

The effects of butorphanol + isoflurane and medetomidine+isoflurane anesthetic agents on cardiopulmonary, hematological, biochemical parameters in pigeons

Efectos de los agentes anestésicos butorfanol + isoflurano y medetomidina+isoflurano sobre los parámetros cardiopulmonares, hematológicos y bioquímicos en palomas

Kübra DİKMEN-İLGİNOĞLU* , Ali HAYAT 

¹Harran University, Faculty of Veterinary Medicine, Department of Surgery, Şanlıurfa, Türkiye

*Corresponding authors: kubradikmen@harran.edu.tr

ABSTRACT

To develop a safe and balanced anesthetic combination in avian and to evaluate the effects of these combinations on various systems. Twenty clinically healthy adult pigeons (1–2 years old, 448.9 ± 41.2 g) were randomly divided into two groups. Group I received butorphanol (2 mg/kg, IM), followed 10 minutes later by 2 % isoflurane via face mask. Group II was given medetomidine (0.2 mg/kg, IM), followed by the same isoflurane protocol. Cardiopulmonary, hematological, biochemical values, and reflexes were monitored and analyzed. Significant reductions in heart rate and cloacal temperature were observed in both groups. In the II group, respiratory rate and end-tidal CO₂ values also decreased significantly compared to baseline (P < 0.05). When the groups were compared: respiratory rate, cloacal temperature, end-tidal CO₂, systolic blood pressure, diastolic blood pressure, mean blood pressure and oxygen saturation values showed significant differences. Haematological and biochemical results showed that the decrease in red blood cell in the I group and the increase in aspartate aminotransferase in the II group compared with T0 were statistically significant. Significant differences were also found between groups in red blood cell, hemoglobin, and hematocrit. It was also observed that medetomidine caused a further decrease in reflexes. The I protocol demonstrated milder depressive effects on cardiopulmonary and hematological systems, suggesting it may be a safer anesthetic option in pigeons.

Key words: Anesthesia; butorphanol; isoflurane; medetomidine; pigeons.

RESUMEN

Con el objetivo de desarrollar una combinación anestésica segura y equilibrada en aves y evaluar los efectos de estas combinaciones en diversos sistemas, se llevó a cabo esta investigación. Para ello se utilizaron veinte palomas adultas clínicamente sanas (1-2 años de edad, 448,9 ± 41,2 g) las cuales fueron divididas aleatoriamente en dos grupos. El grupo I recibió butorfanol (2 mg/kg, IM), seguido 10 minutos después de isoflurano al 2 % mediante mascarilla facial. El grupo II recibió medetomidina (0,2 mg/kg, IM), seguida del mismo protocolo de isoflurano. Se monitorizaron y analizaron los valores cardiopulmonares, hematológicos, bioquímicos y reflejos. Los resultados obtenidos nos muestran reducciones significativas de la frecuencia cardíaca y la temperatura cloacal en ambos grupos. En el grupo II, la frecuencia respiratoria y los valores de dióxido de carbono al final de la espiración también disminuyeron significativamente en comparación con el valor inicial (P < 0,05). Al comparar los dos grupos, se observaron diferencias significativas en los valores de frecuencia respiratoria, temperatura cloacal, CO₂ al final de la espiración, presión arterial sistólica, presión arterial diastólica, presión arterial media y saturación de oxígeno. Los resultados hematológicos y bioquímicos mostraron que la disminución de glóbulos rojos en el grupo I y el aumento de aspartato aminotransferasa en el grupo II, en comparación con T0, fueron estadísticamente significativos. También se observaron diferencias significativas entre los grupos en glóbulos rojos, hemoglobina y hematocrito. Asimismo, se observó que medetomidina provocó una mayor disminución de los reflejos. Se concluye que el protocolo I demostró efectos depresores más leves en los sistemas cardiopulmonar y hematológico, lo que sugiere que podría ser una opción anestésica más segura en palomas.

Palabras clave: Anestesia; butorfanol; isoflurano; medetomidina; palomas.

INTRODUCTION

Anesthesia applications and methods are employed in avian and mammalian species for diagnostic, therapeutic, and prognostic purposes [1, 2]. General anesthesia represents one of the most significant of these methodologies and is now extensively employed in avians. Inhalation anesthesia, which has become a popular and prevalent general anesthesia method in recent years, is being employed with increasing frequency in avians for reasons such as speed, efficacy and rapid recovery [3, 4].

