Glasgow Composite Measure Pain Scale score and comaprison between several adjuvants in association with bupivacaine

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Abstract: Objective: To compare the analgesic and systemic effects during the post-operative period of epidural anesthesia performed with bupivacaine alone or with fentanyl, ketamine or dexmedetomidine in forty male mongrel dogs. **Material and Methods**: Dogs were randomly allocated into 4 groups (n=10) received bupivacaine (BG)1.5 mg/kg alone or in addition to ketamine HCL (BKG) 2mg/kg or fentanyl HCL (BFG) 2 µg / kg or dexmedetomidine (BDG) HCL 1.13 µg / kg according to randomization into the lumbosacral space. Systolic and Diastolic blood pressures were evaluated. Dogs were scored for analgesia using Glasgow Composite Measure Pain Scale score (CMPS – SF). **Results**: Systolic blood pressure showed significant decrease in BFG compared with the other treatment groups. Median (IQR) CMPS - SF scores for dogs in the BDG were significantly lower ($p < 0.05$) compared with dogs in the BKG, BFG or BG groups. **Conclusion and Clinical Relevance:** The results clarified that the dexmedetomidine added to bupivacaine was superior to the other adjuvants with sufficient analgesia last up to the first 24 hours post-operative.

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Key words: Glasgow Composite Measure Pain Scale score, bupivacaine, pain, dog.

1. Introduction

In animals, post operative pain is presumed to peak during the first 24 hours after surgey and this is the time period studied in most clinical trials ***(Slingsby et al., 2006)***. Post operative analgesia is of utmost importance because pain causes various deleterious effects that hinder the recovery of the patient ***(Hansen 2005)***. Among these harmful are negative protein balance, decreased food intake, release of stress hormones, possibility of self – mutilation, weight loss delayed healing of a surgical wound, immunosuppression, and increase in arterial blood pressure ***(Gaynor, 1999)***

The aim of the study was to evaluate The usefulness of different epidural regimens based on local anesthetic bupivacaine in association with various adjuvants ; opioids (Fentanyl), phencyclidine (ketamine) and α_2-agonist (dexmedetomidine) for assessment of analgesia. Our hypothesis Based on our previous knowledge about properties of dexmedetomidine that epidural bupivacaine - dexmedetomidine analgesia will be superior to bupivacaine-fentanyl, bupivacaine- ketamine or plain bupivacaine analgesia regarding the quality of postoperative analgesia and attenuation of inflammatory mediators release after different surgical procedures.

2. Material and methods

Material and Methods

Adult 20 healthy mongrel dogs were obtained from commercial supplier**,** they were individually housed in rod floored stainless steel cages with collection pans beneath each cage containing dust reduced wood shavings as beddings. The experimental animals were kept in a room under controlled environment.

II – Study Design

The selected dogs were randomly allocated into four groups of 10 dogs each. The randomization was carried out by a computer random generator number method according to the epidural medication regimen.

Control Group:

Had received bupivacaine at a dose of 1.5 mg/kg (Bucaine 0.5%, vial Weimar, German) + placebo.

Ketamine group:

Had received a combination of ketamine HCL at a dose of 2mg/kg and bupivacaine at a dose of 1.5 mg/kg.

Fentanyl Group:

Had received a combination of fentanyl HCL at a dose of 2 µg / kg and bupivacaine at a dose of 1.5 mg/kg.

Dexmedetomidine Group:

Had received a combination of dexmedetomidine HCL at a dose of 1.13 µg / kg and bupivacaine at a dose of 1.5 mg/kg.

On the day of the experiment, The dog was placed in sternal position, A 22 Gauge spinal needle was inserted. Once the needle is considered to be in the epidural space, it was carefully examined for the presence of clear cerebro-spinal fluid (CSF) or blood before injection. For all groups, the prepared drugs were administered epidurally within one minute with continous evaluation of any resistance during injection; dogs were maintained in sternal recumbency for 15 minutes to facilitate the uniform spread of the drugs.

Systolic and diastolic arterial blood pressures measured by use of an oscillometric indirect method with the appropriate-sized cuff placed above the elbow joint; were evaluated at different times: before administration of epidural drug, 15 minutes post administration, at end by 1,2,3,4 and 24 hrspost operative.

