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COMPARATIVE EVALUATION OF FENTANYL AND BUPRENORPHINE CRI WITH ISOFLURANE ANAESTHESIA IN DOG

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Abstract: The present investigation was conducted on 12 clinical cases of dogs. These dogs were randomly divided into 2 equal groups (n=6). All the dogs were pre-medicated with Xylazine @ 1 mg/kg IM and were induced IV with Propofol @ 4 mg/kg and maintained with Isoflurane. In group 1 CRI of inj. fentanyl @2.5 µg/kg/hr IV and in group 2, CRI of inj. Buprenorphine @ 2.5 µg /kg/hr IV were used. Assessment of anaesthesia was done based on the duration of anaesthesia, time to lift head, time to attend sternal recumbency, time to stand up and time for complete recovery. Clinico-physiological (HR, RT and RR), Hematological (Hb and PCV) and biochemical (ALT, AST, BUN and Creatinine) parameters were recorded before surgery, during surgery, complete surgery and complete recovery. All the physiological and hemato-biochemical parameters were preserved within their normal acceptable range throughout the study.

Keywords: Fentanyl, Buprenorphine, Constant Rate Infusion (CRI), Propofol, Xylazine, Dog.

INTRODUCTION

Anesthesia is a reversible depression of the Central Nervous System that causes immobilization, loss of sensation, analgesia and relaxation of muscle. No anaesthetic agent has been introduced without unfavorable effects, appropriate selection and combination of anaesthetic is thus essential for wellbeing of patient (Shinde *et al* 2018). As multimodal analgesic approach, various drugs can be administered in combination by constant rate infusion (CRI) as a part of intraoprative analgesia (Dyson, 2008 and Patil *et al* 2023). It is superior to the intermittent dosing and keeps the therapeutic concentration stable in tissue or plasma (Patil *et al* 2023). Nowadays inhalant anaesthetic agents frequently club with CRI, the inhalant anaesthetics are regulated quickly and predictably, similarly has quicker recovery (Ilkiw, 1999). The constant rate infusion (CRI) approach allows continuous administration of low-dose of drug, which is effective in the treatment of hospitalized patients who have preexisting or ongoing medical pain (Reddy *et al.*,2021). Fentanyl is a potent synthetic opioid

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with strong agonist properties at μ receptors having ultra-short action (Patle *et al* 2021). Buprenorphine has a slow onset of peak effect and a longer duration of action with ceiling effect (Nunamaker *et al.*,2014). Xylazine is an alpha-2-adrenoceptor agonist commonly used as a sedative and pre-anaesthetic analgesic. The combination with opoid enhances their analgesic and sedative effects (Parrah *et al*., 2017). Considering the weakness and strength of above drugs the study has been outlined.

MATERIAL AND METHOD

The dogs were divided into two equal groups (n=6) irrespective of their age, sex, breed and type of surgical intervention. All dogs received an injection of xylazine @ 1 mg/kg body weight by the intramuscular route,10 minutes later anaesthesia was induced intravenously with an injection of propofol @ 4 mg/kg /body weight. Endotracheal intubation was performed in each dog after induction of anaesthesia.

In group 1 the maintenance of anaesthesia was carried out with the automatic constant rate infusion pump by infusing fentanyl @ 2.5 μg/kg/hr through an intravenous route along with isoflurane anaesthesia. In group 2, dogs were maintained with the automatic constant rate infusing pump by infusing buprenorphine @ 2.5 μg/kg/hr through an intravenous route along with isoflurane anaesthesia.

PARAMETERS STUDIED

Assessment of anaesthesia was done on the basis of duration of anaesthesia. It was noted as the time taken from the onset of induction of anaesthesia to the time to extubation. Time to lift head was noted as the time taken for the lifting of the head from the discontinuation of the flow of anaesthesia, time to attend sternal recumbency was time taken by the animal to attend sternal recumbency after discontinuation of the anaesthesia. Time to stand up was a time required for the animal to stand on its four quarters without assistance after discontinuing the anaesthesia. The time for complete recovery (minutes) was noted as the time elapsed from discontinuing the flow of anaesthesia until the dog walked on his own without assistance. Clinico-physiological, heamatological and biochemical parameters were recorded before surgery, during surgery, after complete surgery and at complete recovery.

Stastical analysis was performed using statistical package for social sciences (SPSS 21.0 software). Two way ANOVA was used to comapare the differences of means between intervals.

