Over the last few years we have investigated the effects of opioids in different species using the reduction of MAC as a tool. This does not prove that the drugs are or are not analgesics but the information generated has been interesting and appears to be similar to data generated by other methods.

In horses Dr. E.P. Steffey looked at morphine given as a bolus injection and found that MAC was not decreased by doses which had caused significant reductions in other species [1,2]. We did further experiments using alfentanil by continuous infusion and found that, even with doses that exceeded the maximum effect in other species, there was no change in MAC [3]. Thinking that perhaps the analgesic effect and the central stimulation caused by opioids in horses might be acting against each other we pursued the role of kappa agonists in horses. It had previously been shown that a pure kappa agonists provided analgesia without locomotor stimulation [4] so we looked at a combination of a mu agonist and a kappa agonist to see if the latter would decrease locomotor stimulation [5]. This did not work and in fact the horses became more ataxic with the combination. Work by Drs Johnson and Taylor [6] suggested that the EEG changes with alfentanil during halothane anesthesia were similar to those seen in other species suggesting that the central action of the drug was not different in horses. Previous work had suggested that the central excitation associated with opioids was mediated by dopamine. With the idea that if one could depress this response the analgesic effect would be more readily visible, we tested two dopamine antagonists on the locomotor effect of alfentanil [7]. The result was that the dopamine antagonists did not blunt the response and even contributed to some increased locomotor activity, particularly when combined.

In cats we looked at the effect of 4 different opioids (morphine, butorphanol, U50488H and buprenorphine) on the MAC of isoflurane. These drugs were given in 2 different doses as bolus injections. We showed that morphine decreased MAC by about 30% [8] while butorphanol decreased MAC by about 20% - both different from results in the dog. We pursued the mu agonists further by using alfentanil at various infusion rates and were able to show again that, despite very high doses, there was a ceiling effect on MAC reduction in the range of 30 - 35% [9]. A further result of this experiment was that we found that the cats did not get manic even after these very high doses of alfentanil and this has allowed us to be more aggressive in using higher doses of opioids in a clinical setting. Further experiments in cats examined the effect of epidural morphine on MAC [10] and showed that there was no difference with a dose of 0.1 vs 0.2 mg/kg suggesting a ceiling effect at 0.1 mg/kg. It was also interesting that the maximum effect was similar to the maximum reduction seen with systemic opioids (about 30%). The effect of fentanyl patches was also examined in cats and showed that placement of the patch about 24 hours prior to anesthesia gave a 17% reduction in MAC [11] suggesting that there would be some definite intraoperative benefit to this use of fentanyl. Since the opioids did not seem to provide an ideal reduction in anesthetic requirement we did some further experiments looking at ketamine to see if it could be used intraoperatively to reduce the need for other anesthetics [12,13].

References


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