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# Haematobiochemical Changes during Pain Management with Intraperitoneal Bupivacaine and Bupivacaine-dexmedetomidine in Dogs

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## ABSTRACT

**Background:** There is no gold standard to evaluate postoperative pain in animals. The study was conducted to evaluate haematobiochemical changes following intraperitoneal bupivacaine and bupivacaine-dexmedetomidine in dogs.

**Methods:** Eighteen clinical cases of dogs requiring laparotomy were randomly divided into three groups *viz*. Group-B, BD and N comprising of six dogs in each. The animals were premedicated with glycopyrrolate, meloxicam and diazepam. Anaesthetic induction and maintenance was done by using propofol. Intraperitoneally bupivacaine, bupivacaine-dexmedetomidine and normal saline were infused in the three groups. The blood samples were collected prior to pre-medication at 0 min (base line), 30 min (after induction), 2 hrs and 24 hrs interval after intraperitoneal administration of drugs for estimation of haematobiochemical parameters.

**Result:** The bupivacaine and dexmedetomidine combination reduces the serum glucose and cortisol level which might be indicative of lowered pain response.

**Key words:** Bupivacaine, Dexmedetomidine, Dogs, Intraperitoneal.

## INTRODUCTION

Evaluation and management of pain in animals is a challenging task due to their inability to verbalize the discomfort. Recognition and assessment of pain have always been an integral part of animal welfare has been growing considerably (Hansen, 2003). The World Small Animal Veterinary Association and Global Pain Council has recommended intraperitoneal and incisional administration of local anaesthetics for feline and canine pain management as one of the multimodal analgesic approaches to ease post-operative pain. These methods are safe, simple and cost efficient. Intraperitoneal administration of local anaesthetic agents decreases early postoperative reduces pain scores as well as enhance time to first involvement of analgesia following abdominal surgery (Benito *et al*., 2018). Higher blood glucose and cortisol level in bitches after surgery has been common and could be due to post-operative stress and pain (Benjamin, 2001 and Marcovich *et al*., 2001). Intraperitoneal local anaesthetics and alpha - 2 adrenoceptor agonist may be a better option to relieve immediate postoperative pain as these agents lacks the side effects produced by other agents like NSAIDs and opioids such as gastritis and drug dependence (Malhotra *et al*., 2007). The present study was undertaken with the objective to find out haematobiochemical changes during pain management with intraperitoneal bupivacaine and dexmedetomidine in dogs.

## MATERIALS AND METHODS

The study was conducted in the Teaching Veterinary Clinical Complex and Department of Veterinary Surgery and Radiology, College of Veterinary Sciences and Animal Husbandry, Central Agricultural University, Selesih, Aizawl, Mizoram. The study was conducted in total 18 clinical cases of dogs requiring laparotomy procedure. The animals were divided into 3 groups *viz*. Group-B, Group-BD and Group-N comprising of 6 animals in each. Before the laparotomy and anaesthetic trial, all of the animals were fasted for 12 hours for food and 4 hours for water.

All the animals were premedicated with glycopyrrolate @ 0.01 mg/kg b. wt and meloxicam @ 0.2 mg/kg b. wt through intramuscular route after 10 minutes diazepam was administered @ 1 mg/kg b. wt intravenously. Induction was

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done by using propofol @ 5 mg/kg b. wt intravenously or till effect and the anaesthesia was maintained with incremental doses of propofol whenever required. After laparotomy incision of uniform length, intraperitoneal bupivacaine @ 2 mg/kg with equal volume of normal saline in Group B, bupivacaine and dexmedetomidine @ 2 mg/kg and 1 µg/kg with equal volume of normal saline in Group BD and only normal saline in Group N was administered.

