CLINICAL EVALUATION OF DEXMEDETO MIDINE-PROP O FOL
ANAESTHESIA FOR OVARIOHYSTERECTOMY IN BITCHES

THESIS

Submitted

in partial fulfillment of the requirements for the Degree of

MASTER OF VETERINARY SCIENCE

IN

VETERINARY SURGERY AND RADIOLOGY

BY

CHETAN VASUDEORAO PATOND

Enroll. No. V/09/042

DEPARTMENT OF VETERINARY SURGERY AND RADIOLOGY

NAGPUR VETERINARY COLLEGE, NAGPUR
MAHARASHTRA ANIMAL AND FISHERY SCIENCES
UNIVERSITY, NAGPUR - 440001.
(INDIA)
2016
DECLARATION OF STUDENT

I hereby declare that the experimental research work and interpretation of the thesis entitled CLINICAL EVALUATION OF DEXMEDETOMIDINE-PROPOFOL ANAESTHESIA FOR OVARIOHYSTERECTOMY IN BITCHES or part thereof has not been submitted for any other degree or diploma of any University, nor the data have been derived from any thesis/publication of any University or scientific organization. The sources of materials used and all assistance received during the course of investigation have been duly acknowledged.

Date: [Date]

Signature

(CHETAN VASUDEORAO PATOND)

Enrolment No: V/09/042

Counter signed by

(Dr. P. T. Jadhao)
Chairman,
Advisory Committee
with date
DECLARATION OF ADVISORY COMMITTEE

Shri. CHETAN VASUDEORAO PATOND has satisfactorily prosecuted his course of research for a period of not less than two semester and that the thesis entitled CLINICAL EVALUATION OF DEXMEDETOomidine - PROPOFOL FOR OVARIOHYSTERECTOMY IN BITCHES submitted by him is the result of research work is sufficient to warrant its presentation to the examination in the subject of Veterinary Surgery & Radiology for the award of MASTER OF VETERINARY SCIENCE degree by the Maharashtra Animal and Fishery Sciences University, Nagpur.

We also certify that the thesis or part thereof has not been previously submitted by him/her for a degree of any other University.

Place: Nagpur
Date:

(Dr. P. T. JADHAO)
Advisor/Guide
Professor & Head
Department of Veterinary Surgery and Radiology

Advisory Committee

<table>
<thead>
<tr>
<th>Name</th>
<th>Designation</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dr. P. T. Jadhao</td>
<td>Professor &amp; Head Dept. of Surgery &amp; Radiology.</td>
<td></td>
</tr>
<tr>
<td>(Chairman)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Dr. M. S. Dhakate</td>
<td>Hospital Superintendent, TVCC, NVC, Nagpur.</td>
<td></td>
</tr>
<tr>
<td>(Member)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Dr. C. H. Pawashe</td>
<td>Assistant Professor Dept. ARGO, I/c Stem Cell Lab. BVC, Mumbai.</td>
<td></td>
</tr>
<tr>
<td>(Member)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Dr. S. P. Salvekar</td>
<td>Assistant Professor Dept. of Surgery &amp; Radiology.</td>
<td></td>
</tr>
<tr>
<td>(Member)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Dr. N. V. Kurkure</td>
<td>Associate Professor Dept.of Vet.Pathology</td>
<td></td>
</tr>
<tr>
<td>(Member)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CERTIFICATE

This is to certify that the thesis entitled **CLINICAL EVALUATION OF DEXMEDETOMIDINE -PROPOFOL ANAESTHESIA FOR OVARIOHYSTERECTOMY IN BITCHES** submitted by Shri. CHETAN VASUDEORAO PATOND to the Maharashtra Animal and Fishery Sciences University in partial fulfillment of the requirement for the degree of **MASTER OF VETERINARY SCIENCE** has been approved by the Student's Advisory Committee after examination in collaboration with the External Examiner.

Name & signature of External Examiner

Signature with seal

Head of Department

Advisory Committee

<table>
<thead>
<tr>
<th>Name</th>
<th>Designation</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dr. P. T. Jadhao (Chairman)</td>
<td>Professor &amp; Head Dept. of Surgery &amp; Radiology.</td>
<td></td>
</tr>
<tr>
<td>2. Dr. M. S. Dhakate (Member)</td>
<td>Hospital Superintendent, TVCC, NVC, Nagpur.</td>
<td></td>
</tr>
<tr>
<td>3. Dr. C. H. Pawashe (Member)</td>
<td>Assistant Professor Dept. ARGO, I/c Stem Cell Lab. BVC, Mumbai.</td>
<td></td>
</tr>
<tr>
<td>4. Dr. S. P. Salvekar (Member)</td>
<td>Assistant Professor Dept. of Surgery &amp; Radiology.</td>
<td></td>
</tr>
<tr>
<td>5. Dr. N. V. Kurkure (Member)</td>
<td>Associate Professor Dept. of Vet. Pathology</td>
<td></td>
</tr>
</tbody>
</table>

(Add text)

Associate Dean
Nagpur Veterinary College, Nagpur.
ACKNOWLEDGEMENT

A completed thesis bears a single name of the student but the process is always accomplished in combination with the dedicated work of people. The work presented in this thesis would not have been possible without each of the following people. I take this opportunity to extend my sincere gratitude and appreciation to all those who made this possible.

To begin with I must offer my profoundest gratitude to my advisor and research guide Dr. P. T. Jadhao, Professor and Head, Dept of Surgery and Radiology, Nagpur Veterinary College, Nagpur. From finding an appropriate topic to the end of thesis, sir offered me unreserved support, encouragement and guidance which led to completion of my thesis step by step. His enthusiasm, integral view on research and his mission for providing high-quality work has made a deep impression on me. His words can always inspire me and bring me to a higher level of thinking. Without his kind and patient instructions, I would not have been able to finish my thesis.

I am indebted to Dr. M. S. Dhakate for being my pillar of support throughout the two years of my master’s course. His trust, faith and belief in me have made me a very confident person at the end. I express my heart-felt gratitude to Dr. B. M. Gahlod for his constant advice, ideas, constructive criticism, patience and guidance.

I take this opportunity to express my deep sense of gratitude to my energetic teachers and advisors Dr. S. V. Upadhye, Dr. S. B. Akhare and Dr. C. H. Pawshe for their all-time valuable insight and guidance for bequeathing me with knowledge, experience and timely advice during the entire course.

My special words of thanks to Dr. Shalaka Salvekar for being with me throughout the PG and for scientific inputs, personal helps, friendly nature and immense support during my thesis completion.

Sincere thanks are due to Dr. S. S. Pitlawar, Dr. M. V. Kamble and Dr. G. S. Khante for their insightful inputs, genuine interest for the enrichment during my post-graduation.
I would like to thank Dr. N. P. Dakshinkar for providing facilities during research. I owe my sincere thanks to Dr. G. R. Bhojne. I shall always be an admirer of his dedication, sincere, simple and critical outlook towards science will always remain an inspiration for me.

My sincere thanks to Dr. N. V. Kurkure for his invaluable support, encouragement. The help rendered by Dr. S. W. Kolte is highly appreciable for allowing me to work in laboratory without which I would not have been able to complete my thesis. I want to thank Mr. S.N. Gawande and Mr. D. V. Patil for their support during resource collection and guideline for thesis completion. My heartfelt thanks to my seniors, Dr. Shridhar Budhe and Dr. Shashikant Jadhav for their guidance, encouragement and training me at every possible step.

My special regards to Smt. Shilpa Dev and Dinesh for their timely help with the numerous processing of samples during my studies.

I am forever thankful to my colleagues Dr. Shamakant Hire, Dr. Mayur Kate and Dr. Bikash Agrawal for always standing by my side and sharing a great relationship. No words can rightly capture the gratitude I feel for my colleagues Pawan Pawade, Amit Karmankar, Prashant Choudhary, Kalyani Thakur and Pratik Bodakhe. They were with me at every good and bad step.

I am extremely thankful to Achut Biradar and Sanjana Karve for their immense help during my thesis. Sincere thanks to Pratik Ingle Patil, Sidhant Jamdale for their timely help at every possible time. I express my sincere accolades to Amol Jaybhaye, Sushrut Shirbhate, Shradhey Shirankar, Satish Harkal, Kunal Kamble, Mahesh Bipate, Sachin Bache, Harish Thakare, who have been a mode of constant support and a boost of enthusiasm in me throughout these two years.

I will remain thankful to Rahul Shinde for sharing great friendship and for sharing my work. I am extremely blessed to have Ruby, Ally and all the animals that have taught me compassion, kindness, humanity and gave me a chance to experience their unconditional love.
I am deeply indebted to Gordan D’Souza and Jane D’Souza and their family for their unending support and for treating me like their own son. No words of gratitude can ever be enough for you.

I owe my deepest gratitude to Dr. Ushma Patel for her eternal support, motivation and help at every possible step. She was always there in all good and bad times. Sincere thanks to Mr. Deepak Patel, Mrs. Leena Patel, Reema and Aniket for their immense support, encouragement and for sharing my work.

Lastly I would like to express deep sense of gratitude to my parents and brother, their patience and sacrifice will remain my inspiration throughout my life. They formed a part of my vision and taught me good things that really matter in life. Their infallible love and support has always been my strength. I am very much grateful to for their constant inspiration and encouragement.

I thank one and all who helped me directly or indirectly in my research work. Last but not the least my thankful salutations to the Lord Almighty for giving me a chance and inclination to pursue this program.

Place: Nagpur

Date: Chetan V. Patond
TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>CHAPTER</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I) INTRODUCTION</td>
<td>01-03</td>
</tr>
<tr>
<td>II) REVIEW OF LITERATURE</td>
<td>04-12</td>
</tr>
<tr>
<td>III) MATERIALS AND METHODS</td>
<td>13-20</td>
</tr>
<tr>
<td>IV) RESULTS AND DISCUSSION</td>
<td>21-49</td>
</tr>
<tr>
<td>V) SUMMARY AND CONCLUSIONS</td>
<td>50-56</td>
</tr>
<tr>
<td>A) BIBLIOGRAPHY</td>
<td>I-XVII</td>
</tr>
<tr>
<td>B) VITA</td>
<td>XVIII</td>
</tr>
<tr>
<td>C) THESIS ABSTRACT</td>
<td></td>
</tr>
<tr>
<td>(i) ENGLISH ABSTRACT</td>
<td>XIX-XX</td>
</tr>
<tr>
<td>(ii) MARATHI ABSTRACT</td>
<td>XXI-XXIII</td>
</tr>
<tr>
<td>Table No.</td>
<td>PARTICULARS</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1</td>
<td>Anaesthetic protocol used in the present study</td>
</tr>
<tr>
<td>2</td>
<td>Visual Examination: Simple Descriptive Scale for sedation.</td>
</tr>
<tr>
<td>3</td>
<td>Evaluation of pedal reflex.</td>
</tr>
<tr>
<td>4</td>
<td>Gradation of pedal reflex.</td>
</tr>
<tr>
<td>5</td>
<td>Evaluation of palpebral reflex.</td>
</tr>
<tr>
<td>6</td>
<td>Gradation of palpebral reflex</td>
</tr>
<tr>
<td>7</td>
<td>Simple Descriptive Scale: To grade the quality of recovery</td>
</tr>
<tr>
<td>8</td>
<td>Mean ± S.E. of Degree of sedation in different groups.</td>
</tr>
<tr>
<td>9</td>
<td>Mean ± S.E. of Pedal Reflex Score in different groups.</td>
</tr>
<tr>
<td>10</td>
<td>Mean ± S.E. of Palpebral reflex score in different groups</td>
</tr>
<tr>
<td>11</td>
<td>Evaluation of Corneal reflex in different groups.</td>
</tr>
<tr>
<td>12</td>
<td>Mean ± S.E. of Induction time (In Minutes) in different groups</td>
</tr>
<tr>
<td>13</td>
<td>Mean ± S.E. of Total Induction Dose (mg) of propofol in different groups</td>
</tr>
<tr>
<td>14</td>
<td>Mean ± S.E. of Duration of anaesthesia (In Minutes) in different groups</td>
</tr>
<tr>
<td>15</td>
<td>Mean ± S.E. of Recovery time (In minutes)in different groups</td>
</tr>
<tr>
<td>16</td>
<td>Mean ± S.E. of Recovery Quality Score in different groups</td>
</tr>
<tr>
<td>17</td>
<td>Mean ± S.E. of Rectal Temperature (°F) in different groups</td>
</tr>
<tr>
<td>18</td>
<td>Mean ±S.E. of Heart rate (Beats/min) in different groups</td>
</tr>
<tr>
<td>19</td>
<td>Mean ± S.E. of Respiration rate (Breaths/min) in different groups</td>
</tr>
<tr>
<td>20</td>
<td>Mean ± S.E. of Haemoglobin (gm%) in different groups</td>
</tr>
<tr>
<td>21</td>
<td>Mean ± S.E. of Total Erythrocyte Count (×10¹²/L) in different groups</td>
</tr>
<tr>
<td>22</td>
<td>Mean ± S.E. of Total Leukocyte Count (×10⁹/L) in different groups</td>
</tr>
<tr>
<td>23</td>
<td>Mean ± S.E. of Neutrophil (%) in different groups</td>
</tr>
<tr>
<td>24</td>
<td>Mean ± S.E. of Lymphocyte (%) in different groups</td>
</tr>
<tr>
<td>25</td>
<td>Mean ± S.E. of Monocyte (%) in different groups</td>
</tr>
<tr>
<td>26</td>
<td>Mean ± S.E. of Eosinophil(%)in different groups</td>
</tr>
<tr>
<td></td>
<td>Description</td>
</tr>
<tr>
<td>---</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>27</td>
<td>Mean ± S.E. of Platelet Count ((\times 10^9/L)) in different groups</td>
</tr>
<tr>
<td>28</td>
<td>Mean ± S.E. of SGOT (IU/L) in different groups</td>
</tr>
<tr>
<td>29</td>
<td>Mean ± S.E. of SGPT (IU/L) in different groups</td>
</tr>
<tr>
<td>30</td>
<td>Mean ± S.E. of BUN (mg/dl) in different groups</td>
</tr>
<tr>
<td>31</td>
<td>Mean ± S.E. of Serum Creatinine (mg/dl) in different groups</td>
</tr>
<tr>
<td>32</td>
<td>Mean ± S.E. of Blood Glucose (mg/dl) in different groups</td>
</tr>
<tr>
<td>33</td>
<td>Mean ± S.E. of Total Serum Calcium (mg/dl) in different groups</td>
</tr>
<tr>
<td>Table No.</td>
<td>Particulars</td>
</tr>
<tr>
<td>----------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1</td>
<td>Mean ± S.E. of Sedation score in different groups</td>
</tr>
<tr>
<td>2</td>
<td>Mean ± S.E. of Pedal reflex score in different groups</td>
</tr>
<tr>
<td>3</td>
<td>Mean ± S.E. of Palpebral reflex score in different groups</td>
</tr>
<tr>
<td>4</td>
<td>Mean ± S.E. of Induction time (In Minutes) in different groups</td>
</tr>
<tr>
<td>5</td>
<td>Mean ± S.E. of Total induction doses of propofol (mg) in different groups</td>
</tr>
<tr>
<td>6</td>
<td>Mean ± S.E. of Duration of anaesthesia (In Minutes) in different groups</td>
</tr>
<tr>
<td>7</td>
<td>Mean ± S.E. of Recovery time (In minutes) in different groups</td>
</tr>
<tr>
<td>8</td>
<td>Mean ± S.E. of Recovery Quality Score in different groups</td>
</tr>
<tr>
<td>9</td>
<td>Mean ± S.E. of Rectal Temperature (°F) in different groups</td>
</tr>
<tr>
<td>10</td>
<td>Mean ± S.E. of Heart Rate (Beats/min) in different groups</td>
</tr>
<tr>
<td>11</td>
<td>Mean ± S.E. of Respiration Rate (Breaths/min) in different groups</td>
</tr>
<tr>
<td>12</td>
<td>Mean ± S.E. of Haemoglobin (gm %) in different groups</td>
</tr>
<tr>
<td>13</td>
<td>Mean ± S.E. of Total Erythrocyte Count (×10^{12}/) in different groups</td>
</tr>
<tr>
<td>14</td>
<td>Mean ± S.E. of Total Leukocyte Count (×10^9/L)</td>
</tr>
<tr>
<td>15</td>
<td>Mean ± S.E. of Differential Leukocyte Count (%) in different groups</td>
</tr>
<tr>
<td>16</td>
<td>Mean ± S.E. of Platelet Count (×10^9/L) in different groups</td>
</tr>
<tr>
<td>17</td>
<td>Mean ± S.E. of SGOT (IU/L) in different groups</td>
</tr>
<tr>
<td>18</td>
<td>Mean ± S.E. of SGPT (IU/L) in different groups</td>
</tr>
<tr>
<td>19</td>
<td>Mean ± S.E. of BUN (mg/dl) in different groups</td>
</tr>
<tr>
<td>20</td>
<td>Mean ± S.E. of Serum Creatinine (mg/dl) in different groups</td>
</tr>
<tr>
<td>21</td>
<td>Mean ± S.E. of Blood Glucose (mg/dl) in different groups</td>
</tr>
<tr>
<td>22</td>
<td>Mean ± S.E. of Calcium (mg/dl) in different groups</td>
</tr>
</tbody>
</table>
# LIST OF PLATE

