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SHORT COMMUNICATION

A preliminary trial of the sedation induced by intranasal administration of midazolam alone or in combination with dexmedetomidine and reversal by atipamezole for a short-term immobilization in pigeons

Slavomir Hornak, Tomas Liptak, Valent Ledecky, Rudolf Hromada, Jan Bilek, David Mazensky & Vladimir Petrovic

Clinic of Small Animals, University of Veterinary Medicine and Pharmacy, Kosice, Slovak Republic

Correspondence: Slavomir Hornak, Clinic of Small Animals, University of Veterinary Medicine and Pharmacy, Komenskeho 73, 041 81 Kosice, Slovak Republic. E-mail: hornak@uvm.sk

Abstract

Objective To assess the sedative and immobilization effect of intranasal administration (INS) of midazolam (MID) without or with INS dexmedetomidine (DXM), and some physiological changes induced by the drugs. The ability of INS atipamezole to reverse the DXM component was also assessed.

Study design Prospective 'blinded' experimental study.

Animals In total, 15 pigeons.

Methods Pigeons were sedated by INS MID alone at a dose of 5 mg kg^{-1} (group MID, $n = 6$) or in combination with INS DXM at a dose 80 μg kg^{-1} (group MID-DXM, $n = 6$). Measurements were made of heart rate (HR), respiratory rate (f_R) and cloacal temperature (CT). The degree of sedation was assessed at 15 minutes prior to, immediately after, and at intervals until 100 minutes after drug administrations. Following MID-DXM, INS atipamezole (250 μg kg^{-1}) was administered and the same indices measured 5 and 10 minutes later.

Results MID had no effect on HR and f_R, and although CT decreased, it remained within physiological range. MID-DXM caused significant falls in HR, f_R and CT that persisted until the end of sedation. Atipamezole antagonized sedation and cardiorespiratory side effects of MID-DXM within 10 minutes of application. In addition, for MID compared to MID-DXM, the lowest sedation scores [10 (7–14) and 10.5 (5–14) *versus* 2 (1–4) and 2 (1–5)] were achieved in the 10th and 20th minute *versus* the 20th and 30th minute of the sedation, respectively.

Conclusions and clinical relevance MID alone, given INS had minimal side effects on vital functions but caused inadequate immobilization of pigeons for restraint in dorsal recumbency. MID-DXM caused an effective degree of immobilization from 20 to 30 minutes after administration, at which time birds tolerated postural changes without resistance. Atipamezole antagonized both side effects and sedation, but complete recovery had not occurred within 10 minutes after its application.

Keywords atipamezole, dexmedetomidine, immobilization, midazolam, sedation score.

Introduction

Sedation/immobilization for diagnostic and therapeutic purposes often is required in avian practices, particularly for investigations which require the birds to be placed in different recumbent positions,

for example for blood collection, and for clinical and radiological investigations. Recent advances in avian sedation, anaesthesia and analgesia are well reviewed by Lierz & Korbel (2012) and suggest that intranasal (INS) application seems to be a suitable mode of administration of drugs and can be used to facilitate diagnostic procedures requiring a short-term immobilization.

Water-soluble benzodiazepines, such as midazolam (MID), have sedative, anxiolytic, and muscle relaxant effects in avian species, and are a good choice for INS administration. Alpha-2-adrenergic receptor agonists, such as dexmedetomidine (DXM), are used for sedation and analgesia but are not recommended as a single immobilization agent for birds (Pollock et al. 2001). Regardless of administration routes, the benefits and disadvantages of the application of MID with DXM are well known both in veterinary and human medicine. However experimental trials performed on birds studying the additive and/or synergistic sedative effects of MID and DXM when given in combination are lacking. For these reasons, this study was conducted to evaluate the sedative effects of INS MID alone, or in combination with INS DXM (MID-DXM) and to investigate if either protocol can produce adequate immobilization of pigeons such as to enable the maintenance of postural changes following positioning without unacceptable physiological side effects. The study also investigated the effects of reversal of the DXM by INS atipamezole (ATI).

Materials and methods

Study design, animals and husbandry

The present study was conducted on 15 unsexed healthy adult pigeons. Body weights ranged from 327 to 540 g (mean ± SD, 445 ± 53 g) and were measured before sedation for the calculation of effective doses of drugs. All pigeons were kept in a quiet room at standard room temperature (23 °C) and light regime (16 hours light:8 hours dark). The birds were housed in individual cages with free access to water and to a wheat-based diet.

The experiment was conducted in accordance with established standards for use of animals and birds. The protocol was approved by the local ethical and scientific authorities. The degree of sedation/immobilization of the birds was monitored and examined in a well-lit, quiet room to avoid possible stress inducing factors (e.g. noise, movement). Administration of drugs was preceded by fasting for one hour. Each bird was examined to adjudge its vital functions but and only these pigeons which had basal values (BV) of heart rate (HR), respiratory rate (f_R) and cloacal temperature (CT) within their physiological ranges according to Vogel et al. (1994) were used for the sedation protocols. Only three pigeons (one by one) were sedated per day and after recovery they were excluded from the study, thus no bird was sedated more than once.

The group MID received INS MID (Midazolam Torrex, Torrex Chiesi Pharma GmbH, Austria) at the dose of 5 mg kg^{-1}. The group MID-DXM received INS MID 5 mg kg^{-1} in combination with DXM (Dexdor, Orion Pharma, Finland) at the dose of 80 μg kg^{-1} INS.

The drugs were administered as follows: the pigeons were captured by hands covered by a towel, and the birds were initially restrained in a dorsal position with one hand restraining the head while the other hand held the body and both wings. The drugs were slowly administered into nares using a micropipette (Transferpette S Digital Pipette, Brandtech Scientific, Essex, UK). In group MID-DXM, MID was applied to one nostril and DXM to the other. In group MID-DXM, ATI (Antisedan Vet, Orion Pharma) at the dose of 250 μg kg^{-1} was applied INS after 100 minutes.

Sedation monitoring – parameters and scoring

Physiological variables were measured 15 minutes before (BV), immediately after (0), and at 5, 10, 20, 30, 45, 60, 80 and 100 minutes after the drugs administration (+5, +10, +20, +30, +45, +60, +80, +100, respectively). In addition, in group MID-DXM only, they were also measured 5 and 10 minutes after the ATI adminstration (ATI+5 and ATI+10, respectively). The physiolgical variables measured were HR (beats $minute^{-1}$), f_R (breaths $minute^{-1}$) and CT (°C). Body reflexes (except for time 0) were evaluated by the reflex score chart according to Korbel (1998) with some amendments (Table 1; Appendix S1), resulting in a 25-point sedation scale on which the highest score indicates full consciousness of healthy pigeons. The depth of sedation and the level of immobilization were assessed according to the criteria described by Pollock et al. (2001) and Prather (2012). Each bird was assessed in the same manner for all body reflexes. One evaluator stimulated the body reflexes and then assessed them, together with additional assessement by two expe-