A variety of agents are used for inhalation anesthesia, with isoflurane (ISO) being one of the most significant. It offers the benefits of reliability and ease of administration [5, 6]. The capacity to utilize ISO in conjunction with a range of preanaesthetic agents enhances the reliability of general anesthesia procedures. Furthermore, the effects of ISO were assessed in studies conducted in avians, wherein it was demonstrated that its induction was rapid, alterations in the depth of anesthesia could be readily and expeditiously regulated, the time required for recovery was brief, and it exhibited minimal cardiovascular side effects [7, 8].

Although there are studies on ISO in avians in the literature, these studies were limited to pigeons. Furthermore, the effect of ISO in combination with different preanaesthetic agents remains unknown, necessitating the development of new studies. In addition, the efficacy of these agents on haematological and biochemical values in avians has yet to be investigated [9, 10].

Preanaesthetic agents are commonly used in avian and have become a standard component of diagnostic and therapeutic procedures [11]. Butorphanol (BUT) is a member of the opioid class and a preanaesthetic agent that can be used for analgesia in avians [2, 8]. In mammals, the combination of BUT with inhalational anesthetic agents has been shown to provide balanced anesthesia. Additionally, it has been demonstrated that the drug can be safely used, as it lessens the frequency of autonomic side effects and hypotension [12].

Medetomidine (MED) is a preanaesthetic in the alpha 2 adrenergic agonist group that has been the subject of extensive investigation in mammals. It has been reported to have anticonvulsant effects and provide safe sedation and comfortable awakening [13]. Furthermore, although some studies involving the combination of MED and ISO in mammals have reported that they can be used safely, there is a paucity of studies on avian species [14, 15].

The objective of this study was to examine the effects of BUTISO (BUT + ISO) and MEDISO (MED + ISO) anesthetics on cardiopulmonary, haematological, biochemical and reflex values in pigeons. Furthermore, this study aimed to contribute to the existing literature by establishing an optimal and balanced anesthetic protocol for use in pigeons (*Columbidae*).

MATERIALS AND METHODS

This study was conducted at the Harran University Animal Experiments Research Centre (HDAM) Farm Animals and Poultry Unit. The study was conducted on a cohort of 20 healthy adult pigeons (*Columba livia*), with an age range of 1-2 years and a

mean body weight (SKS-4502, Sinbo, Türkiye) of 448.9 ± 41.2 g (mean $\pm$ SD).

Pigeons were housed in spacious and airy cages in an HDAM poultry unit. All clinical and parasitological (fecal) examinations were conducted, and the pigeons were housed in a clean, quiet, and stress-free environment at a temperature of 25 °C with ad libitum access to water and feed.

Experimental procedure

In the present study, 10 pigeons in each group were randomly divided into two groups. Group I (n = 10) received an intramuscular (IM) injection of BUT (Butomidor® 10 mg/mL, Richter Pharma AG, Wels, Austria) at a dose of 2 mg/kg into the pectoral muscle using a 1 mL insulin injector with a 28-gauge, 1.27 cm long needle [11]. Anesthesia was maintained for 30 minutes (min) with 2 % ISO (isoflurane USP, Piramal Critical Care, USA) with an oxygen flow of 0.5-1 L/min using a face mask 10 min after the IM injection [16]. Group II (n = 10) received a single dose of MED (Domitor® 1 mg/mL, Orion Farnos, Pharmaceutical-Pfizer Animal Health, Finland) 0.2 mg/kg via intramuscular injection into the pectoral muscle. A 1 mL insulin syringe equipped with a 28-gauge needle measuring 1.27 cm in length was used to administer the injection [11]. Anesthesia was maintained for 30 min with 2 % ISO (isoflurane USP, Piramal Critical Care, USA) with an oxygen flow of 0.5-1 L/min using a face mask 10 min after the intramuscular injection [16].

Measurements

The initial cardiopulmonary, haematological and biochemical measurements were conducted 10 min prior to the administration of anesthesia (T0) in the dorsal recumbent position, with no pressure applied to the head and neck of any of the pigeons.

Cardiopulmonary assessment was performed at 10 min (PRE10) after the preanesthetic agent injections and at 10 min (ISO10), 20 min (ISO20) and 30 min (ISO30) following the administration of ISO. The evaluation was conducted using the Mindray UMEC12VET (Shenzhen Mindray Bio-Medical Electronics Co., Shenzhen, China), a multiparametric monitor. The data pertaining to Heart rate (HR), systolic blood pressure (SAP), diastolic blood pressure (DAP), mean blood pressure (MAP), respiratory rate (RR), oxygen saturation (SpO2), end-tidal carbon dioxide (EtCO2) and cloacal temperature (CT) were recorded at 10-min intervals.