<table>
<thead>
<tr>
<th>Plate No</th>
<th>Particular</th>
<th>After page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Drugs used during the Study</td>
<td>13</td>
</tr>
<tr>
<td>2</td>
<td>Placement of Intravenous Catheter in dog</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>Clinical Examination Before Anesthesia</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>Use of Multipara monitor During Anaesthesia / Surgery</td>
<td>28</td>
</tr>
<tr>
<td>5</td>
<td>Rostroventral movement of eyeball, wet cornea and relax jaw during anaesthesia indicating moderate depth anaesthesia</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>Central Position of eyeball and dry Cornea during anaesthesia indicting deep surgical plane of anaesthesia in Group 2 dog.</td>
<td>26</td>
</tr>
<tr>
<td>7</td>
<td>Excellent Muscle Relaxation During Ovariohysterectomy</td>
<td>29</td>
</tr>
<tr>
<td>8</td>
<td>Ovariohysterectomy Surgical Procedure</td>
<td>29</td>
</tr>
<tr>
<td>9-11</td>
<td>Recovery From Anaesthesia</td>
<td>30</td>
</tr>
<tr>
<td>12</td>
<td>Pinkish Tongue During Anaesthesia Indicating normoxia and Normal Perfusion</td>
<td>29</td>
</tr>
<tr>
<td>13</td>
<td>Cyanotic tongue during anaesthesia in group III dogs.</td>
<td>29</td>
</tr>
</tbody>
</table>
LIST OF ABBREVIATIONS

A : During Anaesthesia
BA : Before Anaesthesia
S : Sedation
R : Recovery
& : and
@ : at the rate
b.wt/bw : Body Weight
ml : Milliliter
gm% : Gram per cent
mmol/l : Milimol per liter
IV : Intravenous/ Intravenously
ml/kg : Milliliter per kilogram
% : Per cent
@ : At the rate of
NaCl : Sodium Chloride
Ca : Calcium
lb : Pound
mEq : MiliEquivalent
/min : Per minute
kg : Kilogram
gm/dl : Gram per deciliter
mg/dl : Miligram per deciliter
gm : Gram
w/w : Weight to weight
gm/l : Gram per liter
°F : Degree Fahrenheit
PCV : Packed Cell Volume
Hb : Haemoglobin
Ca : Calcium ion
mg/l : Milligram per liter
Cumm : Cubic millimeter
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.E.</td>
<td>Standard error</td>
</tr>
<tr>
<td>et al.</td>
<td>Other workers</td>
</tr>
<tr>
<td>Fig</td>
<td>Figure</td>
</tr>
<tr>
<td>Inj.</td>
<td>Injection</td>
</tr>
<tr>
<td>Viz.</td>
<td>As follows</td>
</tr>
<tr>
<td>±</td>
<td>Plus Minus</td>
</tr>
<tr>
<td>TVCC</td>
<td>Teaching Veterinary Clinical Complex</td>
</tr>
<tr>
<td>TEC</td>
<td>Total Erythrocyte Count</td>
</tr>
<tr>
<td>TLC</td>
<td>Total Leukocyte Count</td>
</tr>
<tr>
<td>RBC</td>
<td>Red Blood Cells</td>
</tr>
<tr>
<td>WBC</td>
<td>White Blood Cells</td>
</tr>
<tr>
<td>Etc.</td>
<td>Etcetera</td>
</tr>
<tr>
<td>µg/mcg</td>
<td>Microgram</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>S/C</td>
<td>Subcutaneous/ Subcutaneously</td>
</tr>
</tbody>
</table>
The history and origin of human anaesthesia as well as animal anaesthesia is vague. The concept of anaesthesia is in practice from centuries together. The aim to reduce the suffering of animals due to pain during the surgery resulted in the development of veterinary anaesthesia. By the end of 19th century, various anaesthetic agents such as ether, chloroform and chloral hydrate were used by veterinary surgeons to reduce the pain and struggling of animal during the surgical procedures. Since 1930 with the discovery of barbiturates and phenothiazine group of drugs opened new era for veterinary anaesthesia. However, further discovery of tranquilizers, opioids, muscle relaxants, dissociate anaesthesia, inhalant anaesthesia and alpha-2 agonist made anaesthesia and its recovery safer (Tranquili et al., 2007).

Anaesthesia is a state of unconsciousness produced by a process of controlled reversible drug induced intoxication of the central nervous system in which the patient neither perceives nor recalls to the noxious stimulus (Hall et al., 1991). A surgical manipulation requires extensive effort to prevent or eliminate pain in animals. Pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage (Thurmon et al., 1996). The prevention and control of pain i.e. analgesia is a central point to the practice of anaesthesia.

Surgical anesthesia is therefore employed to alleviate pain during surgery and is characterized by unconsciousness, good muscle relaxation and alleviation of pain. Use of preanaesthetics is also well known for alleviation of pain and stress not only before surgery but also during surgery & recovery. Pre-anaesthetics produces anxiolysis, facilitates the handling, promotes immobility, hyporeflexia through muscle relaxation, reducing catecholamine release thus pre-op stress. Preanaesthetics by virtue of these qualities smoothens the induction, maintenance and recovery from anaesthesia and also reduce the general anaesthetic requirement thus reducing their side effects.
Basal anaesthesia thus developed by the combination of various preanaesthetics play an important role in the intra-operative as well as post-operative surgical pain and prepares surgical patient for total anaesthesia.

Tramadol, an opioid analgesic is useful prior to, during and after surgery to prevent transmission of painful stimuli. Hence, the concept of pre-emptive analgesics is crucial in the management of peri-operative and post-operative pain and it is popularly incorporated in basal anaesthetic regimen (Hellyer et al., 2003). Tramadol is an opioid receptor agonists and it also inhibits serotonin reuptake and nor-epinephrine reuptake which enhances the inhibitory effects on pain transmission in the spinal cord. Intravenous and epidural administration of tramadol (2mg/kg) in dogs undergoing soft tissue and orthopedic surgery provided effective post-operative analgesia (Vettorato et al., 2010) and 2mg per kg of tramadol had an analgesic potency comparable to that of 0.2mg kg of morphine (Mastrocinque et al., 2003).

Alpha-2 adrenoreceptor agonist or Alpha-2 agonist is an another class of drug widely used as pre-anaesthetics in dogs and other species for their sedative, analgesic, muscle relaxant and anaesthetic sparing effect. Dexmedetomidine, a potent synthetic alpha-2 adrenoreceptor agonist is popular agent in basal anaesthesia due to its sedative, analgesic and muscle relaxation properties (Dugdale, 2010). Incorporation of dexmedetomidine-tramadol combination in anaesthetic regime or alone facilitates comfortable and pain free clinical examinations, minor surgical procedures and markedly reduces the injectable anaesthetic requirement allowing easy orotracheal intubation during major surgeries (Neto, 2009) (Luna et al., 1996).

Dexmedetomidine produces dose-dependent effects without respiratory depression and also provides hemodynamic stability when given intravenously thus is well known as a potentially attractive adjunct for TIVA. Dexmedetomidine is rapidly distributed, 94% protein bound and its concentration ratio between whole blood and plasma is 0.66. It is extensively metabolized in the liver by conjugation (41%), n-methylation (21%), or hydroxylation followed by conjugation and excreted in urine and faeces.

Balanced anestheisa is a state produced by the combination of drugs having different predominant mechanism of action, characterized by
unconsciousness, analgesia and muscle relaxation (Gangwar et al., 2010). In balanced or basal anaesthesia, the disadvantages of each drug when used alone are diminished in combination thus, increasing the depth and safety.

Propofol, an alkyl phenol derivative produces anaesthesia characterized by rapid onset, short duration, lack of cumulative effect on repeated administration, lack of excitatory effects on induction with easy maintenance and faster recovery. The maintenance of surgical anaesthesia with propofol requires repeated bolus injections or a continuous rate infusion (Sandhu. 2011). The induction dose of propofol in unpremedicated dog is 6mg/kg whereas with premedication (10-20 mcg/kg dexmedetomidine) it reduced to induction dose of propofol to 2mg per kg body weight (Thurmon et al., 1996). Dexmedetomidine-Propofol combination can give the better analgesia, narcosis and muscle relaxation which were assessed to be adequate for various surgical procedures (Grimm et al., 2001).

Elective sterilisation of female dogs is one of the most common procedures performed in veterinary practice accomplished by ovariohysterectomy or ovariohysterectomy. Ovariohysterectomy procedure is recommended for the neutering of bitch to avoid reproduction, population control, prevention of diseases of the reproductive tract, and elimination of undesirable behaviors associated with hormonal cycling (Kustritz, 2012).

Ovariohysterectomy at early age i.e. before the exhibition of first heat reduces the predisposition to the pathological conditions like mammary tumours, endometrial hyperplasia–pyometra complex, pseudo-pregnancies, uterine neoplasia and mass lesion involving the ovary. Slatter et al. (2012) added that this factor definitely protects against development of mammary neoplasia only up to the second estrus however it has no significant benefit after 3"estrus.

Considering the above facts, it was proposed to study the effects tramadol-dexmedetomidine as basal anaesthesia to propofol anaesthesia during the major surgery (Ovariohysterectomy) in dogs with the following objectives-

1. To evaluate and compare the tolerability and effectiveness of the Tramadol-Dexmedetomidine-Propofol combination as a TIVA with various dose rates of dexmedetomidine in Dogs.

2. To evaluate the most effective dose of Dexmedetomidine in anaesthetic regimen.
REVIEW OF LITERATURE

Review of literature with respect to this study entitled “Clinical Evaluation of Dexmedetomidine-propofol anaesthesia for Ovariohysterectomy in Bitches” has been cited in the following parts.

2.1 Anaesthesia

Gangwar et al. (2010) defined balanced anesthesia as a state produced by the combination of drugs characterized by unconsciousness, analgesia and muscle relaxation. He observed that the good quality anaesthesia was induced by combination of drugs that having a different predominant mechanism of action. Further he stated, the combination of complementary drugs permits use of a decreased dose of each drug to achieve anesthesia, decreases their commensurate side effects and it also increases the safety of anaesthesia.

Silva et al. (2010) mentioned that the combination of drugs in veterinary anaesthesia has practical applications and its administration as a single drug may be inefficient. He recorded a significant decrease in heart rate and increase in vascular resistance in dogs treated with dexmedetomidine and stated that administration of alpha 2 agonist in combination with other drugs reduces the dosing effect of general anaesthetics. He also found that sedative and analgesic effect of dexmedetomidine was higher than those of levomedetomidine.

Akbar et al. (2014) stated that an ideal surgical anesthesia is a state of central nervous system depression, characterized by the loss of all sensations and consciousness.

2.2 Tramadol

Brockman (1981) studied the effect of xylazine on plasma glucose, glucagons and insulin concentrations in sheep and it was observed that alpha-2 agonists tends to an increase in serum glucose by suppressing insulin release, stimulating glucagon release.
Hall and Clarke (1991) mentioned that the use of opioids may increase the pre-operative sedation and contribute to intra-operative and post-operative analgesia. He also stated that intravenous anaesthesia could be used as an alternative to volatile inhalation anaesthesia due to the possibility of causing atmospheric pollution.

Hellyer et al. (2003) while studying premedication mentioned the importance of preemptive analgesics viz. tramadol in reducing peri-operative and post-operative pain, stress.

Mastrocinque et al. (2003) mentioned that 2mg per kg of tramadol on intravenous administration had an analgesic potency comparable to that of 0.2mg kg of morphine in dogs.

Mastrocinque and Fantoni (2003) compared the effect of intravenous tramadol and morphine administered prior to ovariohysterectomy in dogs and stated that single dose of tramadol was beneficial for post-operative pain where NSAIDs usage is contraindicated.

Ungulecet et al. (2003) compared preemptive analgesic efficacy of tramadol (1mg/kg) with morphine (0.1 mg/kg) after major abdominal surgeries and recorded equivalent analgesia by both the drugs after induction of anaesthesia and during post-operative period without affecting recovery times.

Tranquili et al. (2007) studied that tramadol is a synthetic codeine analogue that is a weak mu-receptor in addition to opioid activity and mentioned tramadol can be used as adjunct analgesic at the dose rate of 2-10mg/kg per day divided in two to three doses in dogs.

McMillan et al. (2008) observed that the main side-effects of tramadol in dogs are mild sedation, nausea, salivation and occasional retching.

Vettorato et al. (2010) confirmed that intravenous and epidural administration of tramadol (2mg/kg) in dogs undergoing soft tissue and orthopedic surgery provided effective post-operative analgesia without any complications.
Choi et al. (2011) studied the effect of tramadol at the rate of 1, 2
and 4 mg per kg body weight with medetomidine-ketamine anaesthesia in 28
dogs. It was concluded that tramadol premedication at a dose of 4mg/kg body
weight can significantly increase the duration of surgical anesthesia with
medetomidine and ketamine in dogs, without imparting significant changes to the
cardiovascular system or recovery from anesthesia.

Buhari et al. (2012) compared the effect of tramadol (3 mg per kg
body weight) after ovariohysterectomy in 12 healthy female dogs by two different
routes (Subcutaneous and IV). A significant decrease in mechanical pain
threshold was observed within each group post-operatively, suggesting that SC
administration of tramadol was as effective as IV administration.

Capik and Nagy (2016) compared the analgesic effect of tramadol
(2mg/kg) and buprenorphine (0.2 mg/kg) when administered 30 minutes prior to
TIVA with midazolam Hcl (0.3mg/kg), Xylazine Hcl ( 0.5 mg/kg) and propofol
(0.2mg/kg/min) along with induction dose of 2mg/kg propofol anaesthesia in
dogs. They observed that tramadol provides significantly better analgesia and
lower depressive effect on cardiovascular system, respiratory system and vital
functions of body allowing controlled management of the continuous intravenous
propofol anaesthesia.

2.3 Dexmedetomidine

Brockman (1981) studied the effect of xylazine on plasma glucose,
glucagons and insulin concentrations in sheep and it was observed that alpha-2
agonists tends to an increase in serum glucose by suppressing insulin release,
stimulating glucagon release.

Hall and Clarke (1991) mentioned that medetomidine may
produce profound sedation and greatly decreases the dose of general
anaesthesia used subsequently.

Wagner et al. (1991) reported the pooling of circulatory blood cells
in the spleen or other reservoirs secondary to sympathetic activity during alpha 2
agonist use may results in decrease in Hb, PCV and total leukocyte count.
However, Naghibi et al. (2002) reasoned vasodilatation at the level of
microcirculation which leads passage of many Red Blood Cell’s (RBC’s) from
circulation that may cause decrease in Haemoglobin (Hb) level measured in peripheral veins, called as plasma skimming.

Skarda and Muir (1994) reported that, dexmedetomidine preserves blood flow to the most vital organs (brain, heart, liver and kidney) at the expense of organs like skin and pancreas.

Lawrence et al. (1996) reported that the alpha 2-adrenergic agonist dexmedetomidine decreases not only heart rate, myocardial contractility, and oxygen demand but also cardiac output, caused a dose-dependent decrease in heart rate in canines. Whereas mean arterial pressure (MAP) increased significantly. Further they reported that dexmedetomidine @ 1ug/kg decreased blood flow to the kidneys by 25% and in the skin by 50% in both groups and @10 ug/kg dose caused slightly larger decreases blood flow through arteriovenous anastomoses (“lung flow”) by 90%. They reported reduction in blood flow to the skeletal muscle in dogs receiving chloralose and urethane (CU) along with dexmedetomidine.

Pypendop and Verstegen (1998) said that α2-agonist, medetomidine produces the dose dependent changes in cardiovascular functions where the cardiovascular effects are best described in two phases: an initial peripheral phase characterized by vasoconstriction, increased blood pressure and reflex bradycardia and subsequent phase characterized by decreased sympathetic tone, heart rate and blood pressure.

Redondo et al. (1999) also stated that premedication with medetomidine decreases the induction doses of propofol by over 50% in dogs and also mentioned that administration of medetomiine IM at a dose of 20 ug/kg decreases the amount of propofol required for intubation to 1.8 mg/kg.

