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Comparison of xylazine and dexmedetomidine as a premedicant for general anaesthesia in dogs

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ABSTRACT

Adult dogs (32) of either sex, divided into 2 groups were used for evaluation of anesthetic efficacy of xylazine (1mg/kg IV) and dexmedetomidine (375µg/m^2 IV) in atropine-butorphanol premedicated and ketamine (till effect IV) induced dogs which were further maintained on halothane. Clinical parameters and reflexes (induction dose, intubation time, jaw relaxation, pedal, palpebral and photo-pupillary) were measured at baseline (pre-operative), just after induction and at 5, 15, 30 and 45 min after the start of halothane. Similarly, haemato-biochemical parameters were measured at baseline (pre-operative), intraoperative and postoperative phase along with recovery parameters. On comparative basis, induction dose of ketamine was 3.7 and 2.9 mg/kg body weight and intubation time 81.29±6.22 and 45.87±3.95 sec in group BXK and BDK groups respectively. Uniform and pronounced muscle relaxation along with excellent sedation was found in both the groups. All haemato-biochemical parameters remained within normal range except hyperglycaemia was observed during late phase in both groups. Mean vaporizer concentration of halothane was 2 and 1.26% in BXK and BDK group respectively. Following discontinuation of the halothane, all the recovery times of BDK group took significantly lesser time than group BXK along with superior quality of recovery.

Key words: Dexmedetomidine, Dogs, Haemato-biochemical, Induction, Recovery, Xylazine

Veterinary anesthesia is an ever-changing and advancing science. Periodically re-evaluating anesthesia choices, methods and monitoring techniques is important for every veterinary practice. Good quality anesthesia consists of — good muscle relaxation, adequate analgesia and sedation along with smooth induction and safer recovery (Fleknell 2009). Alpha 2-adrenoceptor agonists may provide an attractive alternative to anesthetic adjunctive agents now in use because of their anesthetic-sparing and hemodynamic-stabilizing effects (Gertler *et al*. 2001). Currently, xylazine and medetomidine are used at relatively low doses, alone or in combination with other drugs (benzodiazepines, opioids), to induce sedation for minor diagnostic and surgical procedures, and as adjuncts to injectable (ketamine, thiopental, propofol) and inhalational (halothane, isoflurane) anesthetics (Lemke 2004). The drugs with greater degree of the selectivity towards alpha α-2 receptors, show less undesirable neurological effects (Virtanen *et al.* 1988, Ko *et al.* 1997) while undertaking any anesthetic maneuver. Schwartz and Clarke (1998) reported that medetomidine showed about 100 times stronger affinity for all α-2 subtype receptors than xylazine and (Kuusela *et al.* 2001) dexmedetomidine is at least as safe and effective as medetomidine for use as a premedicant in dogs. The purpose of this study is to revisit and compare the earlier and latest alpha-2 agonist in combinations with other adjuncts to have a safe clinical anesthesia on the basis of induction, haemato-biochemical and recovery parameters in dogs.

MATERIALS AND METHODS

Client owned 32 adult dogs of either sex, were divided into 2 groups having 17 animals in BXK group and 15 animals in group BDK. Animals of BXK group received xylazine (1mg/kg I/V) while the animals of group BDK received dexmedetomidine (375µg/m^2 I/V) as premedicant after administration of atropine (0.04mg/kg S/C) and butorphanol (0.2mg/kg I/M). Anaesthesia was induced by ketamine (till effect I/V) and maintained with halothane. Various surgical procedures during the test anesthetic regimens are listed in Table 1.

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Table 1. Surgical procedures performed under BXK or BDK anesthesia in dogs

Surgical procedures	No of cases	BXK group	BDK group
Elective surgery	15	7	8
Fractures	6	5	1
Canine pyometra complex	4	1	3
Tumors	4	3	1
Scrotal ablation	2	1	1
Dental scaling	1	——	1
Duration of surgery	39–43 min	Duration of anesthesia	45.0 min

Various reflexes were assessed on the basis of scoring system shown in Table 2.

Blood (0.5 ml and 5ml) was collected from the cephalic vein of each animal containing 3% EDTA and heparin respectively at baseline, intra operative and post operative period. The haemato-biochemical parameters viz. haemoglobin, packed cell volume, total erythrocyte count, glucose, aspartate aminotransferase, alanine aminotransferase, blood urea nitrogen, creatinine, total protein and alkaline phosphatase were estimated using commercially available kits on RA-50 blood chemistry analyzer while sodium, potassium and chloride were estimated on photometer. The mean vaporizer concentration of the halothane on co-axial re-breathing system circuit was recorded following induction. Following discontinuation of the halothane, the various recovery parameters like time to extubation, head raise reflex, sternal and standing time were measured along with quality of recovery on the basis of scoring system shown in Table 3.

SAS(r) 9.2 TS Level 2M2 was used for data analysis. Paired t test by ANOVA (Fisher's test/Cochran's test) was used for within group comparison from base line value and Simple t-test by ANOVA for between group comparison. All non-parametric data were analysed using Exact Wilcoxon 2 sample test.

