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RESEARCH ARTICLE

Studies on Clinicophysiological and Haematobiochemical Evaluation of Bupivacine , Ropivacaine and Ropivacaine-Xylazine Combination as an Epidural Analgesic in Dogs.

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Abstract

The study was conducted on six apparently healthy dogs of either sex weighing between 10-15 kg. In treatmentI bupivacaine hydrochloride @ 2 mg/kg body. wt.,in treatment II ropivacaine hydrochloride @ 0.22 mg/kg body wt.and in treatment IIIropivacaine hydrochloride 0.5% @ 0.22 mg/kg and xylazine @ 0.75mg/kg was injected in the lumbosacral space. Clinico physiological parameters viz. rectal temperature (°F), pulse rate (per min) ,heart rate (per min) and Respiration rate, (per min) were recorded at 0, 20, 40, 60, 80, 120,180, 240 300, 360, 480 minutes.Haematobiochemical parameters viz. Hb, PCV, TEC, blood glucose, total protein, ALT, ALP, bilirubin, BUN and creatinine were studied in treatment I, II and III respectively. Quick onset and longer duration of analgesia duration was observed in treatment III due to some synergetic effect observed in treatment III as compared to treatment I and II. Also in treatment III there was significantly($P<0.05$) changes in haematobiochemical parameters.

Introduction

In dogs, general anaesthesia is generally used but in case of older, weak, toxaemic and debilitated animals, epidural analgesia is employed. Injection of anaesthetic within spinal canal but outside the duramatar is termed as epidural or extradural anaesthesia. Epidural analgeia is commonly employed to desensitize hind quarters in animals. The present study was planned to focus on clinicophysiologicaland haematobiochemical alterations due to the effect of drugs.

Material and Methods

The study was conducted on six apparently healthy dogs of either sex weighing between 10-15 kg. Each experimental animal was subjected to three treatments and each treatment lasted for three days at an interval of 8 days. In treatment I bupivacaine hydrochloride @ 2 mg/kg body.Wt, in treatment II Ropivacaine hydrochloride @ 0.22 mg/kg body and in treatment III ropivacaine hydrochloride @ 0.22 mg/kg and xylazine @ 0.75mg/kg simultaneously were injected in the lumbosacral space.The rectal temperature (°F), pulse rate (per min) and respiration rate, (per min) was recorded at 0, 20, 40, 60, 80, 120,180, 240 300, 360 and 480 minutes The "0" hrs values from each animal was recorded immediately before the start of the treatment, as the control value.The onset and duration of analgesia and recovery was determined by the pin prickmethod.Haematobiochemical parameters viz. Hb, PCV, TEC , TLC blood glucose, Total protein, ALT, ALP, bilirubin, BUN and creatinine were studied.5 ml of blood was collected from each animal from cephalic vein. About 2ml of blood was poured in a sterile vial containing anticoagulant (EDTA) @ 2mg/ml of blood for hematological studies. Remaining blood was collected in a centrifuge tube and was allowed for clotting .After clotting it was centrifuged @ 2500 rpm for 10 minutes and the serum was collected in sterile vials and kept at -20^0 C till biochemical estimation.Eight blood samples from each animal for each treatment was collected at 0 hrs.,15 min., 3 hrs., ,6hrs., 12 hrs., 24hrs., 36hrs.and 72 hours for haemato-biochemical studies.Statistical analysis was done as per method described by Snedecor and Cochran (1994).

Result and Discussion

1.Clinicophysiological Parameters:-

The onset of analgesia was 1.037 ± 0.02, 1.23 ± 0.02 and 0.87 ± 0.1 minutes in treatment I (Bupivacaine group),in treatment II (Ropivacaine group) and in reatment III (Ropivacaine – Xylazine group)respectively. The epidural administration of Bupivacaine,Ropivacaine and Ropivacaine-Xylazine induced analgesic effect which lasted for 128.83 ±3.64 , 135.83 ± 3.39 min and 202.50 ± 5.88 min in treatment I,II and III respectively.Results of the clinical studies showed that onset of analgesia was quick in group III, as compared to bupivacaine and ropivacaine group. The analgesic effect also lasted maximum in group III. Therefore, clinical studies revealed that ropivacaine–xylazinegroup was better than bupivacaine and Ropivacaine.Ropivacaine and xylazine group showed some synergistic effect and effect was better than other groups, same finding was observed by Duke *et al.* (2000).