Kuusela et al. (2002) studied the dogs premedicated with dexmedetomidine with propofol induced anaesthesia and maintained by propofol infusion or isoflurane for one hour. The recordings were analyzed for ventricular premature complexes, atrio-ventricular blocks and mean heart rate/hour (HR). In most recordings, no ventricular arrhythmias were detected.
Naghibi et al. (2002) reasoned vasodilatation at the level of microcirculation which leads passage of many Red Blood Cell’s (RBC’s) from circulation that may cause decrease in Haemoglobin (Hb) level measured in peripheral veins, which is also called as plasma skimming.

Villela et al. (2003) studied that dexmedetomidine induces a dose-dependent decrease in heart rate, inhibits isoflurane-induced systemic vascular resistance (SVR) and prevents hyper dynamic responses in experimental dogs.

Surbhi et al. (2010) mentioned that alpha 2 agonist decreases the hemoglobin and packed cell volume values which occurs due to pooling of circulating erythrocytes in the spleen or other reservoirs secondary to decreased sympathetic stimulation.

Sandhu (2011) mentioned that dexmedetomidine is having 8 times higher affinity than other alpha-2 receptors and twice the potency as medetomidine. It is relatively unique in its ability to provide sedation without causing respiratory depression and in combination with other CNS drugs it reduces requirement of general anaesthesia.

Artigas et al. (2012) conducted study on forty-two animals with no ocular abnormalities and concluded that dexmedetomidine@ 5 μg/kg was found to be an excellent option for surgery or diagnostic ocular procedures in dogs.

Restitutti et al. (2012) studied the effect of dexmedetomidine @ 10 μg/Kg intravenously in healthy laboratory beagle dogs in combination with 500 μg/kg MK-467 in the same syringe (DMK) and reported significant increase in plasma glucose at 120 min but reduction in plasma insulin level at 35 and 60 min. This reduction was transient for DMK, whereas persistent in dexmedetomidine.

Hunt et al. (2014) reported that dexmedetomidine when given intravenously reduced the incidences of poor recoveries from anaesthesia and extended the period of post-anaesthetic sedation confounded post-operative behavioral expression of pain in dogs.

Jena et al. (2014) evaluate the clinico-physiological parameters in Xylazine (0.5mg/kg) and dexmedetomidine (10mcg/kg) intravenously premedication for propofol anaesthesia. It was observed that pedal reflex scores
increased non-significantly after administration of Xylazine/ dexmedetomidine and started to abolish at 10 mins, followed by complete abolishment from 15 to 75 mins and then remained sluggish until the end. The palpebral reflexes scores were increase non-significantly (p>0.05) from 10) mins up to 60 min in group X and 75 min in group D which was followed by non-significant (p>0.05) decrease in palpebral reflexes score. The corneal reflexes were observed to be followed the similar trend like other clinical reflexes. Jaw tone was remained sluggish in dexmedetomidine group till 10 minutes followed by complete abolishment after administration of propofol.

2.4 Propofol

Hall and chambers (1987) reported that the continuous infusion of propofol to maintain the anaesthesia in healthy dogs was safe with rapid, excitement free, complete recovery.

Concas et al. (1991) also mentioned that propofol induces depression by enhancing the effects of the inhibitory neurotransmitter GABA and decreases the brains metabolic activity.

Hall et al. (1991) described propofol being commonly used in dogs as the free flowing oil in water emulsion which does not give rise to histamine liberation. Further they reported that propofol was found compatible with all the adjuvant drugs and produces anaesthesia of 18 minutes duration on single dose but produces dose dependent respiratory depression.

Smith et al. (1993) in contrast stated that propofol does not provide analgesia therefore painful procedure should not be performed when given alone and express the necessity of pre-medication preferably with opioids and alpha 2 agonists to provide analgesia and dose sparing effect on propofol. Further they reported excitement during induction or recovery, pain on injection, occasionally tremors and myoclonic activity as side effects of propofol and advised that should be given with pre-medication. Further they observed rapid recovery in propofol treated animals with little or no hangover effect compared to thiobarbiturates.
Benson (2000) studied mechanisms that maintain glucose homeostasis are during perioperative period and reported alpha-2 agonists induce increase in serum glucose by suppression of insulin release and by stimulation of glucagon release.

Bayan et al. (2002) studied haematological and biochemical changes during propofol anaesthesia in dog and reported increase in blood glucose level after the start of surgery due to cortisol and catecholamine mediated gluconeogenesis and glycogenolysis as well as due to decreased peripheral use of glucose.

Sano et al. (2003) reported propofol as highly desirable general anaesthetic agent with rapid onset, short duration of action, lack of accumulation on repeated administration and lack of excitatory effects on induction. They further mentioned that premedication with medetomidine produced excellent sedation, smooth administration of propofol reducing the induction dose of propofol.

Khan et al. (2006) recorded the decrease in the haemoglobin level and TLC count during medazolam - propofol anaesthesia in canines.

Kumar (2007) mentioned that propofol can be use for induction and maintenance of general anaesthesia with advantage of rapid induction and recovery times but has poor analgesic effect and requires addition of analgesic in anaesthetic regimen.

Tranquili et al. (2007) described that propofol being lipophilic in nature causes rapid onset, short duration of action due to rapid uptake in CNS, rapid distribution from brain to other tissues and efficient elimination from plasma by extra-hepatic sites of metabolism. They further added that premedication with opioids and alpha-2 agonist (medetomidine) causes analgesia and substantial decrease of induction dose to 2-4 mg per kg IV with complete recovery in approximately 20 minutes.

Singh et al. (2013) in contradiction reported an increase in packed cell volume of goats treated with alpha 2 agonists. Their findings were attributed to increased urine production due to activation of capillary fluid shift mechanism or due to release of the splenic red blood cells reservoir.
Sharma and Bhardwaj (2010) comparatively evaluated propofol alone and with xylazine or midazolam in healthy dogs and reported increase in Total Leukocyte Count (TLC) midazolam treated dogs.

Surbhi et al. (2010) studied physiological and biochemical effects of medetomidine, butorphenol, propofol anaesthesia in dogs undergoing orthopaedic surgery and reported decrease in TLC count.

Sandhu (2011) stated that propofol (2, 6-diisopropyl phenol) as a non-barbiturate non-dissociative intravenous milky emulsion primarily used for induction and maintenance of anaesthesia. He reported the onset of anaesthesia was smooth excitement free and within 20-60 seconds with very smooth and rapid recovery in 5-10 minutes due to both its rapid distribution and metabolism. Further he mentioned propofol has cardiovascular depressant properties and causes direct myocardial depression and peripheral vasodilation leading to arterial hypotension and decrease in TLC but it does not impair hepatic and renal functions. He advised injecting propofol over a period of 20 – 30 seconds rather than fast bolus reduces the incidence of apnoea.

Jena et al. (2014) evaluated and compared the hemodynamic and haematobichemical effects of xylazine (0.5mg/kg) and dexmedetomidine (10mcg/kg) with propofol as TIVA in 12 apparently healthy dogs. He reported that the induction dose of propofol required was more in dogs premedicated with xylazine (3.17mg/kg) than dexmedetomidine (2.72 mg/kg). Further he reported quicker recovery in dexmedetomidine group than xylazine and recorded no significant statistical difference in physiological, hemodynamic, haemato-biochemical parameters in both the group.

2.5 Ovariohysterectomy

Concannon (1995) stated that surgical sterilization of domestic animals has been considered to be the most common, reliable, effective and the least controversial method.

Pollari et al. (1996) mentioned that ovariectomy (OVX) and ovariohysterectomy (OVH) are the two surgical techniques routinely performed for the surgical sterilization of female animals. Since general anaesthesia,
laparotomy and organ removal are performed during the surgeries, complications related to these issues like anaesthetic problems, haemorrhage, dehiscence, delayed wound healing, suture abscesses and infections are similar to any abdominal surgery.

Fox et al. (2000) recommended Ovariohysterectomy (OHE) in veterinary practice and mentioned the presence of some degree of post-op pain

Mathews et al. (2001) stated that the degree of pain varies with amount of trauma to tissue and pain threshold of the individual animal and expressed the necessity of complimentary analgesia with anaesthesia for management of intra-operative and post-operative pain.

Kustritz (2012) recommended elective sterilization of female dogs by Ovariohysterectomy before first heat for population control, prevention of diseases of the reproductive tract, elimination of undesirable behaviors associated with hormonal cycling. He further opined ovariohysterectomy at early age i.e. before the exhibition of first heat reduces the predisposition to the pathological conditions like mammary tumours, endometrial hyperplasia–pyometra complex, pseudo-pregnancies, uterine neoplasia and mass lesion involving the ovary.

Sontas et al. (2007) studied ovarian remnant syndrome in dogs and suggested that this long term complication of Ovariohysterectomy (OVH) could be due to incomplete removal of ovarian cortex.
MATERIALS AND METHODS

The present study was conducted on eighteen healthy clinical cases of spaying (Ovariohysterectomy) in bitches at Teaching Veterinary Clinical Complex, Nagpur Veterinary College, Nagpur. The bitches were divided into three equal groups (6 in each Group) and subjected to thorough clinical examination and haemato-biochemical examination before the surgery. Ovariohysterectomy was performed as a major surgical procedure in all the three groups. The study was initiated as below.

3.1 Selection of dogs

Eighteen apparently healthy female dogs, weighing 15 ± 2 kg presented for ovariohysterectomy at Teaching Veterinary Clinical Complex, Nagpur Veterinary College, Nagpur were included in this study. The dogs were randomly divided in three groups of six dogs each.

A thorough history with respect to the deworming, vaccination, previous heat, pregnancy, whelping and diseased conditions (if any) of the dog, was recorded. All the animals were subjected to clinical examination prior to the surgery and physiological parameters were recorded as reference.

3.2 Preparation of Animal

All the dogs in the study were fasted for twelve hours and water withheld for eight hours prior to surgery. The surgical site was prepared by clipping, shaving and scrubbed by using Savlon and painted with Betadine prior to surgery. Intracath catheter was fixed in the cephalic vein for easy administration of the drugs as per anaesthetic protocol (plate 3).

3.3 Anaesthetic Protocol

All the animals in the study were given Atropine Sulphate\(^1\) @ 0.04 mg per kg body weight subcutaneously and inj. Tramadol\(^2\) @ 3 mg/kg body weight intravenously. Four minutes later inj. Dexmedetomidine\(^3\) was administered intravenously @ 5ug/kg, 10ug/kg and 15ug/kg in Group I, Group II and Group III

1\(^{Atro\ (Atropine\ Sulphate\ 0.6\ mg/1ml):\ LaboratePharamaceuticles\ India\ Ltd.\ H.P.,\ India.}\n2\(^{TRASMATA\ (Tramadol\ 50mg/2ml):\ IntasPharmaceuticles\ Ltd.\ Ahmedabad,\ India.}\n3\(^{DEXTOMID\ (DexametomidineHcl\ 200\ mcg/2ml):\ Neon\ Laboratories\ Ltd,\ Mumbai,\ India.}\)
Plate No.1: Drugs used during the study (from left) Inj. Atropine, Inj. TRAMATAS, Inj. DEXTOMID and Inj. TROYPOFOL.

Plate No.2: Placement of Intravenous catheter in the cephalic vein.
respectively. Intravenous infusion of Propofol was given till the effect to get the surgical stage of anaesthesia and bolus intermittent dosage for the maintenance of anaesthesia as and when required. The induction dose was recorded for all the dogs (Plate 1).

Table 1: Anaesthetic protocol used in the present study

<table>
<thead>
<tr>
<th>Group</th>
<th>Bitches</th>
<th>Protocol</th>
</tr>
</thead>
</table>
| Group I | 6 | Inj. Tramadol: 3mg/kg Body Weight IV  
Inj. Dexmedetomidine: 5ug/kg Body Weight IV  
Inj. Propofol: Till the effect with further maintenance by intermittent bolus dosage |
| Group II | 6 | Inj. Tramadol: 3mg/kg Body Weight IV  
Inj. Dexmedetomidine: 10ug/kg Body Weight IV  
Inj. Propofol: Till the effect with further maintenance by intermittent bolus dosage |
| Group III | 6 | Inj. Tramadol: 3mg/kg Body Weight IV  
Inj. Dexmedetomidine: 15ug/kg Body Weight IV  
Inj. Propofol: Till the effect with further maintenance by intermittent bolus dosage |

All the dogs were subjected to ovariohysterectomy as per the standard procedure described by Fossum et al. (2013). This was accomplished through a ventral midline incision on abdomen. The ligaments of the uterus and ovaries were broken down, the blood vessels were ligated and organs were removed. The abdominal wall, subcutaneous layer and skin were sutured in routine manner.

3.4 Evaluation of Parameters

The various clinical, physiological, haematological and biochemical parameters were recorded immediately before (BA) and on 05th minutes after sedation (S) with dexmedetomidine, 20th during anaesthesia (A) and at 60th minutes following complete recovery(R). The following observations were recorded in all the animals under study.

1 TROYPOFOL (Propofol 1% w/v) TroikaaPharamaceuticles Ltd. Deharadun, India.
3.4.1 Visual Examination: To grade the quality of sedation.

Simple visual examination was carried out by using Simple Descriptive Scale described by Hunt *et al.* (2014) to grade the quality of sedation.

Table 2: Simple Descriptive Test - To grade the degree of sedation

<table>
<thead>
<tr>
<th>SN</th>
<th>Description</th>
<th>Quality</th>
<th>SDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-----</td>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Dog is relaxed, but could be roused and could walk with little or no ataxia.</td>
<td>Mild</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Dog is in sternal or lateral recumbancy, but can be roused and have obvious signs of ataxia.</td>
<td>Moderate</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>No response to stimulation</td>
<td>Good</td>
<td>3</td>
</tr>
</tbody>
</table>

3.4.2 Evaluation of Reflexes:

In the present study, various reflexes were evaluated to grade the quality of sedation, analgesia, muscle relaxation and anaesthesia in dogs.

A. Pedal Reflexes:

The evaluation and gradation of pedal reflexes were done in terms of analgesia as per the numerical scale described by Ahmad *et al.* (2013).

Table 3: Evaluation of pedal reflex

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pedal Reflex</td>
<td>Intact and strong (strong withdrawal)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Intact but weak (animal responding slowly)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Intact but very light (slow and occasional response)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Abolished completely (no response)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>---</td>
<td>4</td>
</tr>
</tbody>
</table>
Table 4: Gradation of pedal reflex from score.

<table>
<thead>
<tr>
<th>S.N.</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No Analgesia</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Very Mild Analgesia</td>
<td>&gt;0&lt;1</td>
</tr>
<tr>
<td>3</td>
<td>Mild Analgesia</td>
<td>=1 &lt;2</td>
</tr>
<tr>
<td>4</td>
<td>Moderate Analgesia</td>
<td>=2 &lt;3</td>
</tr>
<tr>
<td>5</td>
<td>Complete Analgesia</td>
<td>3</td>
</tr>
</tbody>
</table>

B. Palpebral Reflex:

The evaluation and gradation of palpebral reflex was done as per the numerical scale described by Ahmad et al. (2013).

Table 5: Evaluation of palpebral reflex score.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpebral Reflex</td>
<td>Intact and Strong (Quick Blink)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Intact But Weak (Slow Response)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Very Weak (Very Slow And Occasional Response)</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Abolished (No Response)</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 6: Gradation of palpebral reflex from score.

<table>
<thead>
<tr>
<th>S.N.</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No Sedation</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Mild Sedation</td>
<td>&gt;0&lt;1</td>
</tr>
<tr>
<td>3</td>
<td>Moderate sedation</td>
<td>=1 &lt;2</td>
</tr>
<tr>
<td>4</td>
<td>Deep Sedation</td>
<td>=2 &lt;3</td>
</tr>
<tr>
<td>5</td>
<td>Very Deep</td>
<td>&gt;3</td>
</tr>
</tbody>
</table>

C. Corneal Reflex

The corneal reflex, also known as the blink reflex, is an involuntary blinking of the eyelids elicited by stimulation. The evaluation of corneal reflex was done as present (P), Sluggish(S) and Absent (A) as mentioned in Guedel’s classification described by Clarke et al. (2014).
3.4.3 Clinical Parameters

Following parameters were studied to evaluate the efficacy of tramadol-dexmedetomidine-propofol anaesthetic combination clinically.

A. Onset of anaesthesia (In Seconds)
   Onset of anaesthesia i.e. induction time was recorded as time interval (In Seconds) between the intravenous injection of propofol to disappearance of the pedal reflex as per Kim et al. (1999) with xylazine and propofol anesthetics.

B. Induction Dose
   The amount of propofol (mg) required for transition from conscious to the anaesthetized state of animal was considered as induction dose. The induction doses of propofol were recorded in all the three groups.