To assess heart rate, electrodes were attached to the skin on the anterior surface of both wings and to the skin fold on the inner surface of both thighs (femur) in the legs. The cloacal temperature was measured using a thermometer (Shenzhen Mindray Bio-Medical Electronics Co., Shenzhen, China) placed in the cloaca. Blood pressure was measured indirectly via the use of a medium-sized blood pressure cuff with wings, which was placed on the dorsal metatarsal artery of the right leg. For the purpose of monitoring the SpO2 of the blood, a pulse oximeter probe was positioned on the muscle of the right radius bone.

To measure EtCO2 levels, an EtCO2 tube was placed on the nasal passages to cover the entire beak and was monitored [17, 18]. To avoid any potential impact on the cardiopulmonary values

being monitored, reflex control and blood sampling procedures were conducted subsequent to recording the aforementioned cardiopulmonary values.

A series of hematologic and biochemical evaluations were conducted prior to the administration of anesthesia (T0), at PRE10 and ISO30. A total of 2 mL of blood was collected from the brachial vein for subsequent biochemical and haematological analyses [19]. White blood cell (WBC), red blood cell (RBC), hemoglobin (HGB), and hematocrit (HCT) values were determined from 1 mL of venous blood samples with K3EDTA for hemogram analysis using an MS4 autoanalyzer (CFE 279, Hematology Analyzer, France).

For the purpose of biochemical analysis, 1 mL of blood was collected and placed in gel tubes devoid of anticoagulants. The separation of serum was achieved through centrifugation, employing a Nüve (NF 400R, Türkiye) apparatus at a rotation speed of 3000 rpm for 10 min. Biochemical analysis was conducted using at SPOTCHEM EZ SP-4430 (Arkray Inc., Kyoto, Japan) biochemistry analyzer to measure alanine aminotransferase (ALT), aspartate aminotransferase (AST) and glucose (GLU) parameters.

The reflex level was determined by modifying the reflex assessment methodology reported by Martel *et al.* [20]. Accordingly, the following reflexes were evaluated: eyelid spacing (degree of eyelid opening and closing by touching the eyelid margin at the medial canthus with a dry cotton swab), pedal reflex (degree of leg pulling when the fingers were pulled), wing pulling reflex (degree of wing gathering when the wings were pulled outward), response to needle picking (sensation check with needle picking on one leg), and head and neck posture (degree of head-neck movement).

Clinically tested reflex grades were scored as 0: No response to stimuli; 1: very little and partial response to stimuli; 2: vivid and responsive to stimuli.

Statistical analysis

The data were evaluated using the SPSS 22.1 statistical software Package for the Windows®. The Shapiro-Wilk normality test was used to ascertain whether the data were parametric. As the data did not satisfy the parametric test assumptions, the disparities between the experimental groups (BUTISO and MEDISO) in all measured quantitative characteristics were ascertained using the Kruskal-Wallis and Mann-Whitney U tests. Differences between measurements taken on the same pigeon at different times were determined separately for each experimental group using the Friedman test.

In the case of variables exhibiting significant differences in the Friedman test, pairwise comparisons were performed using the Wilcoxon test, with the exception of those pertaining to differences between baseline and other measurements. The results of the study are presented as the mean $\pm$ SD and median values. The threshold for statistical significance was set at $P < 0.05$.

RESULTS AND DISCUSSION

The evaluation of cardiopulmonary parameters showed a meaningful difference in SAP, DAP, and MAP levels between the groups at the PRE10 and ISO10 stages ($P < 0.05$). Statistical analysis revealed notable differences in respiratory rate between the two groups at ISO10 and ISO20. Similarly, SpO₂ levels showed a significant variation between ISO20 and ISO30. In addition, EtCO₂ and cloacal temperature measurements differed significantly between the groups across all evaluated time points.

In the intragroup analysis, heart rate showed a statistically meaningful reduction in the BUTISO and MEDISO groups at PRE10, ISO10, ISO20, and ISO30 ($P < 0.05$). While there was a reduction in respiratory rate in both groups, this decline was statistically significant in the MEDISO group at PRE10, ISO10,

TABLE I
Cardiopulmonary parameters in pigeons administered butorphanol + isoflurane and medetomidine + isoflurane, presented as median and mean $\pm$ SD at different time points.

