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Original Article

Comparative Evaluation of the Biochemical Effects of Ketamine Plus Ketoprofen and Midazolam in the Premedication of Pigeons

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ABSTRACT

The present study was conducted with the aim of comparing the effects of premedication with ketoprofen and midazolam in birds. A total of 24 male pigeons with an approximate weight of 300 g were divided into four equal groups. The control group (Group I) was injected with ketamine alone. Groups II-IV were injected with ketoprofen alone, ketoprofen+ketamine, and midazolam+ketamine, respectively. The biochemical changes in the four groups were evaluated after intramuscular drug injections at different anesthetic levels. A record of biochemical changes was maintained for each group. Blood samples were taken before and after the administration of the medications in order to measure the levels of serum alkaline phosphatase (ALP), oxaloacetate transaminase (OT), prothrombin time (PT), glucose (GLU), lactate dehydrogenase (LDH), albumin (Alb), total protein (TP), and gamma-glutamyl transferase (GGTF). The results showed significant differences in the mean levels of ALP, OT, PT, GLU, LDH, Alb, and TP after anesthesia, compared to that before anesthesia. Therefore, ketoprofen+ketamine can be used for the induction of anesthesia in birds.

Keywords: Serum Analysis, Ketamine, Ketoprofen, Midazolam, Pigeons

Évaluation Comparative des Effets de la Kétamine, Combinée au Kétoprofène et au Midazolam dans la Prémédication des Pigeons

Résumé: Cette étude a été menée fin but de comparer les effets de la prémédication avec le kétoprofène et le midazolam chez les oiseaux. Au total, 24 pigeons mâles d'un poids approximatif de 300 g ont été répartis en quatre groupes égaux. Le groupe témoin (Groupe I) a été injecté avec de la kétamine seule. Les groupes II-IV ont reçu respectivement une injection de kétoprofène seul, de kétoprofène combiné à la kétamine et de midazolam combiné à la kétamine. Les modifications biochimiques dans les quatre groupes ont été évaluées après des injections intramusculaires à différents niveaux d'anesthésie. Les modifications observées ont été ensuite enregistrées pour chaque groupe. Des échantillons de sang ont été prélevés avant et après l'administration des médicaments afin de mesurer les taux de phosphatase alcaline sérique (PAL), oxaloacétate transaminase (OT), taux de prothrombine (TP), glucose (GLU), lactate déshydrogénase (LDH), albumine (Alb), protéine totale (PT) et gamma-glutamyltranspeptidase (γ-GT). Les résultats ont montré des différences significatives dans les niveaux moyens de PAL, d'OT, de TP, de GLU, de LDH, d'Alb et de PT après anesthésie, comparés à ceux avant l'anesthésie. Par conséquent, le kétoprofène combiné à la kétamine peut être utilisé pour l'induction de l'anesthésie chez les oiseaux.

Mots-clés: Analyse du Sérum, Kétamine, Kétoprofène, Midazolam, Pigeons

INTRODUCTION

Many studies have demonstrated the effects of anesthetic agents on metabolic, hemodynamic, and cardiovascular parameters in avian veterinary practice (Maiti et al., 2006; Kamiloglu et al., 2008; Azizpour and Hassani, 2012; Yayla et al., 2012). Although several anesthetic agents are often used to induce anesthesia, the use of safe and effective anesthetic methods and administration route in small pet birds is as important for successful treatment as the surgical procedure itself. When compared to inhaled anesthetics, injectable agents not only are cheaper, but also provide faster induction of anesthesia and require less equipment (Forbes, 1998). Since birds have pneumatic bones, the use of inhaled anesthetics leads to the dispersal of anesthetic gasses in the environment and threatens the health of the surgeons and operating room personnel (Gali et al., 2014). Ketamine is a potent inhibitor of gamma-aminobutyrate binding in the central nervous system that induces amnesia and anesthesia stages I and II, but not stage III. Due to these properties, ketamine is rarely used alone because it is associated with poor muscle relaxation, muscle tremors, myotonic contractions, opisthotonus, and rough recoveries (Sandmeier, 2000). Premedication with midazolam has shown to be more effective in reducing anxiety and improving compliance with anesthesia. The beneficial effects of midazolam include sedation, anxiolysis, and reduction of postoperative vomiting (Yuen et al., 2008). Ketoprofen (2-[3-benzoylphenyl]-propionic acid) is a nonsteroidal anti-inflammatory drug (NSAID) exerting antipyretic, anti-inflammatory, and pain-killing effects (Kang et al., 2008). This medication is mainly used to treat musculoskeletal pain caused by soft tissue injury, osteoarthritis, or other bone and joint problems (Vane and Botting, 1995). The NSAIDs are generally cyclooxygenase-1 and/or -2 (COX-1 and COX-2, respectively) inhibitors. Therefore, they would decrease the number of induced prostanoids, which will in turn inhibit the gastric cytoprotective functions, primary platelet plug formation, and modulation of renal vascular tone (Vane and Botting, 1995). Some recent studies have also highlighted the potential effects of COX-2 on maintaining gastrointestinal (GI) integrity (Dubois et al., 1998), promoting ulcer healing (24), and treating induced colitis in rats (Reuter et al., 1996). Despite the anti-prostaglandin properties of COX-2, a seven-day course of ketoprofen administration was reported to be less damaging to the gastroduodenal mucosa than the NSAID prototype aspirin (Forsyth et al., 1996). The aim of this study aimed to compare the biochemical effects of ketamine+ketoprofen and midazolam+ketamin in the premedication of pigeons.