C. Duration of anaesthesia (In Minutes):
   The duration of anaesthesia was recorded as the time interval (in minutes) between the disappearance and return of the pedal reflex. (As described by Adetunji et al. 2002)

D. Quality of Anaesthesia
   The quality of anaesthesia was graded by observing different physiological parameters at different intervals, presence or absence of various reflexes, degree of muscle relaxation and complications if any.

E. Recovery (In Minutes)
   Recovery time was recorded as time interval (in minutes) between the last bolus injection or cessation of infusion of propofol and the dog’s ability to stand and walk.

F. Quality of Recovery
   The quality of recovery was observed as per the simple descriptive Scale (SDS) described by Hunt et al. (2014) as mentioned below.
Table 7: Simple Descriptive Scale: To grade the quality of recovery

<table>
<thead>
<tr>
<th>S.N.</th>
<th>Description</th>
<th>Quality</th>
<th>SDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dog shows major signs of excitement during recovery to sternal recumbancy such as thrashing in cage or moving around rapidly unaware of surroundings, growling; which does not respond to gentle handling.</td>
<td>Poor</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Dog shows some signs of excitement during recovery to sternal recumbancy such as thrashing in cage or moving around rapidly unaware of surroundings, growling; but responds to gentle handling by calming down</td>
<td>Moderate</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Mild signs of excitement which resolves quickly and dog become calm.</td>
<td>Good</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>Dog is calm and relaxed during recovery.</td>
<td>Excellent</td>
<td>3</td>
</tr>
</tbody>
</table>

3.5 Physiological parameters:

All the physiological parameters were recorded immediately before and after administration of tramadol-dexmedetomidine, at 20 minutes during depth of anaesthesia and at recovery. The following physiological parameters were recorded:

A. Rectal temperature (°F)

The rectal temperature was measured in °F immediately before and after administration of tramadol-dexmedetomidine, at 20 minutes during depth of anaesthesia and at recovery.

B. Heart rate (beats/min)

The heart rate (beats/minutes) was recorded immediately before and after administration of tramadol-dexmedetomidine, at 20 minutes during depth of anaesthesia and at recovery.
C. Respiratory rate (breaths/min)

The respiratory rate (breaths/minutes) was recorded immediately before and after administration of tramadol-dexmedetomidine, at 20 minutes during depth of anaesthesia and at recovery.

3.6 Blood Sample Collection

Two ml blood samples were collected from veins in vacutainer tubes containing EDTA to study the effect on haematology and four ml in vacutainer tubes containing clot activator for serum biochemical examination before and after sedation, during anaesthesia and at recovery as per the protocol. Blood was centrifuge for 6 minutes of after collection at 2500 RPM for the collection of serum samples.

3.7 Haematological parameters

All the haematological parameters were estimated by using MINDRAY BC 2008 VET complete haematology analyzer. Then immediately after collection, the blood was processed for the following parameters:

- Haemoglobin (gm%)
- Total erythrocyte count (cells×10^{12}/L)
- Total leukocyte count (cells×10^{9}/L)
- Differential Leukocyte Count (DLC) (%)
- Total platelet count (Cells×10^{9}/L)

3.8 Biochemical parameters

The biochemical studies on serum glucose were performed first followed by others with the help of Semi-Autoanalyser (STAR-21) using standard kits in all the dogs at different intervals. The kits for serum biochemical examination were supplied by Avantor Diagnostic Ltd, India. (M/s Avantor Performance Materials)**

A. Serum glutamic pyruvate transaminase (SGPT)

Estimation of serum glutamic pyruvate transaminase / alanine transferase was done by IFCC/kinetic method using Star 21 (SEAC) biochemical semi auto analyser and the values were expressed in IU/L.
B. Serum glutamic oxaloacetate transaminase (SGOT)

Estimation of serum glutamic oxaloacetate transaminase / aspartate transferase was done by IFCC/kinetic method by using Star 21 (SEAC) biochemical semi auto analyser and was expressed in IU/L.

C. Blood urea nitrogen (BUN)

The BUN values were estimated by urea UV (GLDH / kinetic) method by using Star 21 (SEAC) biochemical semi auto analyser and the values were expressed in mg/dl.

D. Serum creatinine

The creatinine values were estimated by Jaffe’s / kinetic method using Star 21 (SEAC) biochemical semi auto analyser and the values were expressed in mg/dl.

E. Serum glucose

The serum glucose values were estimated by GOD-POD using Star 21 (SEAC) biochemical semi auto analyser and the values were expressed in mg/dl.

G. Total Serum Calcium

Serum calcium was estimated by using GSCC / kinetic Star 21 (SEAC) biochemical semi auto analyzer and the values were expressed in mg/dl.

3.9 Complications

Intra-operative, post-operative surgical complications and other complications related to drugs and surgery, if any were recorded in all the groups.

3.10 Statistical Analysis

The data recorded during the study was statistically analyzed by using Analysis of Variance as per the Snedecor and Cochran (2000).
RESULTS AND DISCUSSION

The present study was undertaken at Teaching Veterinary Clinical Complex, Nagpur Veterinary College, Nagpur to evaluate the efficacy of dexmedetomidine-propofol anaesthetic combination in dogs presented for Ovariohysterectomy and to study the most effective dose of dexmedetomidine.

Eighteen apparently healthy female dogs were divided randomly in three equal groups of six dogs in each i.e. Group I, Group II and Group III. Intravenous injection of tramadol was given at 0 minute in all the dogs followed by dexmedetomidine at 06 minute intravenously at the dose rate of 5µg, 10µg and 15µg /kg in Group I, Group II and Group III respectively. Anesthesia was induced with propofol at 10th minute till the surgical plane was achieved and the maintenance of the surgical stage was done by incremental bolus of propofol as and when required.

Various clinical, physiological, haematological and serum biochemical parameters were evaluated to study the most effective dose of dexmedetomidine in mentioned anaesthetic regiment. The results of the study were as follows.

4.1 Quality of Sedation

Quality of sedation was graded by comparing different physiological parameters, evaluation reflexes and complications if any at different time intervals, before and after administration of tramadol (3mg/kg) followed by dexmedetomidine at the dose rate of 5µg, 10µg and 15µg per kg in Group I, Group II and Group III respectively. Induction of anaesthesia was done by Intravenous infusion of propofol till effect to achieve the surgical stage of anaesthesia.
Fig. 1: Mean sedation score in different groups.

Fig. 2: Mean of Pedal Reflex Scores in different groups.
4.2 Visual Examination:

The degree of sedation was evaluated as per the simple descriptive Scale (SDS) described by Hunt et al. (2014).

**Table 8: Mean (± SE) degree of sedation in different groups.**

<table>
<thead>
<tr>
<th>Group – I</th>
<th>Group – II</th>
<th>Group – III</th>
<th>CD (0.05)</th>
<th>CD (0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av +/- CE</td>
<td>1.16± 0.16^d</td>
<td>2.83± 0.16^a</td>
<td>3± 0^a</td>
<td>0.290</td>
</tr>
</tbody>
</table>

Capital Letters (Row wise superscripts) - indicates difference between the groups.

The quality of sedation in all the groups was observed smooth, struggle free and without any complications like emesis and salivation. Mild sedation of grade 1 scale was observed in Group I animals which received dexmedetomidine at the dose rate of 5 mcg per kg body weight. The dogs in this group were relaxed but jaw could be opened with great difficulty, could be aroused, showed presence of all the reflexes five minutes post sedation and were able to walk with little or no ataxia (Fig.1).

The dog in Group II where dexmedetomidine was administered at the dose rate of 10 mcg per kg body weight showed obvious signs of ataxia, followed by complete relaxation of jaw, and achieved sternal or lateral recumbancy. The pedal and gag reflexes were sluggish throughout the sedation where as palpebral, corneal were abolished immediately post-sedation. Profound sedation was observed in Group II animals and required very low dose of propofol i.e. 1.6 to 2 mg per kg for induction. Hence, the degree of sedation was found excellent and hence was graded Good i.e. Grade 3 in Group II animals.

The dogs receiving dexmedetomidine at the dose rate 15 mcg in Group III demonstrated excellent sedation with abolishment of most of the reflexes. However, cyanotic tongue, severe bradycardia and arrhythmia like complications were observed in three dogs immediately after intravenous dexmedetomidine injection.

From the study it was observed that Dexmedetomidine in combination with the tramadol proved to be a potent sedative combination producing synergistic analgesic effect in all the three groups. Pypendop (2005) stated that alpha 2 agonist potentiates the analgesia induced by opioids.
Dexmedetomidine at the rate of 10 mcg produced excellent, smooth sedation without any complications in Group II and prepared the dogs well for general anaesthesia. Due to the profound sedative effect of dexmedetomidine the surgical stage of anaesthesia was achieved at the lowest dose of propofol induction. Sano et al. (2003) reported similar findings of potent dose sparing effect of medetomidine, butorphenol in dogs anaesthetized with propofol. In contrast Dewanganet al. (2010) recorded potent sedative, analgesic and muscle relaxant activity In dogs premedicated with alpha-2-adrenergic receptor agonist which was associated with profound bradycardia, decrease cardiac output, salivation, emesis and depression of thermoregulation.

The findings of the study were similar to Netoet al. (2009) who reported moderate to profound sedation lasting up to 30 minutes with dexmedetomidine at the dose rate of 5 mcg per kg and ceiling sedative effect at 10 mcg per kg body weight. He further stated that intravenous dose of dexmedetomidine from 10 to 20 mcg per kg body weight increases the duration but not the intensity of sedation and when combined with opioid substantially reduces the dose of injectable and inhalant anaesthetic requirement. These findings were in accordance with Kuusela et al. (2000).

4.3 Evaluation of Reflexes

In the present study, various reflexes were evaluated to grade the quality of tramadol-dexmedetomidine-propofol anaesthesia to study the effect of various dose rates of dexmedetomidine on quality of sedation, analgesia and anaesthesia in dogs.

A. Pedal Reflexes:

The evaluation and gradation of pedal reflexes were done in terms of analgesia as per the numerical scale described by Ahmad et al. (2013).

The status of pedal reflexes was recorded as a measure of depth of analgesia. It was assessed by observing the reflex to the pinching of inter-digital skin of a hind leg of animal (Kuusela 2003). The response to the pinch of the animal was graded on 0 to 3 score scale (Table) before and after sedation and at 05, 20 and 60 minutes interval during anesthesia.
At each time interval pedal reflex was assessed and score was given as per the gradation of the analgesia as below:

**Table 9: Mean value (± SE) of Pedal Reflex Score in different groups.**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
<th>CD(0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>0± 0(^d)</td>
<td>0± 0(^d)</td>
<td>0± 0(^c)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>1.33± 0.21(^{bb})</td>
<td>2.16± 0.16(^{ba})</td>
<td>2.16± 0.16(^{ba})</td>
<td>0.550</td>
<td>0.761</td>
</tr>
<tr>
<td>A</td>
<td>3± 0(^a)</td>
<td>3± 0(^a)</td>
<td>3± 0(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>1.0± 0(^c)</td>
<td>1.33± 0.21(^c)</td>
<td>1.33± 0.21(^c)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td>0.311</td>
<td>0.396</td>
<td>0.396</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD(0.01)</td>
<td>0.424</td>
<td>0.541</td>
<td>0.541</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Small Letters (Column wise superscripts) - indicates difference within a group.
Capital Letters (Row wise superscripts) - indicates difference between the groups.

The mean (± SE) pedal reflex score before anaesthesia was 0 in dogs of all the three groups indicative of presence strong pedal reflex without analgesia. A statistically significant increase in pedal reflex score was observed in all the three groups 5 minutes post tramadol – dexmedetomidine injection suggestive of sluggish response. From the observations it could be stated that high pedal reflex scores in group II & III than group I were representative of dose dependant analgesic quality of dexmedetomidine and tramadol (Fig. 2).

Absence of pedal reflex and complete analgesia were recorded in all the groups during propofol anaesthesia. Further the pedal reflex was restored to normalcy at recovery. The similar observations were noted by Neto *et al.* (2009) and Akbar *et al.* (2014) by using dexmedetomidine – propofol anesthetic combination in dogs.

**B. Palpebral Reflex:**

The palpebral reflex was recorded at different time intervals before and after sedation, during anaesthesia and at the complete recovery for all the dogs enrolled in the study. The evaluation and gradation of palpebral reflex was done as per the numerical scale described by Ahmad *et al.* (2013).

**Table 10: Mean value (±SE) of Palpebral Reflex Score in different groups.**


The mean palpebral reflex score recorded before sedation was 0 in all the dogs. A significant increase in the score was observed immediately after the sedation which further facilitated significantly during the anaesthesia in all the groups (Fig.3). Significant rise in Palpebral scores were recorded amongst the groups, wherein Group I being the lowest and group III being the highest during sedation. On the basis of the findings it could be concluded that dexmedetomidine produces profound sedation with increasing dose whereas the reflex was completely abolished during the propofol anaesthesia. The findings of this are in line with Ahmad et al. (2003) and Clarke et al. (2014).

C. Corneal Reflex

The corneal reflex, also known as the blink reflex, is an involuntary blinking of the eyelids elicited by stimulation.

Table 11: Evaluation of corneal reflex in different groups.
Fig. 3 Mean of Palpebral Reflex Score in Different groups

Fig. 4 Mean Induction Time in different groups
P- Present, A- Absent, S- Sluggish

In the present study corneal reflex persisted after the sedation in group I where as it was sluggish at higher doses of dexmedetomidine in group II & III. Further the corneal reflex disappeared completely (absent) during the depth of anaesthesia in all the three groups.

As per Guedel’s classifications the absence of corneal reflex at the depth of anaesthesia indicates plane two or three of surgical stage of anaesthesia (Clarke et al. 2014). The rostroventral rotation of eyeball during light and moderate depth of anaesthesia further returns to central position during the deep plane. Similar findings were observed in present study therefore, all the dogs’ attained surgical stage 2 in group I and surgical stage 3 in group II & III (plate 5).

Moens and Coppens (2007) while explaining the clinical signs of depth of anaesthesia described that cornea remains moist in light as well as moderate plane of surgical anaesthesia however the cornea gets dry during the deep anaesthesia with central position of cornea. Similar findings were reported by Tranquili et al. (2007) (Plate 6).

4.3 Evaluation of Clinical Parameters

Following parameters were studied to evaluate the efficacy of tramadol-dexmedetomidine-propofol anaesthetic combination clinically.

A. Onset of anaesthesia (In Seconds)

Onset of anaesthesia i.e. induction time was recorded as time interval (In Seconds) between the injection of propofol intravenously to disappearance of the pedal reflex as per Kim et al. (1999) with xylazine and propofol anesthetics. The onset of anaesthesia in all the dogs was smooth rapid and excitement free without any untoward signs like pain on injection, apnoea, cyanosis, excitement, retching and vomiting etc. in present study. The high lipid solubility may results in rapid blood/brain equilibrium and results in rapid onset of action Langley et al. (1988)

Premedication with tramadol-dexmedetomidine provided a good basal anaesthesia for propofol facilitating stress-free induction with significant level of analgesia during surgery. Davies et al. (1991) reported unusual reactions like
Plate No.5: Rostroventral movement of eyeball, wet cornea and relax jaw during anaesthesia indicating moderate depth anaesthesia.

Plate No.6: Central Position of eyeball and dry Cornea during anaesthesia indicting deep surgical plane of anaesthesia in Group 2 female dog.
apnoea, cyanosis, excitement, retching and vomiting linked with the administration of propofol.

A. Induction Time:

Table 12: Mean value (± SE) of Induction time in different groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD (0.05)</th>
<th>CD (0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av +/- CE</td>
<td>28± 1.26^A</td>
<td>21.83± 1.24^B</td>
<td>20.83± 1.13^B</td>
<td>3.673</td>
<td>5.079</td>
</tr>
</tbody>
</table>

Capital Letters (Row wise superscripts) - indicates difference between the groups.

The mean (± SE) time of induction was 28± 1.26, 21.83± 1.24 and 20.83± 1.13 seconds in Group I, II and III respectively. Statistically significant difference was observed in the induction time amongst group I & II as well as group I & III, but no significant difference in group II & III (Fig. 4). The mean induction time was longest (28± 1.26) in group I whereas shortest (20.83± 1.13) in group III. Similar findings were recorded by Jagtap (2003) and Bell et al. (2011) with and without premedication in dog. Similar findings were recorded by Robinson & Borer-Weir (2013), Watkins et al. (1987). The excitement free induction in alpha 2 agonist premedicated dogs with propofol have been reported earlier by Vaino (1992) and Cullen and Reynoldson (1993).