Pm	Gr					BUTISO					MEDISO				
	T0 median mean $\pm$ SD	PRE10 median mean $\pm$ SD	ISO10 median mean $\pm$ SD	ISO20 median mean $\pm$ SD	ISO30 median mean $\pm$ SD	T0 median mean $\pm$ SD	PRE10 median mean $\pm$ SD	ISO10 median mean $\pm$ SD	ISO20 median mean $\pm$ SD	ISO30 median mean $\pm$ SD	T0 median mean $\pm$ SD	PRE10 median mean $\pm$ SD	ISO10 median mean $\pm$ SD	ISO20 median mean $\pm$ SD	ISO30 median mean $\pm$ SD
HR (beats/min)	275 266 $\pm$ 43	21* 214 $\pm$ 51	150* 152 $\pm$ 50	130* 140 $\pm$ 32	132* 137 $\pm$ 24	280 274 $\pm$ 37	131* 161 $\pm$ 48	163* 152 $\pm$ 41	165* 152 $\pm$ 37	160* 148 $\pm$ 34					
SAP (mmHg)	125 141 $\pm$ 49	147 ^a 156 $\pm$ 47	171 ^a 159 $\pm$ 42	131 142 $\pm$ 35	138 147 $\pm$ 41	127 131 $\pm$ 22	107 ^b 114 $\pm$ 21	124 ^b 124 $\pm$ 16	120 120 $\pm$ 25	134 124 $\pm$ 28					
DAP (mmHg)	84 97 $\pm$ 44	107 ^a 111 $\pm$ 40	112 ^a 102 $\pm$ 37	110 100 $\pm$ 38	101 98 $\pm$ 28	86 88 $\pm$ 28	75 ^b 75 $\pm$ 15	73 ^b 72 $\pm$ 17	68 77 $\pm$ 31	83 81 $\pm$ 31					
MAP (mmHg)	100 113 $\pm$ 42	114 ^a 120 $\pm$ 41	131 ^a 119 $\pm$ 38	116 114 $\pm$ 34	113 115 $\pm$ 28	101 97 $\pm$ 29	83 ^b 86 $\pm$ 15	82 ^b 85 $\pm$ 14	78 87 $\pm$ 28	96 92 $\pm$ 28					
RR (respiration rate/min)	48 47 $\pm$ 14	49 51 $\pm$ 9	34 ^a 35 $\pm$ 9	37 ^a 36 $\pm$ 8	30 31 $\pm$ 9	55 58 $\pm$ 6	39* 35 $\pm$ 9	25 ^{b*} 24 $\pm$ 6	26 ^{b*} 25 $\pm$ 6	23* 22 $\pm$ 8					
SpO ₂ (%)	87 88 $\pm$ 7	91 91 $\pm$ 5	92 93 $\pm$ 5	97 ^a 94 $\pm$ 5	96 ^a 94 $\pm$ 5	90 89 $\pm$ 6	91 88 $\pm$ 7	88 88 $\pm$ 6	85 ^b 87 $\pm$ 6	88 ^b 86 $\pm$ 9					
EtCO ₂ (%)	33 32 $\pm$ 3	34 ^a 35 $\pm$ 8	29 ^a 28 $\pm$ 4	29 ^a 28 $\pm$ 3	29 ^a 26 $\pm$ 6	41 41 $\pm$ 6	39 ^b 39 $\pm$ 3	37 ^b 35 $\pm$ 7	35 ^{b*} 34 $\pm$ 7	34 ^{b*} 33 $\pm$ 6					
CT (°C)	40.3 40.3 $\pm$ 0.8	40.2 ^a 40.2 $\pm$ 0.5	39.8 ^{a*} 39.7 $\pm$ 0.5	39.1 ^{a*} 39.2 $\pm$ 0.6	39 ^{a*} 39 $\pm$ 0.5	41.7 41.5 $\pm$ 0.5	41.5 ^b 41.5 $\pm$ 0.4	40.6 ^{b*} 40.5 $\pm$ 0.6	40.2 ^{b*} 40.3 $\pm$ 0.4	40 ^{b*} 40 $\pm$ 0.5					