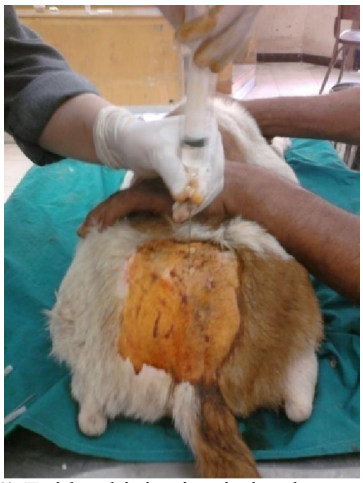

Fig (1) Epidural injection in lumbosacral space in dog

Analgesia was measured at 1,2,3,4,5,24 hoursafter epidural administration of B, BK, BF and BD by using Glasgow Composite Measure Pain Scale score (CMPS-SF) (Appendix I) provides a practical means of assessing acute post-operative pain and provides guidance with regard to analgesic requirement, so improving pain management and welfare. It comprises six behavioural categories with associated descriptive expressions (items): vocalisation (4), attention to wound (5), mobility (5), response to touch (6), demeanour (5) and posture/activity (5). Items are placed in increasing order of pain intensity and numbered accordingly. The observer chooses that item within each category which best describes the dog's behaviour and ranked scores are summed; the maximum pain score is 24. If the total score of CMPS - SF scale was higher than 6 rescue intervention analgesia will be needed ***(Reid et al., 2007)***.

Statistical analysis

Statistical analysis of the data was done by using Statistical Package for Social Science (SPSS) version 17.0. The data were analyzed for normality using Kolmogrov-Smirnov test. Data were represented as the mean ± SD for parametric data like Systolic blood pressure and Diastolic blood pressure. Also non-parametric data were represented as median (IQR) like Glasgow Composite Measure Pain Scale Score. For parametric data, comparisons were carried out by analysis of variance (ANOVA) with the least significance (LSD) post hoc analysis for inter group comparison while for non-parametric data, comparisons were carried out by Kruskal-Wallis H-test followed by Wilcoxon singed rank test for multiple comparison test. Repeated measures ANOVAs were used when data were collected in multiple trials of a single session, followed by the Fisher LSD test. Significance was considered when P value < 0.05.

3. Result:

For blood pressure, between groups, At T15, SAP in BFG was significantly decreased compared with BKG and BDG, for DAP in BG and BFG was significantly decreased than BDG. For analgesia, according to CMPS, a decrease in all groups was observed during the postoperative period and the BDG had significantly lower values than those observed in the B, BK and BF.

4. Discussion:

Results of the present study indicated that: Associated hypotension in dexmedetomidine - bupivacaine, fentanyl - bupivacaine or bupivacaine groups owing to α_2 - adrenoreceptors agonist ***(Venn et al., 2001***), opioid element ***(Trescot et al., 2008)*** or rostral spread of the anesthetics.

The pain score assessed using CMPS which is one of the recommended pain scale that has been validated for the assessment of acute pain in dogs ***(Holton et al., 2001)***, it was shown to be a reliable clinical tool to define different pain intensities and change in pain score over time in a population of dogs undergoing a variety of surgical procedures ***(Murrell et al., 2008).***

Appendix I (CMPS-SF)

SHORT FORM OF THE GLASGOW COMPOSITE PAIN SCALE

Dog's name _____

Hospital Number _____ **Date** / / **Time**

Surgery Yes/No (delete as appropriate)

Procedure or Condition_____

_____

In the sections below please circle the appropriate score in each list and sum these to give the total score.

A. Look at dog in Kennel

Is the dog?

(i)		(ii)	
Quiet	0	Ignoring any wound or painful area	0
Crying or whimpering	1	Looking at wound or painful area	1
Groaning	2	Licking wound or painful area	2
Screaming	3	Rubbing wound or painful area	3
		Chewing wound or painful area	4

In the case of spinal, pelvic or multiple limb fractures, or where assistance is required to aid locomotion do not carry out section **B** and proceed to **C**
Please tick if this is the case ☐ then proceed to C.

B. Put lead on dog and lead out of the kennel.

When the dog rises/walks is it?