B. Induction Dose

The mean (± SE) total induction doses of propofol recorded in all the three groups under is represented in table no. 1 (Fig. 5).

Table 13: The mean (± SE) total induction doses (mg) of propofol.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
<th>CD(0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av +/- CE</td>
<td>32.5± 1.70^A</td>
<td>25.0± 0^B</td>
<td>21.66± 1.05^B</td>
<td>3.492</td>
<td>4.829</td>
</tr>
</tbody>
</table>

Capital Letters (Row wise superscripts) - indicates difference between the groups.

The amount of drug or combination required for transition from conscious to the anaesthetized state of animal was considered as induction dose. The
Fig. 5 Mean total Induction of Dose propofol (mg)

Fig. 6 Mean of Duration of Anaesthesia (Minutes)
mean average total induction dose recorded were 32.5± 1.70, 25.0± 0 and 21.66± 1.05 mg in group I, II & III. Statistically significant difference was observed in the induction dose amongst all the three groups. The total induction dose for group I was highest 34.16± 1.53 mg whereas lowest (25.83± 1.53) in group III (Fig.5). It was extrapolated from the findings that the induction dose of propofol was reduced by the increasing dose of the premedicant. The findings were in accordance with Neto (2009) and Grimm et al (2001). Similar findings were reported by Jagtap (2003) and Kushwaha et al. (2012) in dogs.

A. Duration of anaesthesia (In Minutes):

The mean value was recorded as the time interval (in minutes) between the disappearance and return of the pedal reflex (Adetunji et al. 2002).

Table 14: Mean value (± SE) of duration of anaesthesia (minutes).

<table>
<thead>
<tr>
<th>Av +/- CE</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD (0.05)</th>
<th>CD (0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>26.83±</td>
<td>29.16±</td>
<td>31.33±</td>
<td>0.79B</td>
<td>1.07AB</td>
<td>1.14A</td>
</tr>
</tbody>
</table>

Capital Letters (Row wise superscripts) - indicates difference between the groups.

The mean (± SE) duration of anaesthesia in Group I, II and III were 26.83± 0.79, 29.16± 1.07 and 31.33± 1.14 (Minutes) respectively. Statistically a significant difference (p>0.05) was observed between groups. The duration of anaesthesia was observed lowest in group I and required more incremental bolus dose for maintenance whereas lowest in Group III with minimal incremental boluses of propofol (Fig.6).


B. Quality of Anaesthesia

The quality of anaesthesia was graded by observing different physiological parameters at different intervals, presence or absence of various reflexes, degree of muscle relaxation and complications if any.
Plate 3: Clinical Examination of dog

Plate 4: Use of Multipara monitor During Anaesthesia / Surgery
The plane of anaesthesia was observed to be light in this group and required maintenance with incremental bolus dose of propofol at shorter intervals indicated by reappearance of gag and palpebral reflexes during the surgery. The muscle relaxation was graded poor in group I as the exteriorization and ligation of uterus and ovarian ligation was done with difficulty.

In Group II animals, deep surgical anaesthesia was produced with excellent muscle relaxation, analgesia and loss of all the body reflexes by tramadol – dexmedetomidine (10mcg/kg) – propofol combination. The surgical plane of anaesthesia was achieved with very less dose of propofol at induction. The time duration of the requirement of bolus dose of propofol for maintenance was also prolonged and the animal was observed comfortable and relaxed throughout the surgery without any alteration in the physiological parameters. The exteriorization and ligation of uterus and ovarian ligament could be done easily (Plate 7 and 8).

Good quality of onset of anaesthesia with surgical plane of anesthesia was produced without any alteration in the physiological parameters in group II animals. Therefore, the quality of anaesthesia was graded as excellent in this group II.

Dogs in group III required lowest dose of propofol for induction and maintenance of anaesthesia. However in group III the three dogs experienced cyanosis of tongue (Plate 13) and transient bradycardia during sedation and it also necessitated oxygen with respiratory depression following propofol induction. Significant difference was also observed in physiological parameters.

The combination of preanaesthetic tramadol – dexmedetomidine 10mcg/kg is recommended in dogs to produce basal anaesthesia with excellent sedation and potent analgesia requiring lower doses of propofol with lesser degree of respiratory depression. These findings are in accordance with Jena et al. (2014) and Neto et al. (2009). Synergism between alpha 2 agonist and opioids because of the same location of their receptors in brain as reported by Sinclair (2003) might have reduced the dose of propofol in present study.
Plate No.7: Excellent Muscle Relaxation During Ovariohysterectomy

Plate No.8: Ovariohysterectomy Surgical Procedure
Plate No.12: Pinkish Tongue During Anaesthesia in group II Indicating normoxia and normal Perfusion

Plate No.13: Cyanotic tongue during anaesthesia in group III dogs.
A. Recovery (In Minutes)

Recovery time was recorded as time interval (in min) between the last bolus injection or cessation of infusion of propofol and the dog’s ability to stand and walk.

**Table 15: Mean value (± SE) of Recovery time (minutes).**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD (0.05)</th>
<th>CD (0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av +/− CE</td>
<td>17.58± 0.87</td>
<td>18.66± 1.11</td>
<td>20.08± 1.04</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Capital Letters (Row wise superscripts) - indicates difference between the groups.

The mean (± SE) time required for the recovery in group I, II and III was 17.58± 0.87, 18.66± 1.11 and 20.08± 1.04 minutes respectively. Statistically non-significant increase in recovery time was observed amongst the three groups (Fig. 7).

The recovery was smooth, rapid, without shivering, struggle free in all the dogs. Similar findings are reported by Kelawala and Parsania (1997) and Gomez-Villamandos (2006). The rapid recovery from the anaesthesia is an indicative of quick biodegradation of drug by the hepatic microsomal enzyme system (Watkins *et al.* 1987). Bayan *et al.* (2002) and Kushwaha *et al.* (2012) observed quick recovery of the dogs with propofol-midazolam anaesthesia.

This characteristic rapid recovery could be related to the pharmacokinetics i.e. the high lipid solubility results in rapid and extensive redistribution, which contributes to the termination of the drug’s anaesthetic effect. Propofol is also rapidly cleared by hepatic and extrahepatic metabolism (Sandhu 2011). Therefore, it is evident that smooth and rapid recovery was recorded following tramadol - dexmedetomidine - propofol anaesthesia, irrespective of the dose of premedicant as well as anaesthetic.

B. Quality of Recovery

The quality of recovery was observed as per the simple descriptive Scale (SDS) described by Hunt *et al.* (2014).

The mean Values (± SE) of Recovery Quality Score of different groups presented in table 16.
Fig. 7 Mean of Recovery time (Minutes)

Fig. 8 Mean of Recovery Quality Score
Plate No.9, 10 & 11: Recovery from anaesthesia (Calm and relaxed dog)
Table 16: Mean value (± SE) of Recovery Quality Score.

<table>
<thead>
<tr>
<th>Group</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
<th>CD(0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av +/- CE</td>
<td>2.66± 0.21</td>
<td>3</td>
<td>3</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS-Non-Significant

The overall recovery quality of above anaesthetic combination was good to excellent during the entire study. Statistically, there was no significant difference between the groups. During the study in group I one animal showed mild excitement which resolved quickly in few minutes during recovery. Hence although the recovery time was least in group I the quality of recovery was graded as good (Fig.8) (Plate 9, 10 and 11).

The excellent quality of recovery observed in groups II & III which could be attributed to the synergistic analgesic property of tramadol and dexmedetomidine(Jena et al. 2014). It has recommended the incorporation of an analgesic and muscle relaxant complements to propofol anaesthesia (Clarke et al. 2014). Neto (2009) mentioned that dexmedetomidine analgesic effects last longer when given intravenously and combination with opioid augments the analgesic effect in dogs. Similar findings reported by Grimm et al. (2001).

The treatment with 3mg per kg tramadol alone neither produces clinically relevant sedation (Seddighi et al. 2009) nor affects the recovery time (Choi et al. 2011). Vettorato et al. (2010) reported that intravenous tramadol (2mg/kg) in dogs undergoing soft tissue and orthopedic surgery provided effective post-operative analgesia.

Kushwaha et al. 2012 stated that the recoveries from the propofol anaesthesia were generally rapid and smooth. In this study similar findings were observed and were in accordance with Jena et al. (2014)
4.4 Physiological Parameters:

The following physiological parameters were undertaken during study for the evaluation of anaesthetic combination.

A. Rectal Temperature (°F):

Per rectal temperature (°F) of all the animals under study were recorded before induction, during sedation, during anaesthesia and after recovery. The mean (± SE) temperature recorded in all the groups at above mentioned time points is depicted in the following table with its analysis of variance.

Table 17: Mean (± S E) of Rectal Temperature (°F).

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>101.5± 0.28</td>
<td>102.33± 0.30</td>
<td>101.91± 0.22</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>100.85± 0.35</td>
<td>101.83± 0.26</td>
<td>101.43± 0.18</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>100.58± 0.24&lt;sup&gt;B&lt;/sup&gt;</td>
<td>101.68± 0.32&lt;sup&gt;A&lt;/sup&gt;</td>
<td>101.03± 0.24&lt;sup&gt;AB&lt;/sup&gt;</td>
<td>0.821</td>
</tr>
<tr>
<td>R</td>
<td>101.21± 0.19</td>
<td>101.65± 0.20</td>
<td>101.48± 0.28</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The mean (± SE) rectal temperatures immediately before anaesthesia were 101.5± 0.28, 102.33± 0.30 and 101.91± 0.22 in groups Group I, Group II and Group III respectively. The statistical analysis revealed no significant difference in the temperature within as well as between the groups during sedation. A further decrease in the rectal temperature was observed in all the three groups during anaesthesia at 20 minutes. However a significant decrease (p<0.05) in temperature was observed in Group III during anaesthesia. The slow increased in rectal temperature up to normalcy was observed on 60 minutes at complete recovery. However, all the values were in normal physiological limits in all the three groups at different time points (Fig 9).

The decrease rectal temperature after the administration of preanaesthetics could be attributed to depression of central nervous system in combination with reduction in muscular activity and basal metabolic rate (Singh et al.2009). The further reduction in the temperature may be due to the additive
Fig. 9: Mean Rectal Temperature at different intervals

Fig. 10: Mean of Heart Rate at different intervals

Fig. 11: Mean Respiration Rate (Breaths per min)
effect of preanaesthetic and propofol (Robertson, 1992) or due to the thermoregulatory depressant effect of propofol (Carlson and Chapman, 1981).

The findings of this study are in accordance with Jena et al. (2014), Akbar et al. (2014), Ahmad et al. (2013). The non-significant decrease in temperature in propofol anaesthesia but within a normal acceptable range in all groups was also recorded by Adetunji et al. (2002), Sharma et al. (2007) and Maney et al. (2013) in canines.

A. Heart Rate (Beats per minute)

The mean (± SE) heart rates recorded at various intervals of before and after sedation, during anaesthesia and at recovery are presented in Table 18.

Table 18: Mean (± SE) of heart rate at different intervals.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>120± 3.14aB</td>
<td>126.67± 3.95aAB</td>
<td>140.33± 7.38aA</td>
<td>18.887</td>
</tr>
<tr>
<td>S</td>
<td>88.16± 4.57b</td>
<td>91± 1.98b</td>
<td>95.33± 3.45c</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>98.16± 11.06b</td>
<td>118.17± 12.68a</td>
<td>110.17± 4.10bc</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>103± 5.60abA</td>
<td>127± 10.20abA</td>
<td>122± 8.31bB</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td>24.889</td>
<td>18.202</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD(0.01)</td>
<td>24.829</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Small Letters (Column wise superscripts) - indicates difference within a group.
Capital Letters (Row wise superscripts) - indicates difference between the groups.

The mean heart rates recorded before induction of anaesthesia were 120± 3.14, 126.67± 3.95 and 140.33± 7.38 beats per minute in group I, II and III respectively. A significant decline in heart rate was observed in group II where as marked bradycardia was reported in group III after administration of dexmedetomidine. The highly significant decrease in heart rate after sedation could be attributed to the typical hemodynamic response of alpha 2 agonists mediated by the baroreflex and due to decrease in sympathetic activity. Silva et al. (2010) reported similar findings and summarized that intensity of cardiovascular manifestation after administration of dexmedetomidine depends on dose, route of administration and combination of drugs. Dexmedetomidine
mediated bradycardia might have been prevented due to administration of atropine and combination of tramadol in the present study (Jeff et al. 2001).

Statistically significant decrease in heart rate was observed in all the groups after administration of dexmedetomidine intravenously which was slightly increased after administration of propofol (Fig 10). However heart rate remained within the normal physiological limit in all the three groups. Transient increase in heart rate due to propofol might be due to increase sympathetic tone (Mama et al. 1996) or due to positive chronotropic effect of propofol (Kinjavdekar et al. 2000) or increased myocardial blood flow (Haberer et al. 1993). Braz et al. (2008) reported similar findings of decrease in heart rate and increased in systemic vascular resistance.

B. Respiration Rate (Breaths/min)

The mean (± SE) respiratory rate before administration of anaesthetic protocol was 29.83± 1.90, 33.36± 2.41 and 29.66± 2.44 in group I, II & III respectively are presented in table 19.

Table 19: The mean (± SE) of Respiration Rate (Breaths per min)

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>29.83± 1.90</td>
<td>33.36± 2.411</td>
<td>29.66± 2.44</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>20.33± 2.29</td>
<td>25.66± 1.96</td>
<td>26± 4.56</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>20.66± 2.17</td>
<td>23± 2.04</td>
<td>19.33± 1.52</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>26± 0.73</td>
<td>26± 0.73</td>
<td>24.33± 1.05</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td>5.549</td>
<td>5.624</td>
<td>5.317</td>
<td></td>
</tr>
<tr>
<td>CD(0.01)</td>
<td>7.554</td>
<td>7.670</td>
<td>7.241</td>
<td></td>
</tr>
</tbody>
</table>

There was no effect of tramadol on respiration in all the three groups. However, Capik and Nagy (2016) reported better respiratory stability in dogs premedicated with tramadol.

A significant decline in respiratory rates was observed in all the three groups following the administration of dexmedetomidine irrespective of the dose administered. The reduced respiratory rates persisted during propofol anesthesia.
and surgery but slowly increased to the normal during the recovery. However the respiratory rate remained within normal physiological limits throughout the study (Fig. 11).

The findings of this study were in accordance to Silva et al. (2010) who observed the significant drop in respiratory rate (p<0.05) after administration dexmedetomidine as a preanesthetic to the propofol anaesthesia in dogs.

The depression in respiratory rates after sedation may be due to the direct depression of respiratory centers in the brain (Sinclair 2003, Singh et al. 2013) and further reduction was during anesthesia may be attributed to the adverse effect of respiratory depression by propofol (Suarez et al. 2012, Maney et al., 2013). In contrast, Kuusela et al. (2001) observed dose related depression of respiratory rates in dexmedetomidine sedated dogs.

4.5. Haematological Parameters

The following haematological parameters were studied in all the dogs of three groups immediately before and on 05th, 20th and 60th minutes after the induction of anaesthesia.

A. Haemoglobin estimation (gm/dl)

In the present study, hemoglobin concentration was evaluated of all the groups at different intervals. Average values for hemoglobin concentration in Group I, Group II and Group III at different intervals are presented in Table 20.

| Table 20: Mean value (± SE) of haemoglobin at different time intervals (gm%). |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Group I         | Group II        | Group III       | CD(0.05)        | CD(0.01)        |
| BA              | 13.76± 0.50     | 13.58± 0.99     | 14.2± 0.52a     |                 |                 |
| S               | 12.33± 0.70     | 12.73± 0.95     | 12.26± 0.26b    |                 |                 |
| A               | 12.25± 0.79     | 12.08± 0.82     | 11.66± 0.68b    |                 |                 |
| R               | 11.91± 0.62     | 11.91± 0.93     | 11.3± 0.53b     |                 |                 |
| CD(0.05)        |                 |                 | 1.757           |                 |                 |
The mean (± SE) values of hemoglobin (gm%) before administration of anaesthetic protocol were 13.76±0.50, 13.58±0.99 and 14.2±0.52 in group I, II & III respectively. A non-significant decline in hemoglobin values was observed in group I and group II whereas the significant decrease (p<0.05) in hemoglobin was reported in group III during anesthesia. Comparison amongst the groups revealed non-significant decrease in group III. However, the hemoglobin values ranged in normal physiological limit during this study (Fig 12).

The decrease in the hemoglobin values could be probably due to pooling of circulating erythrocytes in the spleen or other reservoirs secondary to the decreased sympathetic stimulation (Kinjavdekar et al. 2000). Significant transient decline in hemoglobin was also observed by Stephen et al. (1986), Gill et al. (1965), Bayan et al. (2002) and Venugopalan et al. (2002) undergoing propofol anaesthesia.