MATERIALS AND METHODS

Ethical considerations. The pigeons were kept based on the ethics of animal experimentation defined by the Faculty of Specialized Veterinary Sciences of Islamic Azad University, Tehran, Iran. The study protocol was approved by the Animal Ethics Committee of Islamic Azad University. Moreover, the minimum possible number of animals were included in the experiments. Finally, a total of 24 pigeons received antiparasitic drugs.

Animals, housing, and diets. For the purpose of the study, 24 pigeons were randomly divided into four equal groups. Group I, or the control group received an intramuscular (IM) injection of ketamine (40 mg/kg body weight). In Group II, the birds were given an IM injection of ketoprofen (50 mg/kg body weight). Groups III and IV received IM injections of ketamine (40 mg/kg body weight)+ketoprofen (50 mg/kg body weight) and midazolam+ketamine (6 mg/kg body weight), respectively. The animals had access to water on demand. Biochemical parameters were recorded regularly.

Biochemical analysis. In all groups, 1 mL blood samples were obtained from the birds' wing veins (vena cutanea ulnaris) before and 1 h after the administration of the medications (15). The serum levels of alkaline phosphatase (ALP), oxaloacetate transaminase (OT), prothrombin time (PT), glucose (GLU), lactate dehydrogenase (LDH), albumin (Alb),

total protein (TP), and gamma-glutamyltransferase (GGTF) were measured and recorded. The required laboratory kits were all made by Bionic Co. (USA). Serum parameters were measured using BT 1500 (BiotecnicaInstruments, Rome, Italy). Given the side effects of NSAIDs on the liver and kidneys, these enzymes measurement required to evaluation of these drugs safety for pre-anesthesia in compare with midazolam is necessary.

Statistical Analysis. The data were recorded as mean and standard error of mean in Microsoft Excel worksheets. One-way analysis of variance (ANOVA) was applied to analyze the parametric data. P-value less than 0.05 was considered statistically significant. All analyses were performed in SPSS for Windows, version 16.0 (SPSS, Inc., Chicago, IL, USA).

RESULTS

Biochemical parameters. In this study, the determination of the rate of changes in the biochemical variables in the subjects before and after anesthesia was accomplished using biochemical tests. There was no significant difference between the biochemical variables (P>0.05). Therefore, all biochemical variables had a normal distribution; consequently, they were subjected to parametric tests. The four groups had significantly different ALP, OT, PT, GLU, LDH, and Alb levels after anesthesia, compared to those before anesthesia. In this regard, ALP levels were higher in three groups (i.e., ketamine, ketoprofen, and ketoprofen+ketamine) before anesthesia, compared to those after anesthesia. However, regarding the midazolam+ketamine group, ALP level was lower before anesthesia than that after anesthesia. Furthermore, OT and PT were at lower levels before anesthesia in four groups as compared to those after anesthesia. On the other hand, GLU levels were higher in the ketamine and ketoprofen+ketamine groups before anesthesia, compared to those after anesthesia. However, regarding the ketoprofen and midazolam+ketamine groups, the amount of GLU was lower before anesthesia than that after anesthesia. In addition, LDH and Alb levels were higher before anesthesia in all groups than those after anesthesia. In terms of the PRO levels, just three groups (i.e., ketoprofen, ketoprofen + ketamine, and midazolam + ketamine) showed a significant difference after anesthesia in comparison to those after anesthesia. No significant difference was observed in the PRO levels of the ketamine group between the two stages. The ketoprofen and ketoprofen+ketamine groups showed higher PRO levels before anesthesia as compared to those after anesthesia; however, in case of midazolam+ketamine group, this level was lower before anesthesia. Additionally, no significant difference was detected in GGTF levels after anesthesia, compared to the pre-anesthetic measurements in the four research groups. (Table 1).