BUTISO: butorphanol + isoflurane; MEDISO: medetomidine + isoflurane; Pm: parameter; Gr: group; T0: pre-injection baseline; PRE10: 10 min after preanesthetic administration; ISO10, ISO20, ISO30: 10, 20, and 30 min after isoflurane administration. HR: heart rate; SAP: systolic arterial pressure; DAP: diastolic arterial pressure; MAP: mean arterial pressure; RR: respiratory rate; SpO₂: oxygen saturation; EtCO₂: end-tidal carbon dioxide; CT: cloacal temperature. Values within the same row marked with an asterisk (*) indicate statistically significant differences compared to T0 ($P < 0.05$). Values within the same row with different superscript letters (^{a-b}) indicate statistically significant differences between groups ($P < 0.05$).

ISO20 and ISO30. The EtCO₂ value was found to be statistically significant in the MEDISO group at the ISO20 and ISO30 time intervals in compared with T0. A significant decrease in cloacal temperature was indicated at ISO10, ISO20 and ISO30 in both groups ($P < 0.05$). Cardiopulmonary evaluations of both groups at all time intervals are presented in TABLE I.

In light of the growing avian population, there is an increasing need for reliable and balanced anesthesia protocols. This study represents a comprehensive and pioneering investigation in which BUTISO and MEDISO, anesthetics currently employed in other animal species, were comparatively evaluated for cardiopulmonary, haematological, and biochemical values as well as reflexes in pigeons. The objective of the present research was to contribute to the development of an anesthetic protocol that can be applied to pigeons and to support further research on other avian species.

Uzun *et al.* [21], studied the effects of IM MED (200 µg/kg) on electrocardiographic findings, body temperature, respiration and heart rate by administering IM ketamine (120 mg/kg) to pigeons 10 min after administration. The study reported that MED administration resulted in a gradual decrease in body temperature and sudden decrease in heart rate, which as statistically significant at 10 min. This decrease persisted with ketamine administration. In this study, Following MED administration, a notable reduction in respiratory rate was detected at the 10-min mark. However, a notable increase in RR was reported following ketamine administration [21]. Anjana *et al.* [7], evaluated the efficacy of four anesthetic regimens in avian patients: ISO (induction 3-4 % and maintenance 1-2.5 %), sevoflurane (induction 5-7 % and maintenance 3-4 %), BUT (1.5 mg/kg, IM) + ISO (induction 3-4 % and maintenance 1-2.5 %), and BUT (1.5 mg/kg, IM) + sevoflurane (induction 5-7 % and maintenance 3-4 %).

The study revealed that the reduction in heart rate, respiratory rate and cloacal temperature was less pronounced in avian exposed to BUT + ISO and BUT + sevoflurane than in those administered ISO and sevoflurane alone [7].

In a study conducted by Granone *et al.* [1], investigated the physiological responses of red-tailed hawks to different volatile anesthetics (ISO, sevoflurane and desflurane). It has been reported that ISO causes a lower RR (17 ± 7), heart rate (207 ± 51), and CT (39.9 ± 0.8), and there was no statistically significant dissimilarity between the other agents. In the present study, the number of heart-beats decreased after BUT and MED administration. This decrease was abrupt, similar to that reported in studies involving MED administration. It is postulated that this is due to the greater depressive effect of MED on the cardiovascular system [22]. As documented in the literature, the cloacal temperature exhibited a notable decline in both groups over time.

Similarly, a reduction in the RR was observed in all groups, with a notable decrease occurring in the MED administration group. Thus, MED had a greater depressive effect on respiration. In contrast to the findings of Uzun *et al.* [21], who observed an increase in this value with Ketamine administration following MED administration, the present study demonstrated a continued

decrease with ISO administration. This indicated that different drug combinations have disparate effects on respiration. In addition, the RR recorded in this study exceeded that in the ISO-treated red-tailed hawks. This may be attributed to the fact that different avian species possess disparate physiological characteristics [16].

The aim of the study by Joyner *et al.* [23], was to investigate the induction and cardiopulmonary effects of two different inhalation agents in bald eagles. In this study, the authors observed a considerable increase in SAP, DAP and MAP following the administration of ISO and sevoflurane. Conversely, Escobar *et al.* [24], reported a considerable decrease in SAP, DAP and MAP parameters in a crested caracara following the administration of ISO, compared to the pre-induction values ($P < 0.05$).