Respiration Rate

The respiration rate showed a significant (P<0.05) decrease from its pre-treatment value in group I.The respiration rate showed did not differ significantly (P> 0.05) in treatment II. In treatment III, there was a significant (P<0.05) decrease in respiration rate from the control value and reached to its minimum value i.e. 20.66 ± 0.33 at 80 minutes after epidural administration of drugs. Thereafter values started increasing and reached to 31.33 ± 0.42 at 480 minutes.

Similar findings were observed by Kelawala*et al.* (1996), Kumar *et al.* (1975) who reported significant reduction in respiratory rate.Yayla and Kilic (2010) observed that non significantly decrease in respiration rate after administration of ropivacainein dogs.Adetunji*et al.* (2001) observed **that**there was a significant decrease in the respiratory rate upto 75 minutes after epidural administration of bupivacaine @ 2 mg/kg in dogs. Decrease in respiration rate in treatment I and III was observed which may due to depression of respiratory centre by these drugs (Lumb and Jones, 1984). There was no decrease in respiration in ropivacaine group suggestive of its superiority over other two groups.

Pulse Rate

In treatment I, there was a significant (P<0.05) increase in pulse rate after epidural administration of bupivacaine till 60 minutes where the maximum value was recorded. After 60 minute, there was decrease in pulse rate, at 480 minute, the value reached nearly to pre-treatment level.There were non significant alterations in pulse rate in treatment II while as in treatment III the values decreased significantly from 0 to 120 minute and there after value started increasing from 180 minute and reached to maximum at 480 minute pulse rate was observed.

Similar finding were also observed and correlated with Yayla and Kilic (2010).

Similar findings were observed by Hussain and Kumar (1989). Increase in the pulse rate in treatment I, might be due to stimulation of cardio-excitatory centers of the brain or stimulation sympathetic nervous system. Direct stimulation of the CNS as a result of struggling and excitement could be yet another factor responsible for significant increase in the pulse rate. (Short, 1987), Kennely and West (1967) suggested that the opioid has direct effect on sinoaterial and artioventricular conduction causing asystole leading to bradycardia. The central neural mediated mechanism might be primary mechanism of opioid, induced mild to severe bradycardia (Bailey *et al.* 1994) which might be the cause of reduction in pulse rate in treatment III.

Heart rate

In treatment I, there was a significant (P<0.05) increase in heart rate after epidural administration of bupivacaine till 60 minutes when the maximum value was recorded.At 480 minute, the value reached close to pre-treatment level. There was a non significant alteration in heart rate in group II. In group III, the values decreased significantly from 0 to 120 minute and there after value started increasing from 180 minute and reached to maximum at 480 minute.Kelawala*et al.* (1996) also observed decrease in heart rate after epidural administration of xylazine in diazepam premedicated dogs.

The central neural mediated mechanism might be primary mechanism of opioid, induced mild to severe bradycardia (Bailey *et al.*,1994) which might be the cause of reduction in pulse rate in treatment I and II.

Rectal Temperatures

After epidural administration of bupivacaine in treatment I, there was a significant (P<0.05) decrease in rectal temperature up to 80 minutes , there after the value started increasing and reached to maximum at 480 minutes , close to base value. In treatment II, there was non-significant (P>0.05) decrease in rectal temperature. In treatment III, there was a significant (P<0.05) decrease in rectal temperature from 0 to 120

minutes, there after rise in temperature was noticed and the value reached to pre treatment value at 480 minute.

Similar finding were stated by Kelawala*et al.* (1996) after epidural administration of xylazine, Ishiyama*et al.* (1997) observed a non significant decrease in rectal temperature after administration of ropivacaine in dogs.

In the present study the significant decrease in rectal temperature in treatment I and III, might be due to activation of alpha-2 agonists and hypothalamus alpha-receptor, inhibiting the heat conserving mechanism. Reduced metabolic rate and muscle activities might have been resulted in production of less heat in body and depression of thermoregulation resulted in hypothermia (Ponder and Clark, 1980).

2.Haematobiochemical Parameters:-

Haemoglobin Concentration

The haemoglobin concentration did not vary significantly (P>0.05) in treatment Iand II, however in treatment III, after epidural administration of drugs there was a significant (P<0.05) decrease in Hb concentration up to 6 hours, thereafter values started increasing, reaching close to control value at 72 hours.

The present findings of haemoglobin concentration are in accordance with finding of Kumar *et al*. (1997) who reported significant decrease in haemoglobin concentration after administration of xylazine in goats. Similar finding was also observed Fani*et al.* (2008) after administration of epidural administration of bupivacaine, xylazine and ketamine in dogs.