The similar finding was noted by Kushwaha et al. (2012) in medazolam-propofol combination in dogs. However, Singh et al. (2013) observed significant decrease in hemoglobin during propofol anaesthesia with and without premedication and stated that it could be due to sequestration of blood cells in spleen and lungs during anaesthesia.

B. Total Erythrocyte Count (cells/lit)

To study the effect of sedation and anaesthesia on total erythrocyte count blood samples were collected before and at 5 minutes post tramadol-dexmedetomidine sedation, 20 minutes after propofol anaesthesia induction and after complete recovery. Average values of TEC concentration recorded in Group I, Group II and Group III at different intervals are presented in Table 21.

Table 21: Mean value (± SE) of TEC at different time intervals.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
<th>CD(0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>8.04±0.60</td>
<td>7.99±0.63</td>
<td>8.99±0.45&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>6.99±0.55</td>
<td>7.35±0.46</td>
<td>8.13±0.32&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>7.26±0.53</td>
<td>6.99±0.40</td>
<td>7.56±0.42&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>6.79±0.36</td>
<td>6.7±0.48</td>
<td>7.20±0.32&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td></td>
<td></td>
<td>1.150</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fig. 12: Mean Haemoglobin (gm%) in different groups

Fig. 13: Mean of TEC at different interval
The mean (± SE) values of hemoglobin (gm%) before administration of anaesthetic protocol were 13.76± 0.50, 13.58± 0.99 and 14.2± 0.52 in group I, II & III respectively. A non-significant decline in hemoglobin values was observed in group I and group II whereas the significant decrease (p<0.05) in hemoglobin was reported in group III during anesthesia. Comparison amongst the groups revealed non-significant decrease in group III. However, the hemoglobin values ranged in normal physiological limit during this study (Fig 12).

The decrease in the hemoglobin values could be probably due to pooling of circulating erythrocytes in the spleen or other reservoirs secondary to the decreased sympathetic stimulation (Kinjavdekar et al. 2000). Significant transient decline in hemoglobin was also observed by Stephen et al. (1986), Gill et al. (1965), Bayan et al. (2002) and Venugopal et al. (2002) undergoing propofol anaesthesia.

The similar finding was noted by Kushwaha et al. (2012) in medazolam-propofol combination in dogs. However, Singh et al. (2013) observed significant decrease in hemoglobin during propofol anaesthesia with and without premedication and stated that it could be due to sequestration of blood cells in spleen and lungs during anaesthesia.

A. Total Erythrocyte Count (cells/lit)

To study the effect of sedation and anaesthesia on total erythrocyte count blood samples were collected before and at 5 minutes post tramadol-dexmedetomidine sedation, 20 minutes after propofol anaesthesia induction and after complete recovery. Average values of TEC concentration recorded in Group I, Group II and Group III at different intervals are presented in Table 21.

Table 21: Mean value (± SE) of TEC at different time intervals.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
<th>CD(0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>8.04± 0.60</td>
<td>7.99± 0.63</td>
<td>8.99± 0.45&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>6.99± 0.55</td>
<td>7.35± 0.46</td>
<td>8.13± 0.32&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>7.26± 0.53</td>
<td>6.99± 0.40</td>
<td>7.56± 0.42&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>6.79± 0.36</td>
<td>6.7± 0.48</td>
<td>7.20± 0.32&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td></td>
<td></td>
<td>1.150</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fig. 14 Mean of TLC in different groups

Fig. 16: Total Platelet Count
Table 22: Mean value (± SE) of TLC (×10^9/l) at different time intervals.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>21.36± 1.22</td>
<td>20.16± 1.45</td>
<td>17.68± 1.52</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>22.33± 1.66</td>
<td>20.96± 2.14</td>
<td>19.53± 2.2</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>20.83± 1.85</td>
<td>18.04± 1.67</td>
<td>17.05± 1.53</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>21.06± 1.44</td>
<td>17.37± 1.04</td>
<td>17.19± 1.53</td>
<td></td>
</tr>
</tbody>
</table>

A non-significant decrease in total leukocyte count was observed during sedation which was further declined in all the three groups after administration of propofol at 20 minutes. The TLC values returned to the preinduction levels at complete recovery. The variation in TLC values remained within normal physiological limits throughout the study.

The findings of this study were in accordance with Jena *et al.* (2014) who reported decrease in TLC upon administration of dexmedetomidine followed by propofol anaesthesia. The decrease in TLC might be due to enhanced peripheral blood level of adrenaline or nor-adrenaline which suppresses proliferative response of peripheral blood leucocytes or due to increased plasma volume during anaesthesia on account of vasodilatation resulting in vascular pooling (Venugopal et al. 2002) or due to sequestration of blood cells in spleen and lungs (Best and Taylor 1996) and Komar *et al.* (2003).

David *et al.* (1993) and Khan *et al.* (2006) reported decrease in TLC following administration of propofol alone. Similar findings were reported by Kim *et al.* (1999), Ozaydin *et al.* (2001), Jagtap (2003), Bayan *et al.* (2002) and Jain (2003) in dogs. In contrast, Sharma and Bhardwaj (2010) reported increased TLC count which is augmented by Akbar *et al.* (2014) with increasing alteration in TLC upon administration of medetomidine in dogs.
A. Differential Leukocyte Count (%):-

1. Neutrophil %

The mean (± SE) values of neutrophil count as presented in Table 23. Immediately before anaesthesia were 61.16± 1.35, 65.1± 1.0 and 65.13± 1.76 percent in Group I, II and III respectively.

Table 23: Mean value (± SE) of Neutrophil at different time intervals (%).

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>61.16± 1.35c</td>
<td>65.1± 1.0b</td>
<td>65.13± 1.76</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>63.14± 1.47bc</td>
<td>66.17± 0.94ab</td>
<td>67.03± 1.34</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>65.38± 0.75ab</td>
<td>68.46± 1.33a</td>
<td>68.4± 1.12</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>67.7± 1.01a</td>
<td>69.91± 1.15a</td>
<td>70.33± 1.06</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td>3.463</td>
<td>3.308</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Small Letters (Column wise superscripts) - indicates difference within a group.

A significant rise in neutrophil percentage (p<0.05) was recorded in group I and II post sedation and during anaesthesia whereas non-significant increase in neutrophil count was recorded in group III during the study. The increase in neutrophil count lasted till the complete recovery. All values were in normal physiological limits (Fig 15).

These findings are in agreement with Jena et al.(2014). Increased in neutrophil count might be due to severe stress inflicted upon the animal during painful surgeries along with the anaesthetic stress leading to the stimulation of the adrenal cortex and subsequent production of glucocorticoids that acts on circulating neutrophils (Soliman et al, 1965). Similar finding with similar mechanism of action was reported by Sharma and Bhardwaj (2010) in dogs.

Salvekar (2004) recorded increased in neutrophil count during propofol anaesthesia in cats and stated that it could be related to inflammatory response resultant of tissue trauma during surgery. Chitale et al. (1998) recorded a substantial rise in neutrophil in goats at thirty to sixty minutes during anaesthesia propofof which were returned towards pre-administration level within 48 hours. In contrast Akbar et al. (2014) reported decrease in differential leukocyte count.
Fig. 15: Mean of Differential Leukocyte Count

<table>
<thead>
<tr>
<th>Group</th>
<th>Neutrophil%</th>
<th>Lymphocyte %</th>
<th>Monocyte %</th>
<th>Eosinophil %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Neutrophil%
- Lymphocyte %
- Monocyte %
- Eosinophil %

Graph legend:
- Group I
- Group II
- Group III
while studying the effect of different dose levels of medetomidine in relation to time in canines.

1. Lymphocyte %

Average values for lymphocyte count in Group I, Group II and Group III at different intervals are presented in Table 24.

Table 24: Mean value (± SE) of Lymphocyte at different time intervals (%).

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>30.6± 1.14&lt;sup&gt;a&lt;/sup&gt;</td>
<td>28.3± 0.82</td>
<td>28.03± 1.21&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>29.1± 1.40&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>27.25± 0.69</td>
<td>26.71± 0.82&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>27.86± 0.70&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>26.16± 1.08</td>
<td>25.8± 0.72&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>25.91± 1.02&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25.26± 0.95</td>
<td>24.11± 0.66&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td>3.237</td>
<td></td>
<td>2.613</td>
<td></td>
</tr>
</tbody>
</table>

The mean (± SE) lymphocyte percentage before sedation was 30.6± 1.14, 28.3± 0.82 and 28.03± 1.21 in group I, II and III respectively. During sedation and anesthesia a significant decrease in lymphocyte was observed in group I and III whereas a non-significant decrease in lymphocyte was observed in group II. The decrease in lymphocyte percentage persisted even after complete recovery. However, the values of lymphocyte percentage ranged in normal physiological limits during the study (Fig 15).

This drop in lymphocyte count could be attributed to stress response to anaesthesia as reported by Hussain <i>et al.</i> (2010). The findings of this study are in agreement with the results observed by Singh (2009) Hikasa <i>et al.</i> (1996) in cats and Hikasa <i>et al.</i> (1996), Chitale <i>et al.</i> (1998) in goats.

Chang (1984) and Molinan (2006) stated that opioids may suppress immune system cells, like lymphocyte, via an indirect mechanism operating through the central nervous system. Lymphoid organs contains rich supply of sympathetic nerve fibers (Felten <i>et al.</i> 1987) permitting nor-epinephrine (NE) to influence lymphocyte activity Straub <i>et al.</i> (1989). Tramadol inhibits neuronal reuptake of NE and 5-Hydroxytryptamin and may actually facilitate release of
both. Therefore, the increase in concentration of NE may promote the suppression of lymphocytes (Costa et al. 2013)

2. Monocyte and Eosinophil Count (%)

The mean (± SE) monocyte and eosinophil count before anaesthesia in group I were 3.88± 0.33 and 4.21± 0.71, in group II were 3.94± 0.40 and 2.65± 0.13, in group III 3.65± 0.68 and 3.18± 0.63 respectively (Table 25 and 26) (Fig. 15).

Table 25: Mean value (± SE) of Monocyte at different time intervals (%).

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>3.88± 0.33</td>
<td>3.94± 0.40</td>
<td>3.65± 0.68</td>
</tr>
<tr>
<td>S</td>
<td>3.45± 0.30</td>
<td>3.5 ± 0.37</td>
<td>3.26± 0.58</td>
</tr>
<tr>
<td>A</td>
<td>3.08± 0.31</td>
<td>3.1 ± 0.38</td>
<td>3.18± 0.55</td>
</tr>
<tr>
<td>R</td>
<td>2.85± 0.22</td>
<td>2.8 ± 0.27</td>
<td>3.05± 0.62</td>
</tr>
</tbody>
</table>

Table 26: Mean value (± SE) of Eosinophil at different time intervals. (%)

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>4.21± 0.71</td>
<td>2.65± 0.13</td>
<td>3.18± 0.63</td>
</tr>
<tr>
<td>S</td>
<td>3.88± 0.70</td>
<td>2.5 ± 0.17</td>
<td>2.98± 059</td>
</tr>
<tr>
<td>A</td>
<td>3.4± 0.60</td>
<td>2.2 ± 0.15</td>
<td>2.61± 0.47</td>
</tr>
<tr>
<td>R</td>
<td>3.2± 0.54</td>
<td>2.2 ± 0.08</td>
<td>2.5± 0.37</td>
</tr>
</tbody>
</table>

Statistically non-significant difference was observed in monocyte and eosinophil counts during sedation, anaesthesia and complete recovery. Sharma et al. (2010) reported non-significant changes in DLC levels with xylazine-propofol anaesthesia in dogs.

Jena et al. (2014) compared the alpha 2 agonists, dexmedetomidine and Xylazine preanesthetics to the propofol anaesthesia and recorded the decrease in eosinophilic count in dexmedetomidine-propofol anaesthesia whereas non-significant increase in dogs treated with xylazine-propofol.
A. Total Platelet Count

The mean platelet count of all dogs in Group I, Group II and Group III was recorded at different intervals are presented in Table 27.

**Table 27: Mean value (± SE) of Platelet Count (×10⁹/l) at different time intervals.**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>261.5± 18.58&lt;sup&gt;a&lt;/sup&gt;</td>
<td>270± 22.90&lt;sup&gt;b&lt;/sup&gt;</td>
<td>273.5± 54.47&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>164± 11.34&lt;sup&gt;b&lt;/sup&gt;</td>
<td>204.6± 28.38&lt;sup&gt;b&lt;/sup&gt;</td>
<td>166.83± 25.27&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>138.33± 11.90&lt;sup&gt;b&lt;/sup&gt;</td>
<td>140.67± 10.57&lt;sup&gt;b&lt;/sup&gt;</td>
<td>141± 13.75&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>159.16± 24.39&lt;sup&gt;b&lt;/sup&gt;</td>
<td>166.83± 14.49&lt;sup&gt;b&lt;/sup&gt;</td>
<td>189.5± 21.04&lt;sup&gt;ab&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td>51.33</td>
<td>68.13</td>
<td>96.03</td>
<td></td>
</tr>
<tr>
<td>CD(0.01)</td>
<td>70.00</td>
<td>92.92</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Small Letters (Column wise superscripts) - indicates difference within a group.

The mean (± SE) platelet count before anaesthesia was 261.5± 18.58, 270± 22.90 and 273.5± 54.47 in group I, II and III respectively. In the present study, on statistical analysis a significant decrease (p<0.05) in platelet count was observed soon after sedation in all the three groups which persisted during anaesthesia. However the values gradually increased during recovery. All the values were in normal physiological limit (Fig 16).

The transient decrease in the platelet count (thrombocytopenia) could be due to temporary sequestration of platelets in the liver (Handagama and Feldman 1988), spleen and lungs during anaesthesia (Tranquili et al., 2007) or due to the increase plasma volume during anaesthesia on account of vasodilatation resulting in vascular pooling (Stephy et al., 1976). The findings of this study were in accordance with Fani et al. (2008).

Morey et al. (2006) reported highly significant decline in platelet concentration to be 8000 platelets/ul during recovery when compared to the concentrations in the same dog during preinduction (240,000 platelets/ul) and post induction (233,000 platelets/ul) of anaesthesia with propofol. Nna et al. (2016) reported non-significant decrease in blood platelet in rat upon tramadol administration. In contrast Hamad et al. (2016) reported slight increased in blood platelets with tramadol.
4.6 Biochemical Parameters

The following serum biochemical parameters were studied in all the dogs of three groups immediately before and on 05th, 20th and 60th minutes after the induction of anaesthesia.

A. Serum Glutamic Oxaloacetic Transaminase (SGOT) (IU/L)

The mean serum SGOT values of all female dogs from Group I, Group II and Group III at different intervals are presented in Table 28.

Table 28: Mean value (± SE) of SGOT values (IU/L) at different time intervals.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>31.53± 5.9</td>
<td>31.36± 3.29</td>
<td>25.90± 2.09</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>32.89± 8.22</td>
<td>33.06± 7.00</td>
<td>26.81± 2.20</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>37.42± 5.7</td>
<td>36.06± 2.59</td>
<td>30.10± 3.38</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>29.31± 6.5</td>
<td>30.26± 7.00</td>
<td>24.74± 2.15</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean (± SE) SGOT values before induction of the anaesthetic protocol were 31.53± 5.9, 31.36± 3.29 and 25.90± 2.09 in groups I, II and III respectively. In the present study statistically non-significant increase in SGOT values were observed during sedation in all the three groups. This increment in SGOT values persisted during propofol anaesthesia and returned to the preinduction levels at recovery. However all the alterations reported were in normal physiological limits (Fig 17).

A non-significant transient increase in SGOT values during sedation and anesthesia in present study could be due to rapid distribution and clearance of propofol by hepatic and extra-hepatic sites (Branson and Gross, 1994). The slight alteration in hepatic values indicates minimum or no effect of propofol on liver and other body tissues (Bayan et al., 2002).
Fig 17: Mean SGOT Values in different groups

Fig 18: Mean SGPT Values in different Groups
Akbar et al. (2014) reported the decrease in enzyme concentration twenty minutes post administration of medetomidine and also reported that the SGOT enzyme response was anesthetic dose dependant.

A. Serum Glutamic-Pyruvic Transaminase (SGPT) (U/L)

SGPT value was estimated of all the bitches from three groups at different intervals.

Table 29: Mean value (± SE) of SGPT values (U/L) at different time intervals.

