Indian Journal of Animal Sciences **84** (9): 944–948, September 2014/Article

Ketamine and its combination with pentazocine and meperidine for epidural anaesthesia in dogs

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Received: 23 March 2014; Accepted: 12 May 2014

ABSTRACT

Clinically healthy dogs (15) of either sex aged about 1 year were randomly grouped into 3 with 5 dogs each to study the effect of epidural administration of ketamine alone and in combination with pentazocine and meperidine on clinic – anaesthetic profile in dogs. Ketamine hydrochloride @3 mg/kg b.wt and ketamine @3mg/kg b.wt in combination with pentazocine lactate @ 0.3 mg/kg b.wt and ketamine @ 3mg/kg b.wt in combination with meperidine @ 1mg/kg b.wt were administered epidurally in animals of group 1, 2 and 3, respectively. Marked alteration in rectal temperature, heart rate and respiration rate were recorded at initial intervals of observations in all the groups, however, these values returned towards normalcy by the end of 120 min of observation. Quicker onset of analgesia was recorded in group 2 (3.68±0.22 min) followed by group 3 (3.88±0.17 min) and group 1 (4.08±0.33 min). The duration of analgesia, standing time and recovery time were significantly longer in group 2 and 3 as compared to group 1. None of the groups showed significant variation in duration of recumbency. The treated animals manifested minimum, transient and occasional untoward reactions. It is concluded that pentazocine and meperidine can be given epidurally in combination with ketamine for effective analgesia in dogs.

Key words: Clinico- anaesthetic changes, Dog, Ketamine, Meperidine, Pentazocine

Geriatric patient is not supposed to be the ideal subject for undergoing general anaesthesia due to the complications that may occur frequently during anaesthesia. These complications may include respiratory arrest, hypoxia, hypercarbia, hypotension that may be the result of congestive heart failure, bradycardia, cardiac arrhythmias, over depression of CNS, and fluid imbalance as well as prolonged recovery. The most frequently used epidural anaesthetic is lignocaine which has excellent diffusion and penetrability, and produces rapid onset and establishment of surgical anaesthesia, but it does not produce prolonged sensory and motor blockade. Therefore, it is not a satisfactory agent for single dose technique for long duration surgical procedure (Adetunji *et al*. 2001). Epidural administration of opioids drugs, a relatively new technique, is used to provide intra and post-operative analgesia (Jones 2001).

The available literature suggested that only sporadic research work has been conducted on the epidural use of meperidine in mare (Roman and William 2001, Rafael *et al.* 2004). The present paper deals with the effect of epidural administration of ketamine alone and in combination with pentazocine and meperidine on clinic – anaesthetic profile in dogs.

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MATERIALS AND METHODS

The experimental study was conducted on 15 clinically healthy mongrel dogs of either sex of about 1 year of age and were randomly divided into 3 groups of 5 dogs each. The dogs were maintained in same management condition in the indoor ward of Ranchi Veterinary College clinics and were kept off- feed and withheld water for 12 and 6 h, respectively, before the commencement of experiment.

Lumbo-sacral region was prepared aseptically and ketamine hydrochloride @ 3 mg/kg b.wt and in combination with pentazocine lactate @ 0.3 mg/kg b.wt and meperidine hydrochloride @ 1 mg/kg b.wt were administered epidurally in groups 1, 2 and 3, respectively. Treated dog was supported in sternal recumbency for at least 2 min following drug injection to ensure a bilateral blockade. The dog was placed at an isolated corner without disturbance to monitor the development and progression of analgesia sequentially.

Rectal temperature (RT), respiration rate (RR) and heart rate (HR) were recorded before and at the time interval of 5, 15, 30, 60, and 120 min following epidural administration of analgesic agents.

Onset of analgesia, duration of analgesia, standing time and recovery time and time of recumbency were noted in

each treated dog on the basis of physical symptoms and reflexes.

The analgesia was scored using a 0–3 numerical rating scale to pin prick response as:

0 - No analgesia, 1 - Mild, 2 – Moderate, 3- Excellent.

Sedation was judged by observing drowsiness and lowering of head and scored using a

0–3 numerical rating scale: 0 - Fully alert, 1- Alert but unable to walk, 2 - Drowsy and unable to stand, 3 - Heavily sedated/asleep.

The data of findings were statistically analysed by one-way analysis of variance (ANOVA) as per Snedecor and Cochran (1994).