(iii)	
Normal	0
Lame	1
Slow or reluctant	2
Stiff	3
It refuses to move	4

C. If it has a wound or painful area including abdomen, apply gentle pressure 2 inches round the site.

Does it?

(iv)	
Do nothing	0
Look round	1
Flinch	2
Growl or guard area	3
Snap	4
Cry	5

D. Overall

Is the dog? (v)		*Is the dog?* (vi)	
Happy and content or happy and bouncy	0	Comfortable	0
Quiet	1	Unsettled	1
Indifferent or non-responsive to surroundings	2	Restless	2
Nervous or anxious or fearful	3	Hunched or tense	3
Depressed or non-responsive to stimulation	4	Rigid	4

Total Score (i+ii+iii+iv+v+vi) = _____

Table (7) CMPS analgesia score in mongrel dogs that received an epidural injection of bupivacaine, bupivacaine - ketmine, bupivacaine - fentanyl and bupivacaine -dexmedetomidine groups.

CMPS	B – **group (n=10)**	BK – **group (n=10)**	BF – **group (n=10)**	BD – **group (n=10)**
T1hr	1 (0.0-2.0)	0 (0.0-0.0) $	0 (0.0-0.0) $	0 (0.0-0.0) $
T2hrs	3 (2.0-4.0) *	0 (0.0-0.0) $	1 (0.0-2.0) *$#	0 (0.0-0.0) $†
T3hrs	5 (2.0-9.0) *	1 (1.0-2.0) *$	4 (2.0-6.0) *#	0 (0.0-0.0) $#†
T4hrs	8 (5.0-10.0) *	2 (1.0-3.0) *$	5 (2.0-7.0) *$#	0 (0.0-0.0) $#†
T5hrs	9 (7.0-12.0) *	2 (1.0-3.0) *$	8 (5.0-11.0) *#	0 (0.0-0.0) $#†
T24hrs	11 (9.0-13.0) *	8 (5.0-10.0) *$	10 (7.0-14.0) *	0 (0.0-0.0) $#†

* significant when compared with basal value (P < 0.05); $ significant when compared with Bupivacaine group (P < 0.05), # significant when compared with Bupivacaine- Ketamine group (P < 0.05), † significant when compared with Bupivacaine – Fentanyl group (P < 0.05). Values are median (IQR).

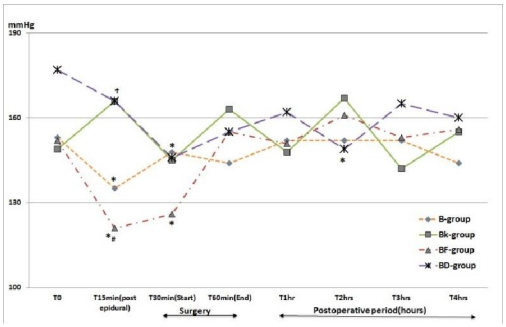

Figure (5) Systolic blood pressure changes in mongrel dogs that received an epidural injection of Bupivacaine (B), Bupivacaine - ketamine (BK), Bupivacaine – Fentanyl (BF) and Bupivacaine – Dexmedetomidine (BD) groups. * significant when compared with basal value (P < 0.05); $ significant when compared with Bupivacaine group (P < 0.05), # significant when compared with Bupivacaine- Ketamine group (P < 0.05), † significant when compared with Bupivacaine – Fentanyl group (P < 0.05). Values are mean ± SD.

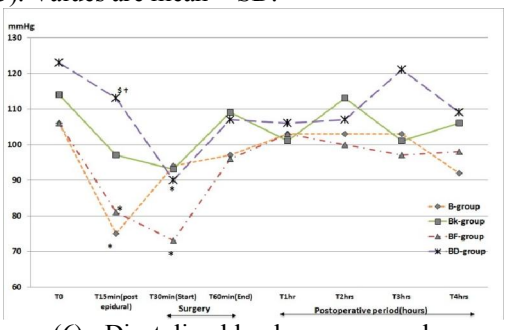

Figure (6) Diastolic blood pressure changes in mongrel dogs that received an epidural injection of Bupivacaine (B), Bupivacaine - ketamine (BK), Bupivacaine – Fentanyl (BF) and Bupivacaine – Dexmedetomidine (BD) groups. * significant when compared with basal value (P < 0.05); $ significant when compared with Bupivacaine group (P < 0.05), # significant when compared with Bupivacaine- Ketamine group (P < 0.05), † significant when compared with Bupivacaine – Fentanyl group (P < 0.05). Values are mean ± SD.

