Enhancing Effect of Butorphanol on Medetomidine-Induced Sedation in Pigs

Minoru SAKAGUCHI*, Ryoei NISHIMURA, Nobuo SASAKI, Toshikazu ISHIKURO†, Hiroshi TAMURA†, and Akira TAKEUCHI

Department of Veterinary Surgery, Faculty of Agriculture, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113 and Laboratory Animal Center, Teikyo University School of Medicine, 2-11-1 Kaga, Itabashi-ku, Tokyo 173, Japan

(Received 31 March 1992/Accepted 7 July 1992)

ABSTRACT. Enhancing effect of an opiate agonist-antagonist butorphanol (0.2 mg/kg) on sedation induced by medetomidine (80 µg/kg) was evaluated in pigs. Butorphanol significantly enhanced the depth of medetomidine-induced sedation and prolonged the duration of that assessed by posture score and spontaneous movement of pigs. The combination of medetomidine and butorphanol produced excellent muscle relaxation and moderate surface analgesia which was enough for procedures with mild pain in pigs.—KEY WORDS: butorphanol, medetomidine, pig.

Medetomidine, a highly selective α2-agonist, has more potent sedative effect than xylazine. From our previous report, medetomidine at a dose of 80 µg/kg of body weight induces satisfactory sedation with lateral recumbency and moderate muscle relaxation without notable side effects in pigs.

It has been reported that the sedative effect of α2-agonist is enhanced by opioid agonist or agonist-antagonist [8], and the combined use of fentanyl and medetomidine induces the condition similar to neurolept-anesthesia in dogs [1]. Butorphanol is a synthetic opioid agonist-antagonist with a significantly more potent analgesic effects than morphine, meperidine or pentazocine in humans, horses and dogs [4]. In horses, xylazine combined with butorphanol produces a synergic analgesic effect and provides good chemical restraint for a standing surgical procedures [2, 5]. Butorphanol has been reported to enhance the anesthesia induced by xylazine-ketamine in pigs [3].

The present study was conducted to examine enhancing effects of butorphanol on medetomidine-induced sedation in pigs.

Five castrated mixed breed pigs of specific pathogen-free (SUMICHIKU Co., Ltd., Japan) with the age ranging from 8 to 13 (mean 10.3) weeks old and the weight ranging from 14.5 to 20.5 (mean 17.5) kg were used in this experiment. The pigs were kept in the conventional environment (room temperature 24.5±1.5°C; humidity 50±15%), fed diet (NS; Nisseiken Co., Ltd., Japan) once a day, and allowed free access to water. The food was withheld at least for 12 h before the experiment.

Prior to the drug administration, pigs were positioned on a canvas sling and after their conditions were stabilized, heart rate (HR), respiratory rate (RR) and rectal temperature (RT) were measured as pre-administration values. After the drug administration, those values were also measured at 5-min intervals for 30 min and then at 10-min intervals for another 60 min.

Butorphanol (Torbugasic; Fort Dodge Laboratories Inc., U.S.A.) at a dose of 0.2 mg/kg of body weight was intramuscularly administered immediately after the intramuscular administration of medetomidine (Domitor; Farmos Ltd., Finland) at a dose of 80 µg/kg mixed with atropine at a dose of 25 µg/kg in the same syringe (MED-BUT). After the onset of sedation appeared, the pigs were moved from the canvas sling to the floor. Sedative effect was assessed by posture score, as lateral recumbency with no spontaneous movement (score=3), lateral recumbency with spontaneous movement (score=2), ventral recumbency or sitting on their hind legs (score=1), and standing or walking (score=0) [7] . Induction time (time from the administration of the drugs to lateral recumbency and lost of spontaneous movement), arousal time (time from the induction of sedation to a return of motor activity and right reflex, indicated by ability of the pigs to raise the head spontaneously) and walk time (time from the arousal to being able to walk spontaneously) were recorded.

When the muscle tone of the jaw was lost, its duration was recorded as muscle relaxation time. Duration of analgesia of the body surface tested by clamping the edge of the muzzle was also recorded. These observations were performed at the same interval as those of the measurements of HR, RR and RT. The recovery condition from the sedation was observed until the pigs could walk normally.

These measurements were compared with the data produced by medetomidine at a dose of 80 µg/kg alone (MED), which we previously reported [7]. Totals of posture score summed up at 30 min intervals were statistically compared using Kruskal-Wallis’s non-parametric method [6]. Other measurements were statistically analyzed by Student’s t-test. HR, RR and RT were also compared with pre-administration values by Student’s paired t-test. Values of P<0.05 were considered to be statistically significant.