RESULTS AND DISCUSSION

The rectal temperature in group 1 showed an increasing trend up to 30 min of observation followed by a decreasing trend to reach to the pre injection level. The value recorded at 15 and 30 min of observation was significantly higher ($P<0.05$) as compared to its base value (Table 1). Ketamine causes tonic and clonic convulsion of limb muscles (Hall and Clark 1991) which might be responsible for increase of temperature at initial intervals of observation in group 1 animals, which is in accordance with the findings of Aithal *et al.*(1998). The animals of groups 2 and 3 manifested a nonsignificant fall in rectal temperature throughout the observation period concurrent with the findings of Amarpal *et al.* (1998) and Atalan *et al.* (2002).

The respiratory frequency in group 1 showed a significant tachypnoea up to 60 min as compared to its base value which simulates with the findings of Amarpal *et al.* (1998). The tachypnoea observed in the present case might be attributed to stimulatory action on the respiratory centre causing increase in respiration rate. The increase in respiration rate might also be due to its rapid absorption and systemic distribution (Aithal *et al.* 1998). The values recorded at 5 and 15 min in group 1 were significantly higher as compared to the corresponding values in groups 2 and 3 (Table 1). Fall in respiration rate in groups 2 and 3 might be ascribed to synergistic respiratory depressant activity of opioids and ketamine. Kappa-opioid agonists are less likely to induce respiratory depression as compared with μ-opioid (meperidine and pentazocine) agonists (Hall and Clark 1991, Pascoe 2000). The opioids follow the slow passive circulation of CSF in the spinal subarachnoid space over 4–6 h interval to reach the cisterns of the brain and then reach the respiratory centre via the ventral pons. Opioid travelling cephalad in CSF may also stream against the rapid and active intracranial CSF circulation to gain retrograde access to the lower ventricle with subsequent rapid access to respiratory centre. A nonsignificant change was reported in horse treated with epidural meperidine (De Rossi *et al.* 2004).

The animals of all the groups showed an increased heart rate during the initial phase of observation post- injection and the maximum increase could be recorded at 5 min (Table 1). The values recorded at 5 and 15 min of observations were significantly higher ($P<0.05$) as compared to their base value in all the groups. This increase in heart rate might be a sequel to rapid absorption and systemic distribution of drugs from epidural space. A significant increase in heart rate was also reported after epidural administration of ketamine (Aithal *et al*. 1998) and ketamine-pethidine (Amarpal *et al.* 1998) in dogs. Increase in heart rate in meperidine group might be due to its atropine like action (Kumar *et al*. 1988). Bradycardia occurring following opioids administration was compensated and antagonized by epidural administration of ketamine causing tachycardia (Sharma *et al*. 2005). A major feature that distinguishes ketamine from other intravenous anaesthetics is stimulation of the cardio vascular system (Reich and Silvay 1989). Ketamine increases arterial pressure, heart rate and cardiac output in a man after intravenous infusion (Idvall *et al*. 1979).

Heart rate and blood pressure did not change significantly in dogs treated with ketamine and midazolam or diazepam combination (Hellyer *et al*. 1991) and in horse treated with epidural meperidine (De Rossi *et al.* 2004).

Sedation was absent throughout the observation period in group 1 animals which is similar to the finding of Aithal

Table 1. Mean ± SE values of rectal temperature (ºF), respiration rate (no. / min) and heart rate (beats / min) in the animals of different groups before and after epidural administration