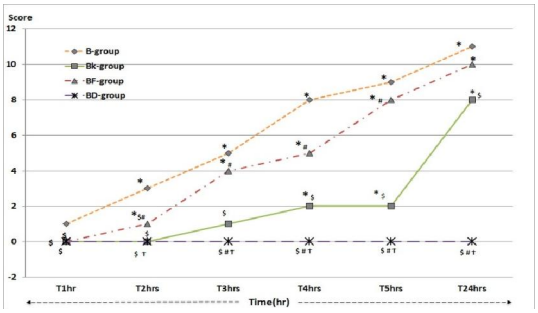

Figure (11) Glasgow Composite Measure Pain Scale Score (CMPS) for postoperative pain assessment in mongrel dogs that received an epidural injection of Bupivacaine (B), Bupivacaine – ketamine (BK), Bupivacaine – Fentanyl (BF) and Bupivacaine – Dexmedetomidine (BD) groups. * significant when compared with basal value (P < 0.05); $ significant when compared with Bupivacaine group (P < 0.05), # significant when compared with Bupivacaine- Ketamine group (P < 0.05), † significant when compared with Bupivacaine – Fentanyl group (P < 0.05). Values are median.

In the present study, dogs in the dexmedetomidine - bupivacaine group had significantly the lower pain scores according to the CMPS compared with dogs in the bupivacaine, fentanyl - bupivacaine or ketamine - bupivacaine. Dogs in the bupivacaine group were the earlier in expressing acute signs of pain 2 hrs post operative post epidural administration followed by dogs in fentanyl - bupivacaine group they expressed acute signs of pain 4 hrs post operative on contrast with ketamine - bupivacaine which had high pain scores 24 hrs post operative.

The result belong to dexmedetomidine - bupivacaine owing to α_2-adrenergic and opioidergic systems have common effect or mechanisms in the locus coeruleus, representing a supraspinal site of action. In the spinal cord, their analgesic effect is related to activation of the descending medullospinal noradrenergic pathways or to the reduction of spinal

sympathetic outflow at presynaptic ganglionic sites ***(Arian et al., 2004)***.

As for the ketamine - bupivacaine group, which showed high pain scores in the first 24 hrs post epidural administration assessment, ***Rai et al., 2007*** described ketamine as a potent analgesic, ketamine is unique in that it has a comparatively and markedly smaller risk of respiratory depression than a similar analgesia produced by a narcotic.

Ketamine has analgesic properties that are mediated by a number of mechanisms. NMDA receptor noncompetitive antagonism accounts for most of its analgesic effects through a use-dependent channel blockade. The affinity of ketamine for NMDA receptors is several-fold higher than that for μ receptors, non-NMDA glutamate receptors, nicotinic and muscarinic cholinergic receptors, and monoaminergic transporter sites ***(Colin et al., 2004)***.

In contrast to this study, a study were performed by ***Cook et al.,(1995)*** comparing the effects of adrenaline, clonidine and ketamine on the duration of caudal analgesia in adjuvant with bupivacaine in children concluded that ketamine produced longer duration of analgesia compared to clonidine and adrenaline.A meta-analysis of 18 trials by ***Curatalo et al (2008)*** comparing epidural fentanyl, adrenaline and clonidine as adjuvants to local anaesthetics concluded that addition of fentanyl decreased the incidence of pain quantitatively during surgery and is a safe.

At the end of this study we conclude that dexmedetomidine in a dose of 1.13μg/kg added to bupivacaine for epidural anesthesia in dogs undergoing surgery, significantly prolongs the duration of post-operative analgesia when compared to 0.6 ml/kg of bupivacaine with ketamine 2 mg/kg or 0.6ml/kg of bupivacaine with fentanyl 2μg/kg or 0.6ml/kg bupivacaine alone without side effects.

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8/21/2013

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