The reduction in Hb % after ropivacaine - xylazine administration might be due to shifting of fluid volume from extravascular compartment to intravascular compartment in order to maintain the normal cardiac output of pooling of circulation blood cells in the spleen or other reservoirs secondary to sympathetic tone (Pratap*et al.*, 2001).

Packed Cell Volume

The Packed cell volume did not vary significantly (P>0.05) in treatment I, II and III after epidural administration of drugs

Similar finding was also stated byFani*et al.* (2008) after administration of epidural administration of bupivacaine, xylazine and ketamine in dogs.

Total Erythrocyte Count

There was no significant change in total erythrocyte count (TEC) in treatment I, II and III. These findings are in accordance withRaghuvanshi, (2008) and (Lumb and Jones, 1984).

Blood Glucose

The blood glucose level was increased significantly (P<0.05) in all the treatmentgroups.Fani*et al.* (2008) showed a significantly increase in blood glucose level after epidural administration of bupivacaine in dogs.

Increase of glucose concentration, might be due to effects of stress induced secretion of cortical hormones from adrenal gland under ACTH. Secreted cortical hormones might have stimulated gluconeogenesis and also reduced consumption of glucose by cells, and both resulted in increased blood glucose concentration (Guyton and Hall, 2006).

Total Protein

There was no significant (P>0.05) variation in the values of total protein in any of the treatment groups.

Similar finding was observed by Raghuvanshi (2008).

The transiently increase in total protein values in the present study might have been due to effect of Xylazine on liver during biotransformation of drug which might have caused increase in total protein levels (Fayed *et al.*, 1989)

Alkaline Phosphatase

There was significant (P<0.05) increase in alkaline phosphatase level in treatment III. In treatment I and II , there was a non significant (P>0.05) increase in alkaline phosphatase level up to 6 hours after that values started decreasing significantly up to 72 hours. Vickers *et al.* (1984) reported that there is a possibility of transient liver damage during biotransformation of xylazine, which may be the cause of rise in ALP values in the present study.

Alanine Amino Transferase (ALT)

In treatment I and II, there was a non-significant (P>0.05) increase in ALTvalues.However in treatment III, there was significant (P<0.05) increase in ALT values up to 6 hours. Chang and Glazko (1974) indicated that the local anesthetic drugs are metabolised by the liver in most of the species and excreted in urine, during this there may be transient damage to liver, thus might be increase in ALT levels.

Total Bilirubin (mg/dl)

There was non significant (P>0.05) decrease in serum bilirubin value upto 6 hours in treatment I, and II However there was a significant (P<0.05) increase in serum bilirubin in treatment III. In the present study therefore, there is possibility that the metabolism of these in the liver might have caused some disruption in the liver parenchymal cells leading to non

significant increase in the serum bilirubin level (Chang and Glazko, 1974).

Blood Urea Nitrogen and Creatinine

In treatment I and II, there was non significant (P>0.05) increase in blood urea nitrogen values after epidural administration of Bupivacaine and Ropivacaine respectively. In treatment III, there was significant (P<0.05) increase in BUN values up to 24 hours.

There was significant (P<0.05) increase in serum creatinine values in treatment III. However, there was non significant increase (P>0.05) in serum creatinine values in treatment I and II up to 3 hours. The increase in creatinine and BUN may be attributed to the temporarily inhibitory effect of drugs on the renal blood flow, which in turn might have caused a rise in serum creatinine and BUN values (Wright, 1965). However, the possibility of renal damage could be ruled out because all the values were under normal physiological limits.

Conclusion

Duration of analgesia was longer in Ropivacaine – Xylazine (III) group as compared to Bupivacaine (I) and Ropivacaine (II) groups. Changes in clinical parameters like temperature, respiration rate and pulse were less significant in Ropivacaine group as compared to Bupivacaine group and Ropivacaine – Xylazine group. There was not much significant changes in haematological parameters in the same group. As for biochemical parameters were concerned except glucose all other parameters showed non significant increase in Ropivacaine group but the values were well within the normal physiological limits. Overall, it is concluded that all drugs used in three treatments produced good analgesia and were also good during surgical procedures and post operative pain alleivation which is most important demand of current research. However, Ropivacaine was better as far as its effects on clinico -physiological and haematobiochenical parameters were concerned. Most importantly, unlike other local **analgesics**, Ropivacaine has no clinically relevant effects on respiratory, cardiovascular, renal and hepatic parameters. So, it is useful in patients with poor cardiopulmonary function including elderly and obese patients with impaired renal and hepatic function.

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