Parameters	Groups	Observation period (min)					
		0	5	15	30	60	120
RT	1	101.50 ± 0.40^{aA}	102.20 ± 0.33^{acA}	103.40 ± 0.54^{bcA}	104.00 ± 0.49^{bcA}	102.16 ± 0.34^{aA}	102.10 ± 0.57^{aA}
	2	101.40 ± 0.61^{aA}	100.80 ± 0.72^{aA}	100.74 ± 0.97^{aA}	100.60 ± 0.46^{aA}	100.40 ± 0.54^{aA}	100.20 ± 1.00^{aA}
	3	100.48 ± 0.56^{aA}	101.20 ± 0.59^{aA}	101.00 ± 0.49^{aA}	100.80 ± 0.18^{aA}	100.60 ± 0.22^{aA}	100.40 ± 0.61^{aA}
RR	1	20.40 ± 0.73^{aA}	24.80 ± 0.66^{bA}	25.40 ± 0.78^{bA}	24.80 ± 0.9^{bA}	23.60 ± 0.83^{bA}	23.00 ± 1.23^{aA}
	2	22.60 ± 1.28^{aA}	18.40 ± 0.36^{bA}	17.40 ± 0.83^{bA}	21.80 ± 1.18^{aA}	22.20 ± 0.9^{aA}	22.60 ± 0.46^{aA}
	3	22.00 ± 0.57^{aA}	18.20 ± 0.33^{bA}	17.80 ± 0.33^{bA}	20.80 ± 0.52^{aA}	21.60 ± 0.73^{aA}	21.80 ± 0.66^{aA}
HR	1	92.40 ± 1.46^{aA}	100.80 ± 0.77^{bA}	101.20 ± 0.91^{bA}	100.40 ± 0.83^{bA}	94.00 ± 1.17^{aA}	93.40 ± 4.09^{aA}
	2	92.00 ± 3.01^{aA}	100.40 ± 0.46^{bA}	101.00 ± 0.40^{bA}	95.20 ± 0.87^{aA}	94.60 ± 1.08^{aA}	93.40 ± 1.61^{aA}
	3	92.40 ± 1.08^{aA}	101.80 ± 0.95^{bA}	102.20 ± 1.04^{bA}	95.80 ± 0.72^{cA}	95.00 ± 0.85^{acA}	94.00 ± 1.17^{acA}

Group 1, ketamine alone; group 2, pentazocine lactate; group 3, meperidine (pethidine). Values bearing similar superscript in a row with small letters and capital letters in a column did not differ significantly ($P>0.05$).

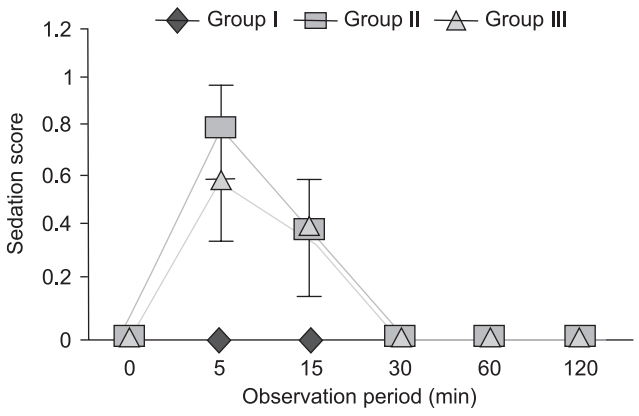

Fig. 1. Sedation after epidural administration in all the groups

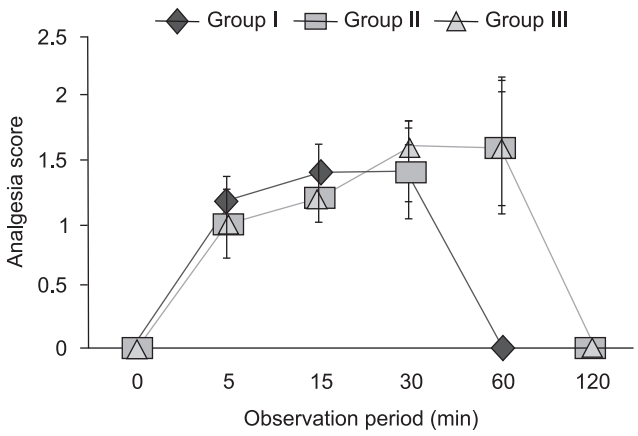

Fig. 2. Analgesia after epidural administration in all the groups

et al. (1999). The maximum sedation could be recorded at 5 min in group 2 (0.80 ± 0.18 min) followed by group 3 (0.60 ± 0.22 min) (Fig.1). The level of sedation gradually decreased in groups 2 and 3 at 15 min post induction and on the subsequent periods of observation. Sedation was not appreciable in any group which simulates, with the findings of Amarpal *et al*. (1998).