<table>
<thead>
<tr>
<th>Group</th>
<th>Group I (U/L)</th>
<th>Group II (U/L)</th>
<th>Group III (U/L)</th>
<th>CD(0.05)</th>
<th>CD(0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>27.57± 4.30</td>
<td>18.97± 3.90</td>
<td>18.33± 1.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>22.8± 2.20$^A$</td>
<td>17.19± 1.64$^B$</td>
<td>14.71± 1.10$^B$</td>
<td>5.153</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>23.65± 2.65</td>
<td>20.88± 2.14</td>
<td>15.87± 1.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>25.29± 2.69$^A$</td>
<td>15.65± 1.71$^B$</td>
<td>14.78± 0.73$^B$</td>
<td>5.708</td>
<td>7.894</td>
</tr>
<tr>
<td>CD(0.05)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The mean (± SE) SGPT values before anaesthesia were 27.57± 4.30, 18.97± 3.90 and 18.33± 1.83 in group I, II, and III respectively (Table 29). Statistically non-significant decrease during sedation and anesthesia followed by gradual increase in SGPT values to pretreatment level were observed during the present study (Fig. 18).

The findings were in agreement with Akbar et al. (2014) who reported increase in the concentration of ALT/SGPT was directly proportionate to the dose of anaesthetic used and recorded decreased ALT values at 20, 40 and 60 minutes after administration of medetomidine in dogs.

Singh et al. (2010) observed no significant difference in medetomidine treated calves, thus reflecting absence of any hepatic toxicity. Bayan et al. (2002) stated that an increased SGPT level within normal range indicates the normal functioning of vital organs like liver during of propofol anaesthesia.
B. Blood Urea Nitrogen

Mean (± SE) values of Blood Urea Nitrogen (BUN) recorded before induction were 17.03± 0.90, 19.59± 3.10 and 9.06± 1.74 in Group I, Group II and Group III respectively (Table 30).

Table 30: Mean value (± SE) of BUN (mg/dl) values at different time intervals.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>17.03± 0.90&lt;sup&gt;b&lt;/sup&gt;</td>
<td>19.59± 3.10</td>
<td>9.06± 1.74</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>20.25± 1.05&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>20.65± 3.35</td>
<td>9.78± 1.64</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>21.68± 1.07&lt;sup&gt;a&lt;/sup&gt;</td>
<td>18.64± 3.88</td>
<td>10.88± 1.95</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>19.38± 0.93&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>17.03± 3.21</td>
<td>8.66± 1.11</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td>2.838</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Small Letters (Column wise superscripts) - indicates difference within a group.

A significant increase in BUN values post induction of anaesthetic protocol was observed in group I whereas there was no significant difference observed in groups II & III and the values returned to pretreatment levels after recovery (Fig. 19). Elevated BUN values in group I could be due to the propofol anaesthesia induced hypotension and reduced blood flow to kidneys leading to retention of nitrogenous substances in blood (Manat and Kelawala, 2004). However the values remained in normal physiological limit. Jena et al. (2014) recorded similar findings in dogs premedicated with dexmedetomidine and anaesthetized with propofol. The results of this study were in accordance with earlier.

Similar findings were recorded by Khan (2006), Akbar et al. (2014) in dogs, Singh et al. (2010) and Raj (2001) in calves and Kumar et al. (2013) in goats.

C. Serum Creatinine

Average values for serum Creatinine levels recorded in Group I, Group II and Group III at different intervals are presented in Table 1.
**Fig 19: Mean BUN Values in different groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>BA</th>
<th>S</th>
<th>A</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>15</td>
<td>20</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>Group III</td>
<td>10</td>
<td>12</td>
<td>15</td>
<td>16</td>
</tr>
</tbody>
</table>

**Fig 20: Mean Serum Creatinine Values in different groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>BA</th>
<th>S</th>
<th>A</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>0.8</td>
<td>1.0</td>
<td>1.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Group II</td>
<td>0.7</td>
<td>0.9</td>
<td>1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>Group III</td>
<td>0.6</td>
<td>0.8</td>
<td>1.0</td>
<td>0.6</td>
</tr>
</tbody>
</table>
Table 31: Mean value (± SE) of Serum Creatinine (mg/dl).

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>0.76± 0.03</td>
<td>0.79± 0.1</td>
<td>0.76± 0.03</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>0.86± 0.04</td>
<td>0.85± 0.11</td>
<td>0.86± 0.04</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>1.05± 0.16</td>
<td>0.88± 0.11</td>
<td>1.05± 0.16</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>0.68± 0.07</td>
<td>0.69± 0.11</td>
<td>0.68± 0.70</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The mean (± SE) serum creatinine level before anaesthesia was 0.76± 0.03, 0.79± 0.1 and 0.76± 0.03 in Group I, II and III respectively. Non-significant increases in serum creatinine level were observed in all the three groups soon after sedation as well as during anaesthesia. The elevated values dropped down restoring to the preinduction level at recovery. However, the values ranged in the normal limits during the whole study (Fig 20).

The fluctuations in creatinine values attributed to inhibitory effect of drugs on renal blood flow, increased creatinine production from muscle damage and amino acids degradation (Restitutti et al., 2012), (Singh et al., 2013).

Kushwaha et al. (2012) and Jena et al. (2014) reported increased in serum creatinine values between ten minutes to sixty minutes followed by declination which was in accordance to the present study. Similar observations reported by Butola (2000) with midazolam-ketamine and Khan (2006) and Akbar et al. (2014) with medetomidine in dogs.
A. Blood Glucose (mg/dl)

Blood Glucose values recorded at various time intervals of the experiment in all three groups are presented in Table 32. The mean (± SE) glucose value before induction were 54.55± 9.55, 61.52± 5.00 and 47.25± 4.15 in groups I, II & III respectively.

Table 32: Mean value (± SE) of Blood Glucose (mg/dl) at different time intervals.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>54.55± 9.55</td>
<td>61.52± 5.00c</td>
<td>47.25± 4.15c</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>68.21± 21</td>
<td>64.65± 7.1bc</td>
<td>64.43± 10.91bc</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>75.03± 9.08</td>
<td>83.19± 8.69b</td>
<td>90.86± 17.37b</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>88.57± 12.89b</td>
<td>110.11± 5.36aAB</td>
<td>146.15± 16.37aA</td>
<td>37.438</td>
</tr>
<tr>
<td>CD (0.05)</td>
<td></td>
<td>19.829</td>
<td>39.204</td>
<td></td>
</tr>
<tr>
<td>CD (0.01)</td>
<td></td>
<td>27.048</td>
<td>53.460</td>
<td></td>
</tr>
</tbody>
</table>

Small Letters (Column wise superscripts) - indicates difference within a group.
Capital Letters (Row wise superscripts) - indicates difference between the groups.

Statistically, a significant elevation in glucose values were recorded in groups II & III whereas a non-significant increase was recorded in group I post sedation, during anesthesia and values continued to rise during recovery (Fig 21). The high rise in glucose in present study could be attributed to decrease membrane transport of glucose during anaesthesia, decreased glucose utilisation, impaired insulin activity and increased blood concentration of adreno-corticoid hormones as reported in dogs Restitutti et al. (2012). Kumar et al. (2013) reported similar findings of increased in glucose levels towards the end of study in goats treated with propofol-ketamine anaesthesia

Kinjavekar et al. (2000) and Mcsweeney et al. (2012) explained the hyperglycaemic effect of medetomidine and dexmedetomidine which occurs due to suppression of insulin release, stimulation of glucagon release, or both, in alpha and beta cells of pancreas respectively. Mirakhur et al. (1984) stated that hyperglycemia could be attributed to the traumatic stress or muscular activity and sympathetic stimulation caused during restraining of animals resulting in increased secretion adreno-corticoid hormones.
Fig 21: Mean of Blood glucose values in different groups

Fig 22: Mean of Total Serum Calcium In different groups
Kushwaha et al. (2012) in dogs and Bayan et al. (2002) in cats observed significant increase in serum glucose levels during propofol anaesthesia.

On the basis of observations it could be stated that propofol aggravates hyperglycemic effect of dexmedetomidine. The findings of this study are in general agreement with that of Kumar et al. (2013), Jena et al. (2014) and Brockman (1981).

A. Total serum Calcium (mg/dl)

The mean Blood Calcium values recorded in all the three groups at different intervals are presented in Table 33.

**Table 33: Mean value (± SE) of total serum calcium (mg/dl) values at different time intervals.**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>CD(0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA</td>
<td>11.70± 1.22</td>
<td>10.97± 1.78</td>
<td>8.43± 1.21</td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>7.77± 0.89</td>
<td>8.93± 0.70</td>
<td>6.76± 1.21</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>7.4± 1.37</td>
<td>7.80± 0.83</td>
<td>5.74± 1.21</td>
<td></td>
</tr>
<tr>
<td>R</td>
<td>9.96± 1.28</td>
<td>9.47± 1.30</td>
<td>7.73± 1.31</td>
<td></td>
</tr>
<tr>
<td>CD(0.05)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The mean value (± SE) calcium before induction was 11.70± 1.22, 10.97± 1.78 and 8.43± 1.21 mg/dl in Group I, II and III respectively. A non-significant decrease in calcium levels were observed in all the three groups immediately after sedation which persisted during anaesthesia. However, the levels slowly increased to preinduction levels following complete recovery in all the three groups. The levels of calcium ranged between the normal physiological limits in the present study (Fig. 22).

The non-significant decrease in total calcium levels could be attributed to soft tissue trauma during surgery (Baines et al., 2012) or induced by propofol anesthesia. Brainard et al. (2007) recorded statistically significant decrease in ionized calcium levels during propofol anesthesia in dogs and cats and further added that this decrease can be evident regardless of anesthetic protocol used.
Thrane et al. (2012) found that xylazine markedly suppressed calcium transients in neocortical astrocytes in rats. Kancir et al. (1985) reported a non-significant decrease in the calcium levels during surgical procedures which were attributed to the alkaline pH during anaesthesia in humans. Lepage et al. (1999) observed that the decrease in serum calcium levels during anaesthesia was accompanied by hypoalbuminemia.
SUMMARY & CONCLUSIONS

The present study entitled “Clinical Evaluation of Dexmedetomidine-Propofol Anaesthesia for Ovariohysterectomy in bitches” was undertaken at Teaching Veterinary Clinical Complex, Nagpur Veterinary College, Nagpur to evaluate and compare the tolerability of dexmedetomidine-propofol combination with various dose rates of dexmedetomidine.

Eighteen apparently healthy female dogs were divided randomly in three equal groups i.e. Group I, Group II and Group III of six dogs in each. Intravenous injection of tramadol was given at 0 minute in all the dogs followed dexmedetomidine at 06 minute at the dose rate of 5mcg, 10mcg and 15mcg/kg in the dogs of Group I, group II & group III respectively. Anaesthesia was induced with propofol at 10th minute to achieve the surgical stage of anaesthesia and maintenance of anesthesia was done by incremental bolus dose of propofol.

During the present study various physiological, haematological and serum biochemical evaluations were carried out to evaluate the most effective dose of dexmedetomidine in anaesthetic regimen. The results of the study were as follows.

In the present study, quality of sedation was graded based on visual examination, presence or absence of reflexes, clinical signs as per simple descriptive scale and complications if any. mild sedation of grade 1 was observed in group I as the animals could be easily aroused and were able to walk with very little or no ataxia.

The dogs in group II treated with dexmedetomidine at 10 mcg/kg dose rate exhibited profound sedation of grade 3 with obvious signs of ataxia, complete relaxation of jaw and achieved sternal or lateral recumbancy with abolition of pedal, palpebral and corneal reflexes immediately post-sedation. The dogs in group III also demonstrated excellent sedation with abolition of most of the reflexes however, it was associated with complications like, cyanotic tongue, severe bradycardia, and arrhythmia hence was graded as 4.

From the study it was observed that Dexmedetomidine in combination with the tramadol proved to be a potent sedative combination producing
synergistic analgesic effect in all the three groups. Dexmedetomidine at the rate of 10 mcg produced excellent, smooth sedation without any complications in group II and prepared the dogs well for induction of general anaesthesia. Due to the profound sedative effect of dexmedetomidine, the surgical stage of anaesthesia was achieved at the lowest dose of propofol induction.

Significantly high pedal reflex scores in group II (2.16±0.16) & III (2.16±0.16) than group I (1.33±0.21) could be considered representative of dose dependant sedation and analgesic quality of dexmedetomidine and tramadol. Complete abolishment of pedal reflex with score 3 was recorded during anaesthesia which further restored to normalcy at recovery.

A significant increase in the palpebral reflex score was observed immediately after the sedation and during the anaesthesia within all the groups. Significant rise in Palpebral scores were recorded amongst the groups, wherein group I being the lowest (1.33±0.21) and group III being the highest (2.83±0.16) during sedation. On the basis of the findings it could be concluded that dexmedetomidine produces profound sedation with increasing dose, whereas the reflex was completely abolished during the propofol anaesthesia.

In the present study corneal reflex persisted after the sedation in group I where as it was sluggish at higher doses of dexmedetomidine in group II & III. Further the corneal reflex disappeared completely (absent) during the depth of anaesthesia in all the three groups.

The mean (±SE) onset of anesthesia was 28±1.26, 21.83±1.24 and 20.83±1.13 seconds in Group I, II and III respectively. Statistically significant difference was observed in the induction time amongst group I & II as well as in group I & III, but no significant difference in group II & III. The mean induction time was longest (28±1.26) in group I whereas shortest (20.0±1.29) in group III.

The onset of anaesthesia in all the dogs was smooth rapid and excitement free without any untoward signs like pain on injection, apnoea, cyanosis, excitement, retching and vomiting etc. in present study. It could be concluded that premedication with tramadol-dexmedetomidine provided a good basal anaesthesia for propofol facilitating stress-free induction with significant level of analgesia during surgery.
The mean average total induction dose recorded were 32.5±1.70, 25.0±0
and 21.66±1.05 mg in group I, II & III. Statistically significant difference was
observed in total induction dose amongst all the three groups. The total induction
dose for Group I was highest 34.16±1.53 mg whereas lowest (25.83±1.53) in
group III. It was extrapolated from the findings that the induction dose of propofol
was reduced by the increasing dose of the premedicant used.

The average duration of anaesthesia in Group I, II and III were
26.83±0.79, 29.16±1.07 and 31.33±1.14 (Minutes) respectively. Statistically a
significant difference (p>0.05) was observed between groups. The duration of
anaesthesia was observed lowest in group I (26.83±0.79) and required more
incremental bolus dose for maintenance whereas longest in Group III
(31.33±1.14) with minimal incremental boluses of propofol.

The quality of anaesthesia was graded by observing different
physiological parameters at different intervals, presence or absence of various
reflexes, degree of muscle relaxation and complications if any.

The plane of anaesthesia was observed to be light in group I due to poor
muscle relaxation and reappearance of gag & palpebral reflexes during surgery
requiring frequent incremental propofol boluses for the maintenance of surgical
plane.

In Group II animals, deep surgical anaesthesia was produced with
excellent muscle relaxation, analgesia and loss of all the body reflexes by
tramadol – dexmedetomidine (10mcg/kg) – propofol combination. The animals
were observed comfortable and relaxed throughout the surgery without any
alteration in the physiological parameters.

The quality of anaesthesia was good in dogs of group III but experienced
complications like cyanosis of tongue and transient bradycardia during sedation
and also necessitated oxygen with respiratory depression following propofol
induction. Significant difference was also observed in physiological parameters.

Good quality of onset of anaesthesia with surgical plane of anesthesia
was produced without any alteration in the physiological parameters in group II
animals. The combination of preanaesthetic tramadol – dexmedetomidine
10mcg/ kg is recommended in dogs to produce basal anaesthesia with excellent
sedation, potent analgesia and muscle relaxation requiring lower doses of propofol with lesser degree of respiratory depression.

The mean (± SE) time required for the recovery in group I, II and III was 17.58±0.87, 18.66±1.11 and 20.08±1.04 minutes respectively. Statistically non-significant increase in recovery time was observed amongst the three groups. The quality of recovery was graded as good in group I whereas excellent quality of recovery observed in groups II & III which could be attributed to the synergistic analgesic property of tramadol and dexmedetomidine. The quality of recovery was smooth, rapid, without shivering, struggle free in all the dogs.

The mean (± SE) rectal temperatures immediately before anaesthesia were 101.5±0.28, 102.33±0.30 and 101.91±0.22 in groups in group I, II and III respectively. A non-significant decline in the rectal temperature was observed in all the three groups during anaesthesia at 20 minutes which gradually increased to normalcy at complete recovery. Statistically no significant difference was observed in the values amongst the groups.

The mean heart rates recorded before induction of anaesthesia were 120±3.14, 126.67±3.95 and 140.33±7.38 beats per minute in group I, II and III respectively. Statistically significant decrease in heart rate was observed within all the three groups but was more pronounced in Group III after administration of dexmedetomidine. Highly significant difference was observed in groups II & III. However, heart rate significantly increased after induction of propofol anesthesia. Statistically no significant difference was observed amongst the three groups.