Figure 1 shows the depth of sedation expressed by the mean posture score, comparing with that produced by MED. Posture score of MED-BUT was significantly higher than that of MED from the time of drug administration to 90 min post-administration. Table 1 shows the results of duration of sedation, muscle relaxation and surface analgesia. Onset of sedation was observed within 5 min after the drug administration in all pigs. Then, they
Fig. 1. Sedative effect of medetomidine-butorphanol (MED-BUT) expressed as the mean of posture score in 5 pigs comparing with that of medetomidine (80 µg/kg) alone (MED) [7]. Vertical lines show SD. Posture score means as follows: 3, lateral recumbency without spontaneous movement; 2, lateral recumbency with spontaneous movement; 1, ventral recumbency or sitting on their hind legs; 0, standing or walking. *: Significantly different (P<0.05) from the score of MED.

Table 1. Effects of medetomidine-butorphanol on the duration (mean±SD, min) of sedation, muscle relaxation and surface analgesia in 5 pigs.

<table>
<thead>
<tr>
<th>Effect</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction time</td>
<td>7.2±5.5</td>
</tr>
<tr>
<td>Arousal time</td>
<td>84.0±15.8</td>
</tr>
<tr>
<td>Walk time</td>
<td>85.2±15.2</td>
</tr>
<tr>
<td>Muscle relaxation</td>
<td>76±15</td>
</tr>
<tr>
<td>Surface analgesia</td>
<td>24±25</td>
</tr>
</tbody>
</table>

a) Time from the administration of the drugs to lateral recumbency and lost of spontaneous movement.

b) Time from the induction of sedation to a return of motor activity and right reflex, indicated by ability of the pigs to raise the head spontaneously.

c) Time from the induction of sedation to being able to walk spontaneously.

d) Significantly different (P<0.05) from walk time of medetomidine alone [7].

e) Tested by clamping the edge of the muzzle.

f) Three pigs lost surface pain (mean value was calculated as the duration in other pigs being 0 min).

gradually and smoothly became quiet and unconcerned to their environment, and showed lateral recumbent position averagely 7.2 min after the administration, at which time the spontaneous movement and muscle tone were lost. The surface pain tested by clamping of the edge of the muzzle was lost in three pigs, whereas the remaining two pigs responded, however the reaction to the pain was weakened. The pigs could walk averagely 1.2 min after arousal, and walk time of MED-BUT was significantly prolonged comparing with MED, however the duration of muscle relaxation was mostly similar to that by MED. The recovery from the sedation was smooth in all pigs without excitation, excessive salivation, vomiting and returning to sleep after walking (after-sleep).

It was demonstrated that butorphanol significantly enhances the depth of sedation until 90 min of post-administration and prolongs walk time compared with MED alone. Muscle relaxation produced by MED was moderate [7], however that by MED-BUT was excellent without significant prolongation of the duration. Although surface analgesia induced by MED-BUT was still not enough for procedures with strong pain, it was enough for those with mild pain such as injection of drugs or blood sampling. More rapid recovery from the sedation without after-sleep were observed in pigs given MED-BUT, while some pigs given MED showed after-sleep [7].

Figure 2 shows the changes in HR, RR and RT. Mean HR values were varying between 110 and 140 beats/min,
and there was a temporary, mild but statistically significant decrease at 5 min after the drug administration. Mean RR values increased suddenly at 5 min to approximately 1.7 times (38 breaths/min) of pre-administration values (23 breaths/min), then increased gradually to twice (46 breaths/min) at 40 min. Animals showed shallower respiratory depth according to the increase in respiratory rate, however respiratory manner was not changed through the experimental period. Mean RT values decreased significantly from 20 min after the drug administration and reached 36.7±0.9°C at 90 min.

Because the changes in HR and RT induced by MED-BUT were similar to those by MED as previously reported [7], butorphanol seemed to have little effect on HR and RT in pigs. On the contrary, the mean RR value increased significantly to twice of the pre-administration value by MED-BUT, while it gradually decreased by MED [7]. Further investigation might be needed to clarify whether this changes was caused by the direct effect on respiratory center or by the indirect effect through changes in the blood gas and acid-base balance.

In conclusion, it is indicated that butorphanol enhances and prolongs medetomidine-induced sedation, and that this combination produces the excellent muscle relaxation and moderate analgesia. Moreover, recovery from the sedation induced by this combination is rapid and smooth.

REFERENCES