The mean induction dose of ketamine utilized to facilitate intubation in BXK group was 3.7 mg.kg b.wt I/V, whereas in group BDK it was 2.9 mg/kg b.wt I/V. The animals of BXK group took 81.29±6.22 sec to allow intubation whereas the animals of group BDK, needed 45.87±3.95 sec, which was significantly ($P<0.01$) lesser than that of BXK group. The administration of xylazine and dexmedetomidine along with opioids has shown to markedly reduce the induction dose of ketamine by 30 to 61% (Amend *et al.* 1972, Dexdomitor NADA 2006).

Jaw relaxation and pedal reflex: Relaxation of the jaw and the status of the pedal reflex were recorded as a measure of muscle relaxation and depth of analgesia respectively. In group BXK, highest score of 3 was attained at 5 min after halothane starts which lasted up to 15 min, thereafter it decreases gradually while in BDK group, highest score of 3 was attained post-induction which remained constant throughout the study. All alpha-2 agonists, including dexmedetomidine are known to produce good muscle relaxation (Lemke 2004) which is attributed to inhibition of

Table 2. The subjective observations of various reflexes assessed on the basis of scoring system (Ahmad *et al.* 2011)

Score/Reflex	0	1	2	3
Jaw relaxation	Not allowing to open the jaws	Resistant to opening the jaws and closed quickly	Less resistance to opening the jaws and closed slowly	No resistance and jaw remained open
Pedal reflex	Intact and strong reflex (strong withdrawal)	Intact but weak reflex (animal responding slowly)	Intact but very light reflex (slow and occasional)	Reflex abolished completely
Palpebral reflex	Intact and strong reflex (quick blink)	Intact but weak reflex (slow response)	Very weak reflex (very slow and occasional)	Reflex abolished completely
Photo pupillary reflex	Constriction of dilated pupil in response to increase in light intensity	Mild constriction of dilated pupil in response to increase in light intensity	Moderate constriction of dilated pupil in response to increase in light intensity	Reflex abolished completely

Table 3. Quality of recovery, assessed on the basis of scoring system

Quality of recovery		
4	Excellent	No ataxia, no struggling, standing as it is fully conscious
3	Good	Slight ataxia or struggling but no serious instability
2	Fair	Some staggering and ataxia, few unsuccessful attempts to stand, ataxia on standing
1	Bad2	Excitement and paddling when recumbent, severe ataxia on standing
0	Bad1	Excited when recumbent, persistent unsuccessful attempts to stand, severe ataxia, falling when standing, aimless walking

intraneuronal transmission of impulses by alpha-2 agonists at the level of CNS (Marjorie 2001) while analgesic action of xylazine might be due to stimulating central presynaptic alpha-2 adrenoceptors which inhibits norepinephrine release from adrenergic nerve terminals (Hsu 1981) whereas analgesic effect by dexmedetomidine is mediated at spinal level and by interruption of nociceptive pathways to the ventral root of the dorsal horn which reduce spinal reflexes (Kending *et al*. 1991). Ahmad *et al.* (2013) and Santosh *et al.* 2012 also stated that dexmedetomidine produced excellent sedation in dogs.

Ocular reflexes: Palpebral reflex score reached 2.0 and 2.20 at 5 min in BXK and BDK group respectively which further depressed to 2.53 and 2.73 at 15 min and was completely depressed with highest score of 3 at 30 min in both the groups which remained constant till the end of the study. Quick and profound sedation which is statically non-significant was produced by xylazine in comparison to dexmedetomidine as shown by photo-pupillary reflex score. Selmi *et al*. (2003) proved that dexmedetomidine or xylazine were very effective sedative-analgesic adjuncts when co-administered with opioid agonists or dissociative.

Haematological-biochemical parameters: In BXK group, only Hb and PCV were significantly low during post-operative phase when compared to the base line values while all haematological parameters remained unchanged in group BDK. The majority of the patients in BXK group were of ASA category-III involving orthopaedic and tumor excision procedures in which the blood loss is more than BDK group in which most of the numbers of surgeries are elective types of surgery. The other reason might be vasodilation at the level of microcirculation and passage of many RBC's from circulation causing decrease in haemoglobin level measured in peripheral veins which is also called as plasma skimming (Naghibi *et al*. 2002).

Glucose: In both groups, significant (P<0.01) increase in blood glucose was recorded during inta-operative and post-operative as compared to their respective base line values. Hyperglycaemia may be attributed to alpha-2 agonists, which can cause an increase in plasma glucose concentration due to their action on alpha-2 receptors in ß cells of pancreas and inhibit the release of insulin and/or increase glucagon release from the α cells (Burton *et al.* 1997). Hyperglycaemia may also be due to the presence of ketamine in combination which has also been reported to cause sympathetic stimulation leading to release of catecholamines and increased glucose concentration in plasma (Ylitalo *et al.* 1976) while in rebreathing system, halothane also induced significant hyperglycaemia due to inhibition of insulin release (Hikasa *et al.* 1998).