The mean (± SE) respiratory rate before administration of anaesthetic protocol was 29.83±1.90, 33.36±2.411 and 29.66±2.44 in group I, II & III respectively. A significant decline in respiratory rates was observed in all the three groups following sedation. The reduced respiratory rates persisted during propofol anesthesia but slowly increased to the normal during the recovery.

The mean (± SE) values of hemoglobin (gm/dl) before administration of anaesthetic protocol were 13.76±0.50, 13.58±0.99 and 14.2±0.52 in group I, II & III respectively. A non-significant decline in hemoglobin values was observed in group I and group II whereas the significant decrease (p<0.05) in hemoglobin was reported in group III during anesthesia. Comparison amongst the groups revealed no significant difference.
The mean (± SE) packed cell volume (PCV) percentage recorded before anaesthesia was 45.25±2.88, 47.45±1.30 and 48.53±0.78 percent in group I, II and III respectively. A non-significant decrease was observed within all the three groups. Statistically there was no significant difference amongst the groups. However the values were in normal physiological limits.

The mean (± SE) total erythrocyte counts (TEC) before induction were 8.04±0.60, 7.99±0.63 and 8.99±0.45×10⁹ Cells per liter in group I, II and III respectively. After sedation a non-significant decline in TEC was observed in group I and II whereas in group III significant decline in total erythrocyte count was observed. However, all the values were in normal physiological range in all the three groups at all the time.

The mean (± SE) total leukocyte count (TLC) before induction of anaesthesia were 21.36±1.22, 20.16±1.45 and 17.68±1.52 cells per liter in group I, II and III respectively. A non-significant decrease in total leukocyte count was observed during sedation which was further declined in all the three groups after administration of propofol at 20 minutes. The TLC values returned to the preinduction levels at complete recovery. The variation in TLC values remained within normal physiological limits throughout the study.

The mean (± SE) values of neutrophil count as presented in table 23. Immediately before anaesthesia were 61.16±1.35, 65.1±1.0 and 65.13±1.76 percent in group I, II and III respectively. A significant rise in neutrophil percentage (p<0.05) was recorded in group I and II post sedation and during anaesthesia whereas non-significant increase in neutrophil count was recorded in group III during the study. The increase in neutrophil count lasted till the complete recovery. All values were in normal physiological limits.

The mean (± SE) lymphocyte percentage before sedation was 30.6±1.14, 28.3±0.82 and 28.03±1.21 in group I, II and III respectively. During sedation and anesthesia a significant decrease in lymphocyte was observed in group I and III whereas a non-significant decrease in lymphocyte was observed in group II. The decrease in lymphocyte percentage persisted even after complete recovery. However, the values of lymphocyte percentage ranged in normal physiological limits during the study.
The mean (± SE) monocyte and eosinophil count before anaesthesia in group I were 3.88±0.33 and 4.21±0.71, in group II were 3.94±0.40 and 2.65±0.13, in group III 3.65±0.68 and 3.18±0.63 respectively. Statistically non-significant difference was observed in monocyte and eosinophil counts during sedation, anaesthesia and complete recovery.

The mean (± SE) platelet count before anaesthesia was 261.5±18.58, 270±22.90 and 273.5±54.47 in Group I, II and III respectively. In the present study, on statistical analysis a significant decrease (p<0.05) in platelet count was observed soon after sedation in all the three groups which persisted during anaesthesia and gradually increased during recovery. All the values were in normal physiological limit.

Mean (± SE) SGOT values before induction of the anaesthetic protocol were 31.53±5.9, 31.36±3.29 and 25.90±2.09 in groups I, II and III respectively. In the present study statistically non-significant increase in SGOT values were observed during sedation in all the three groups. This increment in SGOT values persisted during propofol anaesthesia and returned to the preinduction levels at recovery. However all the alterations reported were in normal physiological limits.

The mean (± SE) SGPT values before anaesthesia were 27.57±4.30, 18.97±3.90 and 18.33±1.83 in group I, II, and III respectively. Statistically non-significant decrease during sedation and anesthesia followed by gradual increase in SGPT values to pretreatment level were observed during the present study.

Mean (± SE) values of Blood Urea Nitrogen (BUN) recorded before induction were 17.03±0.90, 19.59±3.10 and 9.06±1.74 in Group I, Group II and Group III respectively. A significant increase in BUN values post induction of anaesthetic protocol was observed in group I whereas there was no significant difference observed in groups II & III and the values returned to pretreatment levels after recovery.

The mean (± SE) serum creatinine levels before anaesthesia were 0.76±0.03, 0.79±0.1 and 0.76±0.03 in Group I, II and III respectively. Non-significant increases in serum creatinine level were observed in all the three groups soon after sedation as well as during anaesthesia and values dropped
down to pre-induction level at recovery. However, the values ranged in the
normal limits during the whole study.

The mean (± SE) glucose values before induction were
54.55±9.55, 61.52±5.00 and 47.25±4.15 in Groups I, II & III respectively.

Statistically, a significant elevation in glucose values were
recorded in groups II & III whereas a non-significant increase was recorded in
group I post sedation, during anesthesia and values continued to rise during
recovery.

The mean values (± SE) of total calcium before induction was
11.70±1.22, 10.97±1.78 and 8.43±1.21 mg/dl in Group I, II and III respectively. A
non- significant decrease in calcium levels were observed in all the three groups
immediately after sedation which persisted during anaesthesia and slowly
increased to pre-induction levels following complete recovery in all the three
groups. The levels of calcium ranged in normal physiological limits.

Conclusions:
On the basis of the study the following conclusions can be drawn:

1. Tramadol – dexmedetomidine propofol combination could be effectively
tolerated as Total intravenous Anaesthesia (TIVA) in dogs at different
dose rates producing rapid, smooth, safe anaesthesia with uneventful
recovery without alteration in physiological and haemato-biochemical
parameters.

2. The dexmedetomidine at the dose of 10µg produced for
profound/excellent sedation, analgesia with muscle relaxation and can be
recommended as most effective sedative for propofol anaesthesia during
major surgeries.

3. Dexmedetomidine combination with tramadol produced synergistic
analgesic effect which was beneficial for pain management during
recovery.
Bibliography


VITA

The author of this dissertation Mr. Chetan Vasudeorao Patond was born on 21st September 1992 at Village Goregaon, Taluka Murtizapur of Akola district (Maharashtra). He has passed S.S.C and H.S.C. Examination from Maharashtra State Board of Secondary and Higher Secondary Education, Pune in the year 2007 and 2009 respectively. In August 2014 he has completed his graduation (B.V.Sc. & A.H.) from Nagpur Veterinary College, Nagpur under Maharashtra Animal and Fishery Sciences University, Nagpur. He was an active member of NCC during his graduation studies, actively participated in all extension activities. He represented 1 MAH R & V SQN, NCC at Republic Day Camp at New Delhi in 2012. He was an active member of NSS and participated in various activities. He was participated in 6th International Clinical Case Conference 2014 held at Chennai and was awarded with second prize in avian and wild-life section for case paper presentation during under graduation.

He has joined the Department of Surgery & Radiology, Nagpur Veterinary College, Nagpur for post-graduation in November 2014. During his post-graduation he presented the case paper at 8th International Clinical Case Conference 2016 Held at Chennai and was awarded with first prize in companion animal surgery section. He also presented a paper at International Clinical Case Conference 2015, Namakkal, TANUVAS, Chennai. He attended the hands on training programme in bird surgery at Jivdaya Charitable Trust, Ahmedabad. He also actively participated in various workshops during his PG. He has given the active participation in animal welfare activities such as Mass Vaccination Camp, Anti-Rabies Camp, Free Animal Treatment camp, Animal Birth Control Camp, Swatch Bharat Abhiyan, Tree Plantation Programme etc.

He is a registered member of Maharashtra State Veterinary Council (MSVC), Nagpur. Further, he is a life Member of the Indian Society for Veterinary Surgery, Indian Society For Advancement In Canine Practice (ISACP) and a life member of Nagpur Veterinary College Alumni Association. He was also a former member of ISAW.
The present study was undertaken to evaluate the efficacy and tolerability of dexmedetomidine-propofol anaesthesia for ovariohysterectomy in bitches and evaluate the most effective dose of dexmedetomidine in it. Clinical, physiological & haemato-biochemical changes were assessed to study the tolerability of dexmedetomidine-propofol anaesthesia at different dose rates during ovariohysterectomy in eighteen apparently healthy female dogs.

Eighteen apparently healthy dogs were randomly divided in three groups (6 dogs in each). All the dogs premedicated with tramadol (3mg/kg) in combination
with dexmedetomidine at different dose rates of 5, 10 and 15 µg/kg in group I, II and III respectively followed by propofol anaesthesia intravenously.

The onset, quality and duration of sedation, anaesthesia and recovery were studied. Changes in HR, RR, rectal temperature and haematobiochemical parameters were recorded before and at 5 minutes after sedation, at 20 minutes during anaesthesia and at 60 minutes after complete recovery.

The sedation was smooth and excitement or struggle free in all the groups but the quality of sedation was mild in group I, excellent in group II where as in group III it was excellent but associated with untoward signs. Pedal, palpebral and corneal reflexes were sluggish to greater extent after sedation and completely abolished during anaesthesia.

The onset of induction was smooth and rapid in all the groups but was longest (29.16±1.53 seconds) in group I and shortest and approximately same in group II (20.83±1.53) & III (20.0±1.29) with smooth and quicker recovery in all the three groups. A significant difference in the reduction of induction dose of propofol was observed with the increasing dose of dexmedetomidine amongst the groups.

A significant decrease in HR & RR was observed within all the groups post sedation and during anesthesia, whereas there was no significant difference in Temperature, Hb, PCV, TEC, TLC, platelets, lymphocytes, monocytes, eosinophils, SGOT, SGPT, BUN, Serum Creatinine and total calcium values. A significant rise in neutrophils was observed in group 1 after sedation where as significant increase in glucose levels were noted in all the groups immediately after sedation and during anaesthesia. All the values were in normal physiological limits. Therefore Tramadol –dexmedetomidine-propofol combination could be effectively tolerated as Total intravenous Anaesthesia (TIVA) in dogs at different dose rates producing rapid, smooth, safe anaesthesia with uneventful recovery without alteration in physiological and haematobiochemical parameters.

The dexmedetomidine at the dose of 10mcg was found to be produced for profound/excellent sedation, analgesia with muscle relaxation and can be recommended as most effective sedative for propofol anaesthesia during major surgeries. Dexmedetomidine combination with tramadol produced synergistic analgesic effect which was beneficial for pain management during recovery.
مادی شرایط نسبتاً شاخص‌پذیر نمودن دکس‌مید‌ترومیدین–پرپروفیل بلژیکا سانسپراتوری چهارمانتین محصول.

ک. ماه‌نشینی کاشت‌های انجام شده:

پ. پنج‌شنبه، گروه‌هایی از نیروی انتظامی، با توجه به اینکه گروه‌هایی که در آن‌ها به شدت از نیروی انتظامی استفاده می‌شود، به‌طور کلی در ایالات متحده آمریکا و کانادا وجود ندارد، این نیاز است که این کشورها از این نیاز را دارند.
शारीरिक, रक्तविषयक व जीवनसाधनों बदल अदरा मादी स्वास्थ्यवादी करण्यात आला।

सदर अभ्यासकरिता मादी स्वास्थ्य तीन समान गटांमध्ये (प्रत्येकी सहा) विभागण्यात आले. त्यामध्ये पूर्व औषधोपचार मणून इंजेक्शन ट्रॅमीडॉल व इंजेक्शन डेक्समेडेटोमिडीन या समोहन संपोजननाचा बापर करण्यात आला. त्याकरितासाठी ट्रॅमीडॉल हे (अम्फ्रॅमेक्सिल या माच्यास) सर्व स्वास्थ्यवादी देयांत आले व तसेच इंजेक्शन डेक्समेडेटोमिडीन हे पाप, त्याच्या धा यंत्रप्रधान फक्त अनुमोदक अनुमत अनुमोदक देयांत आले होते.

याकरिता समोहन व भूल याची सुरुवात, त्याला लागणारा कालावधी व त्याची पुनःप्राप्ती या सामयिक परिणाम जसे वेळ व वर्तमान बावत अभ्यास करण्यात आला. तसेच या अभ्यासात हदयाची व स्वस्थ्याची गती, शरीराची तापमान, रक्त व जीवनसाधनोंचे घडक यांच्यातील फक्त अनुमोदक निरोधण भुलेच्या आदेश व नंद नंद मिनीटे, वीस मिनीटे व साठ मिनीटे या काळावधीत करण्यात आला.

यामध्ये समोहन करण्यात उपजांक्य अभ्यासाचा उपाय एवढून आला. त्यावरसमोहन करण्यात उपायसारखा अभ्यासाचा परिणाम गट कं. एक मध्ये सौम्य होता तर दोन व तीन मध्ये उत्कृष्ट दर्जाचा होता. परतु गट कं. तीन मध्ये काही प्रतिकृत लक्षणे आढळली.

तसेच असे प्रत्येक निरोधणाचा आले को, बेदना, पाणपणी व डॉ यांच्या आहारी संबंधीत अयोग्यता प्रतिकृत किंवा समोहन दरम्यान मंद होते गेल्या व त्याचा प्रतिसाद भुलेच्या नंतर पुनरुत्पन्न नाहीस झाला. आणि संपूर्ण सद्द्रास्य मिनीटाच्या संपूर्ण चेतनाव्यता परत आली.

या तिथी गटांमध्ये भुलेच्या सुरुवात ही जलद, पासुमुक्त, सहज व सोपी होती तसेच रक्तच्या काळावधी गट कं. एकमध्ये सर्वांत जास्त (२५-२६ सेकंड) व गट कं. दोन व तीन (अनुमोदक २०.४३ व २०.०० सेकंड) मध्ये सर्वांत कमी व अद्वीत मारखाच होता.

या संपोजननाच्या अभ्यासात सर्व गटांमध्ये चेतनाव्यता (पुनःप्राप्ती) ही जलद, सोपी व प्राणजल होती.या अभ्यासात गटांमध्ये भुलेच्या सुरुवात धावणे उपयोगी नव्या या ती गटांमध्ये डेक्समेडेटोमिडीन च्या वापराचा माजवर अवलंबून असल्याचे दिसून आले.

तीनही गटांमध्ये हदयाच्या ट्रॅमीडॉल गतीत व रात्साधनासाधनाच्या दर रक्तच्या प्रभाव पद दिसून आली मात्र शारीरिक तापमान, हिमोगेमोन्याचे, एकूण रात रक्त पेषी, एकूण पांढरा रक्त पेषी, तांडवाचा रक्त पेषी, लिप्मॉसाइट, मोनोसाइट, इंसोसिक्सिल, एस्जी, ओ. डि., एस. जी, पी, ठी., रक्त युरिया, नाप्टोजीन, सिस्म क्रियेटिनाइन व केल्फायम यांच्या मात्रेमध्ये लक्षणीय बदल व फक्त आढळून आला नाही. याव्यतिरिक्त गट कं. एक मध्ये नुसिफेक्ट या पांढरा पेशीच्या प्रभावाचा लक्षणीय बाहु आढळून आली व रात्साधन शाळारेच्या प्रभावात सर्व गटांमध्ये.
लक्षणीय बाह दिसन आली। तथापि या सर्व घटकांमध्ये झालेले बदल सामान्य व शरीराच्या मयदित होते।

सदर अभ्यासांती असे लक्षात आले की, मादी रचनामयाच्या नसवंदीकरिता ट्रांसमॉडल, डेक्समेडेटेमॉडल व प्रोपोफॉल या संयोजनाच्या प्रभावीपणे मादीला घटकांत बदल न करता शिरोपदारे विविध मात्रेमध्ये जलंद, सहज व सुरक्षित आहे.

वरील संयोजननातील डेक्समेडेटेमॉडल आव्यू (२० मि.ग्र./किलो वजनप्रमाणे) सत्ताच समोहन वेदनाशमन आणि स्नायु विश्रांती मिळून जवळ मानावेत स्वेच्छाने प्रक-प्रक मदत करते। प्रोपोफॉल—डेक्समेडेटेमॉडल आव्यूवत्ता संयोजन सर्वव भावासारख्या कृत्यांमध्ये मोठ्या साधनक्षेपणी (मादी रचनामयाच्या नसवंदीसाठी) प्रोपोफॉल या भूमिका आणि भागी व चेतनाक्षेपणे प्राप्त दरम्यान वेदना प्रक्षेपणासाठी सर्वत्र प्रभावीपणे प्राप्त दरम्यान त्यावर ठरते.