

Summary

Introduction: Ideally, general anesthesia and analgesation in specific situations should meet the following requirements: fast and simple induction of analgesia, achievement of the desired suppression of consciousness, minimal cardiovascular effects, preservation of patent airways without the need for mandatory ventilation, and rapid recovery after the application of antagonists. Ketamine is widely used for this purpose, often in combination with benzodiazepines, however, it does possess an undesired psychomimetic effect and lacks a specific antagonist. In veterinary anesthesia ketamine is often used in combination with α_2 agonists, a group of substances with a favourable pharmacological profile in specific situations from an anesthesiologist's point of view. Ketamine in combination with new representatives of α_2 agonists may theoretically be a promising new option for this purpose.

Aim: In rhesus monkeys experiments to assess 1. immobilization by combination of ketamine with α_2 agonists, 2. effect of the addition of hyaluronidase to the above mentioned combinations, and 3. the possibility of reducing ketamine dosage through the addition of a small dose of midazolam while maintaining the effect of immobilization. In the clinical part to assess analgesation with combination of dexmedetomidine - ketamine - midazolam and to compare the results to so far routinely used sufentanil - midazolam analgesation.

Materials and methods: In primate experiments, 95 rhesus monkeys were divided into 7 groups for application of the following combinations of substances via single intramuscular injection: ketamine - medetomidine, the dextroisomer of ketamine - dexmedetomidine, the above combinations with the addition of hyaluronidase, the previous two combinations with the addition of midazolam, and ketamine - naphthylmedetomidine - hyaluronidase group. Behavioral changes, onset of immobilization, and rate of psychomotor recovery - both spontaneous and specific α_2 antagonist induced (atipamezol) - were analysed. Cardiorespiratory functions and undesired side-effects were monitored continuously. In the clinical part, 62 patients undergoing elective endovascular neurointerventions were randomised into two groups for sedation with dexmedetomidine - ketamine - midazolam or sufentanil - midazolam. The characteristics of sedation, effect on cardiorespiratory parameters, and the occurrence of undesired side-effects were analysed. Results were statistically tested using variation analysis, the paired t - test and the chi - square test.

Results: Medetomidine in combination with ketamine resulted in reliable immobilization in all macaques. A decrease in heart rate was recorded, without any major cardiovascular side-effects or respiratory depression. Immobilisation had faster onset in the ketamine dextroisomer group. Addition of hyaluronidase increased the rate of onset of immobilization as well as its duration. Addition of midazolam enabled the dosage of ketamine to be lowered by 50 %. Administration of the α_2 adrenoreceptor antagonist resulted in awakening after 2 – 6 minutes. The combination of naphthylmedetomidine - ketamine - hyaluronidase provided loss of aggressiveness with full manipulability, without loss of consciousness in some cases, cardiorespiratory functions were affected minimally. In the clinical part, dexmedetomidine - ketamine - midazolam provided reliable sedation to the desired degree in the absence of any undesired side-effects. In comparison to sedation using sufentanil - midazolam the decrease in blood pressure and heart rate was significantly greater, however, the number of episodes of hypotension or bradycardia did not differ significantly. Blood pressure showed lower intraindividual variability and patient cooperation during sedation was significantly better.

Conclusion: Immobilization of macaques by combination of ketamine with α_2 agonists appears to be safe and reliable, the rate of onset can be accelerated though the addition of hyaluronidase, the immobilization is antagonisable. In comparison to routine sedation dexmedetomidine - ketamine - midazolam analgesation provides better patient cooperation. The results illustrate the potential of the combination ketamine - α_2 agonist for use in anesthesia in specific situations.