For evaluation of haemato-biochemical parameters the blood samples were collected in sterile EDTA and clot-activator vials from the cephalic or saphenous vein prior to pre-medication at 0 min (base line), 30 min (after induction), 2 hrs and 24 hrs interval after intraperitoneal administration. Automated haematology cell counter MS4e and Automated serum biochemical analyzer DRI-CHEM 4000i was used for the assessment of haemato-biochemical parameters. The following parameters were evaluated haemoglobin (g/dL), packed cell volume (%), total erythrocyte count (millions/cu.mm), total leukocyte count (thousands/cu.mm), differential leukocyte count (%), serum glucose (mg/dL), serum gamma-glutamyl transferase (U/L), serum creatine kinase (U/L), serum creatinine (mg/dL) and serum cortisol (nmol/L). The statistical package for social sciences (SPSS) version 25 was used to analyse the data. The data was analysed by using one-way analysis of variance (ANOVA) and a post-hoc test using Duncan's multiple range tests. The data was displayed as mean standard error and differences were considered statistically significant when $P<0.05$.

## RESULTS AND DISCUSSION

In the present study mean body weight was 10.5±0.23 kg ranging from 9-12 kg and the mean age was 12.4±0.29 months ranging from 11-15 months dogs were included. In all the groups, the mean Hb, PCV and TEC level (Fig 1,2,3) decreased significantly at 30 min and 2 hrs intervals from the baseline value thereafter, increased at 24 hrs intervals. However, the changes were non-significant among the groups at different time period. The decrease in Hb observed in the present study might be due to reduced sympathetic activity resulting in circulating blood cell accumulation in the spleen and other reservoirs, as well as inter-compartmental fluid redistribution to maintain cardiac output or hemodilution as a result of fluid therapy (Singh *et al.,* 2013 and Thejasree *et al.,* 2018). The values were within the physiological limit throughout study period. In all groups the TLC (Fig 4) declined significantly at 30 min of observation followed by gradual increase at 2 hrs and 24 hrs. The granulocyte (Fig 5) increased non-significantly from 0 min to 2 hrs followed by non-significant decrease at 24 hrs in all the groups. Surgical and anaesthetic stress leads to activation of the adrenal cortex and production of glucocorticoids that have an effect on the neutrophils which might have resulted in an initial increase in granulocyte count (Chandrashekarappa *et al.,* 2009). The lymphocyte count (Fig 6) reduced up to 2 hrs followed by slight rise at 24 hrs. However, the changes were statistically non-significant and the values were within the physiological limit. A non-significant decrease was noticed in monocyte count (Fig 7) in all the groups up to 2 hrs followed by slight rise at 24 hrs.

In all the three groups the mean value of serum glucose level (Fig 8) increased significantly at 30 min after induction. The initial rise in glucose level might be due to the hyperglycaemic reflex to surgery is caused by afferent nerve fibres carrying neural impulses from the surgical site to the central nervous system. The efferent connection is mediated both directly and indirectly via sympathetic activity in the liver and catecholamine production from the adrenal glands which mediates gluconeogenesis along with reduced peripheral utilization of glucose (Rimback *et al*., 1986 and Bayan *et al.,* 2002). A significantly lower level of glucose was recorded in Group BD and Group B as compared to Group N at 2 hrs and 24 hrs intervals which might be due to the effect of bupivacaine which might have caused less post-operative biochemical stress caused by the intraperitoneal administration of bupivacaine (Kibar *et al*., 2019). A reduced serum glucose level was also observed by Farokhzad *et al.* (2021) with intraperitoneal lidocaine and tramadol in dogs.

In all the groups the GGT value (Fig 9) increased non-significantly at 30 min of observation period followed by gradual decrease towards the baseline values at 24 hrs. However, the changes in the GGT level were within the physiological limit indicating a minimum or no effect on the hepatic functions.