Alkaline phosphatase: Only in BXK group, ALKP concentration significantly (P<0.01) increased during post-operative phase as compared to the base line value while in BDK group, it increased nonsignificantly and remained within physiological limits. Significant increase can be attributed to the fact that ALKP is not only a liver specific enzyme but also associated with intestine, kidney and bone (Komnenou *et al.* 2005) and due to bone specific enzyme too, in BXKgroup, many patients were of ASA category-III involving orthopaedic procedures.

Sodium: In group BXK group, sodium concentration significantly increased during intra-operative (P<0.05) and post-operative (P<0.01) phase as compared to the base line values whereas in BDK group, no statistically significant alterations were found. The significant increase may be correlated with enhance sodium release after xylazine administration causing diuresis (Standhoy *et al.* 1974). Changes in the other haemato-biochemical parameters were non-significant (Table 4).

The mean vaporizer concentration require to maintain

Table 4. Effects of BXK (n=17) and BDK (n=15) anaesthetic drug combinations on various hemato-biochemical parameters during early and late phase of the study in dogs (mean±SE)

	BXK group (n=17)			BDK group (n=15)		
	Base line	Early phase	Late phase	Base line	Early phase	Late phase
Hb (× 10 g/l)	11.99±0.76	10.77±0.75	9.54±0.61[a]	11.75±0.58	10.19±0.52	10.78±0.68
PCV (× 10^{-2} L/L)	37.10±2.37	34.01±2.32	29.29±1.74[a]	36.06±1.93	31.05±1.58	36.62±2.28
TEC (× 10^{12} g/L)	5.25±0.30	4.69±0.37	4.40±0.37	4.50±0.35	3.92±0.26	4.19±0.37
Glu (mmol/L)	69.11±1.10	76.93±1.27[ab]	73.34±1.37[a]	72.93±1.24	81.73±1.92[ab]	78.93±1.24[ab]
CRTN (mmol/L)	0.99±0.03	1.02±0.03	1.09±0.03	0.98±0.06	1.00±0.07	1.06±0.06
BUN (mmol/L)	15.99±1.75	16.88±2.66	18.22±1.83	25.15±2.94	24.96±3.35	24.97±2.67
TPR (g/l)	5.81±0.35	5.27±0.34	4.90±0.36	5.79±0.58	5.74±0.52	5.68±0.36
ALT (IU/L)	28.75±2.13	31.7±2.42	34.47±2.48	29.67±4.37	30.07±4.35	34.00±4.34
AST (IU/L)	34.88±2.28	35.24±2.37	37.71±2.48	29.33±1.89	32.20±2.31	32.87±2.05
ALKP (IU/L)	132.98±3.28	141.86±3.49	153.81±3.77[ab]	130.00±12.15	120.76±10.73	134.27±12.00
Chloride (mmol/L)	102.22±1.45	108.53±4.40	110.17±3.49	101.93±2.33	108.07±2.85	107.49±2.17
Sodium (mmol/L)	147.95±1.66	157.17±2.26[a]	158.31±3.66[ab]	142.02±2.79	140.14±3.17	142.66±2.90

A, The mean difference from base value is significant (P < 0.05); Ab, the mean difference from base value is significant (P < 0.01).

Table 5. Mean±SE intervals of various anesthetic end points in dogs that received BXK (n=17) and BDK (n=15) combinations in dogs

Recovery parameters	BXK group (n=17)	BDK group (n=15)
Time to extubation (min)	8.71±0.69**	5.87±0.52**
Time to HRR (min)	16.41±1.08**	9.93±0.69**
Time to sternal (min)	27.06±1.23**	16.47±0.97**
Time to standing (min)	46.18±2.11**	31.60±2.12**

* Mean difference between the groups is significant ($P < 0.05$), ** mean difference between the groups is significant ($P < 0.01$).

anaesthesia was 2.00±0.20 and 1.26±0.14% in BXK and BDK group respectively. On comparative basis, time to extubation, head raise reflex, time to sternal and standing were significantly ($P<0.01$) lesser in BDK group animals than the animals of BXK group (Table 5). The reason behind this is rapid biotransformation of xylazine with elimination half life of 30.1 min (Gracia *et al*. 1981) as compared with dexmedetomidine which is having half life of 47 min (Kuusela *et al.* 2000). On the basis of above statement, xylazine requires more percent of halothane to maintain adequate plane of anesthesia than the dexmedetomidine.

In group BXK, the quality of recovery was excellent in majority of dogs (71%) few (23%) had a good recovery score characterized by slight ataxia with one animal showed fair recovery (6%) while in BDK group, quality of recovery was excellent in majority of animals (87%) with only 13% animals had good quality of recovery scores.

It was concluded that co-administration of butorphanol-dexmedetomidine-ketamine produced better and safe induction, muscle relaxation, analgesia with quick induction and recovery in comparison to butorphanol-xylazine-ketamine combination and without alarming changes in haematobiochemical parameters in both the group combinations.

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