RESULT AND DISCUSSION

Assessment of anaesthesia

Duration of anaesthesia (minutes)

The mean values for the duration of anaesthesia for group 1 and group 2 were 53.88 ± 1.24 and 72. 50 ± 3.81 minutes, respectively. The duration of anaesthesia in group 2 was significantly ($p < 0.01$) longer as compared to group 1 (Table 1). These findings are accordance with Kay (1980) and Kukanich and Allen (2014).The surgeries performed under group 1 were less time-consuming as compared to group 2 which might be the reason of prolong duration of anaesthesia in group 2. Moreover, the half-life period of buprenorphine was also more than that of fentanyl.

Table 1: Mean± SE values of duration of anaesthesia in both the groups expressed in minutes

Group 1	Group 2	d.f	T -stat	T-Table (0.01)
53.88 ±1.24	72.50 ±3.81	5	-4.646**	4.032

**-superscript suggests a significant difference at a 1% level ($p<0.01$)

Time to lift head (minutes)

In group 1, the mean time to lift the head by dogs was 15.00 ±1.00 and in group 2 was 56.83 ± 3.91 minutes. The time taken to lift the head in group 1 was significantly shorter ($p<0.01$) as compared with group 2 (Table 2). The findings are accordance with Kukanich and Allen

Group 1	Group 2	d.f	T-stat	T-Table (0.01)
15.00 ±1.00	56.83 ±3.91	5	-10.342**	4.032

(2014), Dehuisser *et al.* (2017) and Vijay *et al.* (2018). This might be attributed to the rapid metabolization of fentanyl as compared to buprenorphine.

Table 2: Mean ± SE values of time to lift head in both the groups expressed in minutes

**-superscript suggests a significant difference at a 1% level ($p<0.01$)

Time to attend sternal recumbency (minutes)

In group 1 and group 2, the mean time to attend the sternal recumbency was 28.66 ± 1.08 and 84.50 ± 3.60 minutes. Dogs in group 2 took significantly ($p<0.01$) longer time to attend the sternal recumbency as compared to group 1 (Table 3). The findings are accordance with Dehuisser *et al.* (2017), Vijay *et al.* (2018) and Velazquez -Delgado *et al*. (2021). This might be due to a larger fraction of fentanyl remaining unbound to plasma protein due to low

protein binding affinity, this unbound fentanyl was available to interact with metabolizing enzymes and waived off quickly (Kukanich and Allen 2014).

Table 3: Mean ± SE values of time to attend sternal recumbency in both groups expressed in minutes

Group 1	Group 2	d.f	T-stat	T-Table (0.01)
28.66 ±1.08	84.50 ± 3.60	5	-14.837**	4.032

**-superscript suggests a significant difference at a 1% level ($p<0.01$)

Time to stand up (minutes)

In group 1, the mean time to stand up was 36.33 ± 0.76 minutes. Whereas, in group 2, the mean time was 116.83± 4.26 minutes. The mean time to stand up in group 2 was significantly ($p<0.01$) longer as compared to group 1(Table 4). The findings are accordance with Hughes and Nolan (1999), Kukanich and Allen (2014), Vijay *et al.* (2018) and Velazquez -Delgado *et al*. (2021). The slow metabolization of buprenorphine as compared to fentanyl might have been responsible for delayed standing in group 2 as compared to group 1.

Table 4: Mean ± SE values of time to stand up a in both the groups expressed in minutes

Group 1	Group 2	d.f	T-stat	T-Table (0.01)
36.33 ± 0.76	116.83± 4.26	5	-14.53**	3.619

**-superscript suggests a significant difference at a 1% level ($p<0.01$).

Time for complete recovery (minutes)

The mean values of time required for complete recovery in group 1 and group 2 were 60.00 ±2.36 and 139.83± 4.46 minutes, respectively. Significantly ($p<0.05$) shorter duration was required for the complete recovery in group 1 as compared to group 2 (Table 5). The findings are accordance with Kukanich and Allen (2014), Thejashree *et al*. (2018) and Vijay *et al.* (2018). The terminal half-life of fentanyl (2.22 h) was shorter than buprenorphine (3.96 h) moreover the protein binding affinity of buprenorphine (95-98%) was higher than the fentanyl (84%) which might be responsible for delayed recovery from anaesthesia in group 2 as compared to group 1.

Table 5: Mean± SE values of time for complete recovery in both the groups expressed in minutes.

Group1	Group 2	d.f	T-stat	T-Table (0.05)
60.00 ±2.36	139.83± 4.46	5	-2.821*	2.571

*-superscript suggests a significant difference at a 1% level ($p<0.05$)

Clinico -physiological parameter

In clinico-physiological parameters, the mean values of heart rate, rectal temperature and respiratory rate were decreased significantly ($p^*<0.05$) within a normal physiological limit.

CONCLUSIONS

The anaesthetic combination at the studied dose rate provides excellent nociception and adequate muscle relaxation essential for soft tissue surgeries in both groups. However, buprenorphine treated group showed prolong recovery time as compared to fentanyl.

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