Significantly increased level of serum creatine kinase (Fig 10) was observed up to 24 hrs in all the groups. At 2 hrs and 24 hrs the serum creatine kinase concentration was higher in Group N followed by Group B and BD. Increase level of creatine kinase during and after surgery might be due to increased muscular exertion, muscle damage or due to stress (Petherick *et al*., 2013). The serum creatinine (Fig 11) increased significantly in all the groups up to 30 min after induction followed by a gradual decrease at 2 hrs and 24 hrs. The initial increase in serum creatinine level might be due to the action of anaesthetic agents which might have decreased the glomerular filtration rate by temporary inhibiting the renal blood flow or might also be due to the effect of muscle damage and degradation of amino acid during surgery (Kinjavdekar *et al*., 2002) and (Gamal and Khalid, 2013). However, the serum creatinine values were within the physiological limit in all the groups.

There was a significant increase in cortisol level (Fig 12) up to 2 hrs from the baseline value and returned towards the pre-induction level at 24 hrs in all the groups. A significantly higher concentration of cortisol was recorded in Group N and Group B as compared to Group BD at 2 hrs and 24 hrs. The changes in the cortisol level were statistically non-significant at 0 min and 30 min but significant at 2 hrs and 24 hrs among the groups. The increase in the cortisol level might be due to the stress, surgical trauma, effects of anaesthetic, anxiety and excitement causing activation of hypothalamic pituitary adrenal axis (Michelsen *et al*., 2012).