Analgesia and anaesthetic indices

In group 1, analgesia was noticed at 5 min which progressed up to 30 min, whereas, in group 2 and 3 the analgesia persisted up to 60 min of observation (Fig. 2). Evidence of analgesia was absent in all the groups by 120 min of observation. The onset of analgesia was noticed with a faster rate in group 2 (3.68 ± 0.22 min) as compared to group 3 (3.88 ± 0.17 min) and group 1 (4.08 ± 0.33 min). The duration of analgesia was maximum in group 2 (24. 40± 0.36 min) as compared to group 3 (24.00 ± 0.40 min) and 1 (21.40 ± 1.15 min) (Table 2), which is in contrast with the findings of DeRossi *et al.* (2004). The duration of analgesia after intrathecal and epidural administration of opioids is dependent upon the agent and its lipophilicity as well as the size of the dose employed (Cousins and Mather 1984). Time of standing was longer in group 2 followed by group 3 and 1. The mean time of standing recorded in group 2 and 3 were significantly higher (P< 0.05) as compared to group 1.

Table 2. Mean ± SE values of anaesthetic indices in the animals of different groups after epidural administration

Anaesthetic parameters	Groups		
	1	2	3
Onset of analgesia (min)	4.08±0.33[a]	3.68±0.22[a]	3.88±0.17[a]
Duration of analgesia (min)	21.40±1.15[a]	24.40±0.36[c]	24.00±0.40[c]
Standing time (min)	23.00±0.75[a]	26.00±1.06[c]	24.60±0.73[c]
Recovery time (min)	31.20±0.91[a]	35.80±2.11[a]	33.40±0.96[a]
Time of recumbency (min)	2.08±0.33[a]	1.68±0.22[a]	1.88±0.17[a]

Values bearing similar superscript in a row with small letters did not differ significantly (P>0.05).

The recovery time was maximum in group 2 followed by group 3 and group 1, which did not vary significantly among themselves. The duration of recumbency did not exhibit any significant variation among the treated groups. However, the maximum recumbency period could be noticed in group 1 and the minimum in group 2. Time to sternal recumbency and time to standing were nonsignificant.

The analgesic properties of ketamine appear to be mediated by action on a number of receptor systems. Ketamine will bind stereospecifically to opioid receptors (Husteveit *et al.* 1995, Forman 1999) as well as cholinergic receptors (muscarinic and nicotinic) (Husteveit *et al.* 1995). Additionally, ketamine may activate the monoaminergic descending inhibitory system (Crisp *et al.* 1991) and produce local anaesthetic effects by blockade of sodium channels (Yaksh 1996). Reduction in post incisional hyperalgesia could be observed for longer time in epidural administration of ketamine (Duque *et al.* 2004). Spinal opiates can alter both the processes by reducing the pre-terminal release of neurotransmitters and hyperpolarizing the post terminal second order neurons (Yaksh 1993). Opioids are the most potent and effective analgesics available and are accepted as appropriate treatment for acute and chronic pain (Collet 2001). N-methyl-D-aspartate (NMDA) receptor activation is essential for central facilitation after nociceptive stimulation and is a key factor in the generation and maintenance of persistent pain stress. Spinal NMDA antagonists might alter post operation pain by removing the facilitatory component (Dickenson 1994). Epidural ketamine alone may be insufficient for adequately reducing the pain state by removing the central facilitation alone (Wong *et al*. 1996). Opioids and ketamine combination can antagonize these 2 distinct components and provide adequate control of post operative pain. Spinal potentiation of opiate receptor activity by NMDA antagonism was reported (Chapman and Dickenson 1992, Sethi *et al.* 2011). Amarpal *et al.* (2003) also used ketamine and pethidine epidurally in dogs and confirmed synergistic

interaction in increasing analgesia.

Untoward reactions like excessive salivation were common in all the groups but more prominent in group 1 followed by groups 2 and 3. Other unwanted side effect like defecation (1) and panting (1) were observed in 40% animals of group 3. Opioids administration often stimulates dogs and less frequently cats to defecate (Thurmon *et al.* 1996). The shivering was common in group 3 followed by group 2 which might be due to depression of hypothalamus producing hypothermia. A variable degree of hallucination was observed in almost all the groups. Ketamine induced depression of the inferior colliculus and medial geniculate nucleus leading to misperception of auditory and visual stimuli, which may be responsible for the reaction (White *et al.* 1982). Chaney (1995) reported 4 side effects like pruritis, nausea, vomiting, urinary retention and respiratory depression after epidural opioids. But in present study untoward reaction were occasionally noticed in all the groups. It is concluded that pentazocine and meperidine can be given epidurally in combination with ketamine for effective analgesia in dogs.

ACKNOWLEDGEMENTS

We thank the Dean of college and Head of the Department for providing requisite facilities to carry out the work.

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