DISCUSSION

Safe and effective premedication methods are highly important for surgical, diagnostic, and clinical procedures (e.g., radiography, wound dressing, blood collection, endoscopy, and fracture repair) in all animals, including small pet birds. Such methods can control pain in chronic inflammatory diseases, mitigate posttraumatic and postoperative discomfort, and reduce the thermoregulatory set point in animals with fever (Kore, 1990). This study aimed to evaluate the serum

Table 1.Various biochemical parameters of four research groups

Group	ALP(µl)	OT(µl)	PT(µl)	GLU(µl)	LDH(µl)	TP(µl)	GGTF(µl)	ALB(µl)
Ketamine	1.264a ±27	2.607b ±244	0.894a ±45	2.280b ±28	2.607b ±588	1.095 ± 1b	0.632a ±1	0.035b ±1.70
Ketoprofen	0.632c ±80	1.414b ±308	4.049c ±84	3.794c ±6	4c± 271	0.24a ±0.09	0.547 ± 0.50b	0.035b ±1.70
Ketoprofen+Ketamine	2.529a ±34	1.264a ±510	6.801a ±58.66	3.405a ±13	5.329a ±621	0.020a ±0.10	1.032 ± 0.66a	0.056a ±0.20
Midazolam+Ketamine	3.162b ±165	3.162a ±504	2.607b ±24	3.033b ±33	1.414c ±265	0.014b ±160	0.816 ± 0.66b	0.040b ±0.9
Sig	0.001	0.001	0.001	0.001	0.001	0.001	0.731	0.001

*a, b- Dissimilar letters in each column indicate significant differences (P<0.05)

biochemical effects of ketoprofen in comparison with those of midazolamon in premedicated pigeons. In a study investigating ketoprofen toxicity in avian species, the administration of ketoprofen did not significantly change uric acid and creatinine levels; however, it caused significant changes in ALT, AST, and ALP levels. Bonina et al. (2002) reported the risk of GI bleeding and/or perforation in ketoprofen therapy. While we did not observe such complications, there was an increase in serum ALT, AST, and ALP levels, which suggested hepatotoxicity. The postmortem of the control group revealed no abnormalities, particularly in the liver, kidneys, and muscles. Similarly, in other studies, the uric acid, creatinine, ALT, AST, and ALP levels were not significantly different in the serum samples collected at different times during the experiments (García Rodríguez, 1998; Bonina et al., 2002). Hernández-Díaz and Rodríguez (2000) assessed the relationship between NSAIDs (i.e., ketoprofen, piroxicam, indomethacin, diclofenac, naproxen, and sulindac) and upper GI bleeding. They found that the risk of GI bleeding was lower in ketoprofen group than that in any other groups. Garcia Rodriguez et al. (2004) examined the relationship between NSAIDs administration and the risk of myocardial infarction in the general population. According to their findings, the risk of myocardial infarction was lower in ketoprofen group than that in piroxicam and diclofenac groups (Garcia Rodriguez et al., 2004). Furthermore, Maiti et al. (2006) evaluated the differential mortality in spectacled and king eiders (Somateria fischeri and Somateria spectabilis, respectively) anesthetized with propofol, bupivacaine, or ketoprofen. During the first four days post-surgery, 4 out of 10 male spectacled eiders and 5 out of 6 male king eiders died. However, during the same period, no female spectacled eiders and only one out of five female king eiders passed away. Their histopathologic findings suggested the presence of severe renal tubular necrosis, acute rhabdomyolysis, and mild visceral gout in two dead male king eiders. They also reported that necropsy findings in the remaining three dead male king eiders were in favor of visceral gout. Some studies have examined the effects of NSAIDs in the treatment of joint inflammatory diseases in the lame backyard chickens. They indicated associations between mortality and the administration of diclofenac, carprofen, and ketoprofen. However, no mortality was reported following meloxicam use. Semrad (1993) studied the efficacy of ketoprofen in the treatment of endotoxemia in neonatal calves. In the mentioned study, the clinical signs of endotoxemia and lipopolysaccharide (LPS)-induced lacticanemia were exacerbated after the intravenous administration of ketoprofen (2.2 mg/kg) and ketorolac promethazine (1.1 mg/kg). However, these agents did not significantly change the degree of LPS-induced leukopenia or hypoglycemia. In a study on rats, Roughan and Paul (2001) evaluated the behavioral effects of laparotomy and the analgesic effects of the postoperative administration of ketoprofen and carprofen. They found that the frequency of particular postoperative behaviors decreased with analgesic treatment and concluded that such behaviors could indicate postoperative pain. Moreover, both agents (i.e., ketoprofen and carprofen) had similar dose-independent effects (Roughan and Paul, 2001).

In the present study, no deaths were recorded in any of the groups. Based on the biochemical analyses, ketoprofen was a suitable premedication drug. Moreover, the base ranking of ketoprofen suggested it as a useful drug for the management of pyrexia and inflammation in poultry and veterinary practice. Ketoprofen has good pharmacological effects among veterinary medicine and may be used instead of other premedication drugs in veterinary practice.

Ethics

I hereby declare all ethical standards have been respected in preparation of the submitted article.

Conflict of Interest

The authors declare that they have no conflict of interest.

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