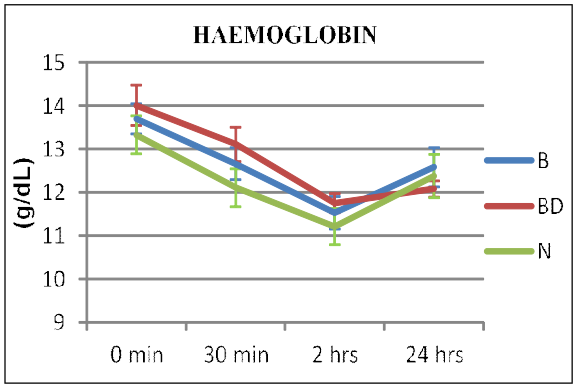


**Fig 1:** Haemoglobin in Group B, BD and N.

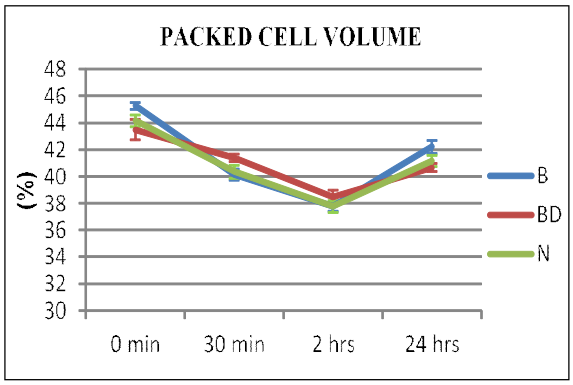


**Fig 2:** Packed cell volume in Group B, BD and N.

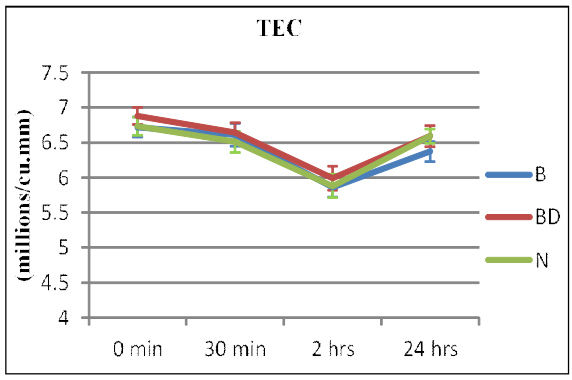


**Fig 3:** TEC in Group B, BD and N.

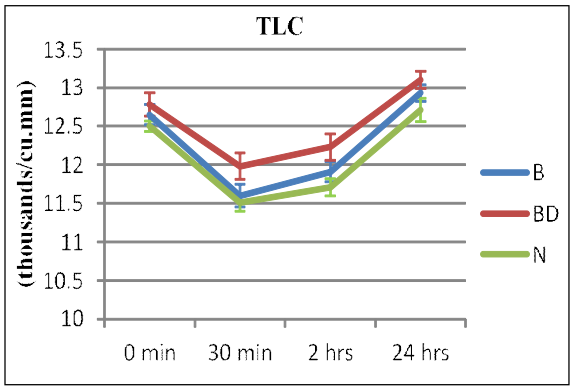


**Fig 4:** TLC in Group B, BD and N.

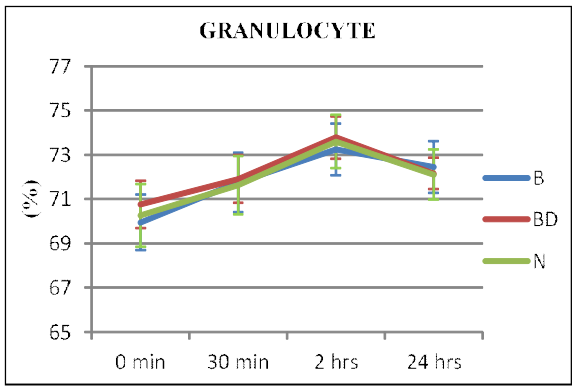


**Fig 5:** Granulocyte count in Group B, BD and N.

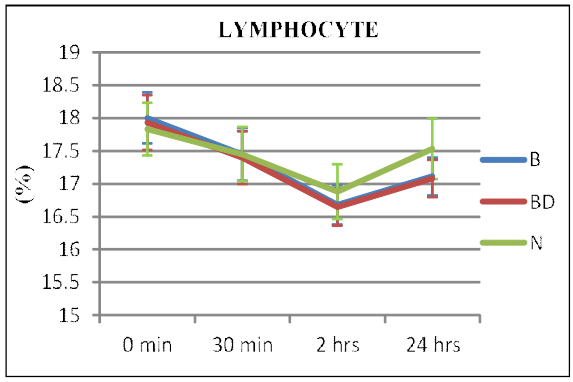


**Fig 6:** Lymphocyte count Group B, BD and N.

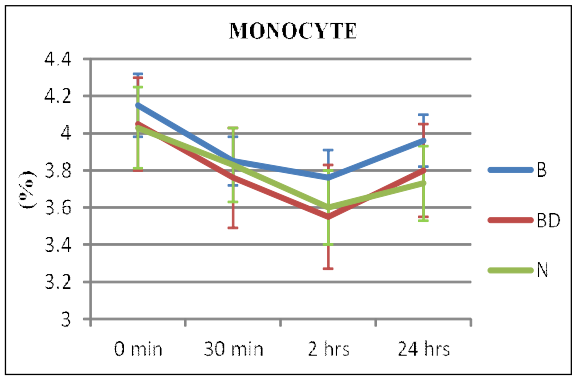


**Fig 7:** Monocyte count in Group B, BD and N.

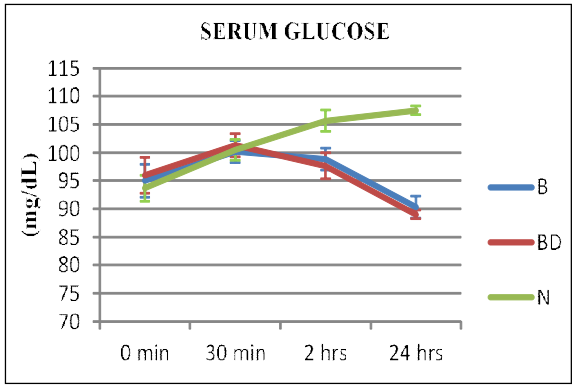


**Fig 8:** Serum glucose in Group B, BD and N.

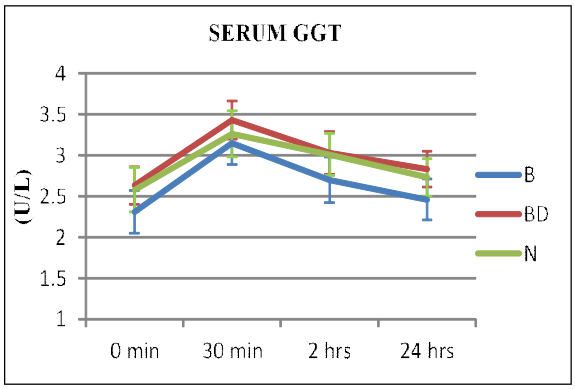


**Fig 9:** Serum GGT in Group B, BD and N.

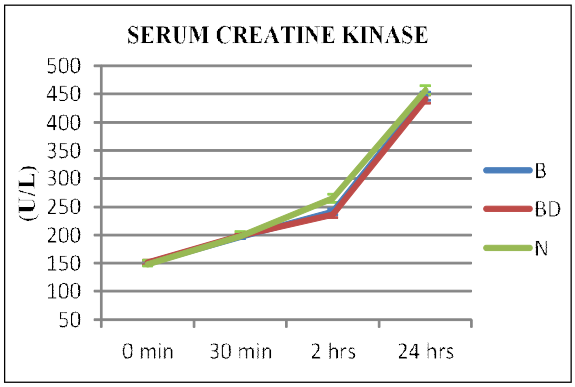


**Fig 10:** Serum creatine kinase in Group B, BD and N.

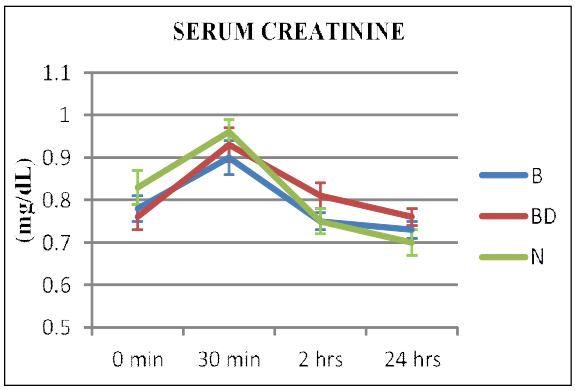


**Fig 11:** Serum creatinine in Group B, BD and N.

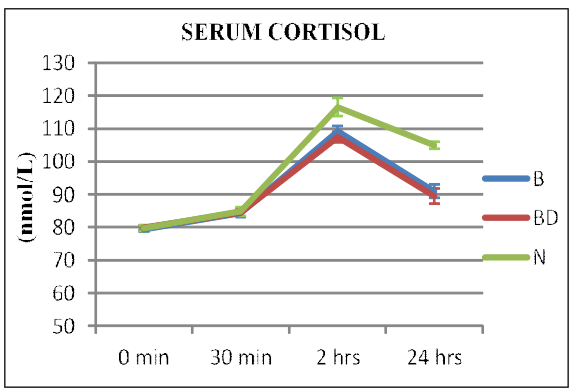


**Fig 12:** Serum cortisol in Group B, BD and N.

A significantly lower level of serum cortisol recorded in Group BD and Group B at 2 hrs and 24 hrs might be indicative of less pain perception or more pain suppression due the effects of bupivacaine and dexmedetomidine. Similar findings were also reported by Kim *et al.* (2012) and Farokhzad *et al.* (2021) with intraperitoneal lidocaine-tramadol, bupivacine and ropivacaine.

## CONCLUSION

In the present study the haematobiochemical changes following intraperitoneal bupivacaine and bupivacaine-dexmedetomidine combination in dogs were within physiological range. The administration of bupivacaine and dexmedetomidine combination reduces the serum glucose and cortisol level which might be indicative of a reduced amount of pain in this group than the other two groups.

### Conflict of interest

All authors declare that they have on conflict of interest.

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