The present study demonstrated distinct cardiovascular responses between the anesthetic protocols. In the BUTISO group, SAP, DAP, and MAP increased following BUT administration and remained elevated during the early stages of ISO anesthesia. In contrast, MED administration produced a marked reduction in arterial blood pressure parameters, consistent with the known cardiovascular depressant effects of α_2 -adrenoceptor agonists [8]. Although blood pressure values in the MEDISO group tended to increase after ISO administration, they remained lower than those observed in the BUTISO group. These findings suggest that MED exerted a stronger influence on cardiovascular function than BUT under the conditions of the present study.

End-tidal CO₂ values remained lower throughout the study compared with baseline measurements, particularly in the MEDISO group. These findings differ from those reported by Botman *et al.* [8], who observed increased EtCO₂ concentrations during ISO anesthesia in pigeons. Variations in anesthetic protocols, monitoring techniques, and individual physiological responses may account for these discrepancies. The lower EtCO₂ values observed in the present study may reflect differences in ventilatory patterns induced by the preanesthetic agents.

It has been previously documented that the administration of ISO has been observed to results in a reduction in SpO₂ values in avians [25]. In the present investigation, a decrease was observed in the MEDISO group, whereas an increase was observed in the BUTISO group. It can be posited that the administration of BUT in pigeons may elicit disparate effects on the SpO₂ value.

Several limitations of the present study should be acknowledged. The relatively small sample size may have limited the statistical power to detect subtle differences between treatment groups. Furthermore, only healthy adult pigeons were included, which may restrict the extrapolation of the findings to other avian species, age groups, or birds with clinical disorders. Additionally, the evaluation period was confined to the anesthetic phase, and recovery characteristics were not comprehensively assessed. Future studies involving larger sample sizes, different avian species, and detailed recovery evaluations are warranted to further establish the safety and clinical applicability of these anesthetic protocols.

The hematological and biochemical parameters of both groups at the specified time points are presented in TABLE II.

The hematological findings demonstrated that RBC values decreased in both groups throughout the anesthetic period, although statistical significance was observed only in the BUTISO group. Similar reductions in RBC and HGB values have previously been reported in birds anesthetized with ISO [9]. The decrease in erythrocyte-related parameters may be associated with transient hemodilution, splenic sequestration, or physiological responses to anesthesia. However, the exact mechanism remains unclear and warrants further investigation.

In contrast to the findings of Sani and Onifade [13], who reported increased RBC counts following MED administration in pigeons, the MEDISO group in the present study showed a mild decline in RBC values. Differences in dosage, drug combinations, sampling time, and experimental conditions may explain these discrepancies.

WBC values exhibited a gradual decline in both groups, although these changes were not statistically significant. Similar observations have been reported in avian studies involving inhalation anesthesia [9]. The modest reduction observed in the present study may reflect transient physiological alterations associated with anesthetic exposure rather than clinically relevant hematological disturbances.

Biochemical analysis revealed relatively stable ALT and GLU concentrations throughout the study. Although AST values

increased in the MEDISO group at ISO30, the magnitude of change was limited and remained within the range reported in previous avian anesthesia studies. Consequently, the observed biochemical alterations suggest that both anesthetic protocols exerted only minor short-term effects on hepatic and metabolic parameters under the conditions of this study.

Overall, the hematological and biochemical findings indicate that both anesthetic combinations were generally well tolerated in healthy pigeons. Nevertheless, additional studies involving larger sample sizes and longer monitoring periods are needed to determine the clinical significance of the observed changes and their potential implications for diseased or compromised birds.

Reflex values for both groups are presented in FIGS. 1 and 2. Reflex evaluation showed that MEDISO produced a more pronounced and faster reduction in reflex responses compared with BUTISO. An early decrease in reflex activity was observed at PRE10 in both groups, and by ISO10 most pigeons exhibited marked reflex suppression, with a stronger effect in the MEDISO group.

TABLE II

Hematological and biochemical parameters of pigeons administered butorphanol + isoflurane and medetomidine + isoflurane, presented as median and mean $\pm$ SD at designated time points.

Gr	BUTISO			MEDISO		
Pm	T0 median mean $\pm$ SD	PRE10 median mean $\pm$ SD	ISO30 median mean $\pm$ SD	T0 median mean $\pm$ SD	PRE10 median mean $\pm$ SD	ISO30 median mean $\pm$ SD
WBC(10^3 /ul)	241 239 $\pm$ 26	237 232 $\pm$ 22	228 227 $\pm$ 29	257 250 $\pm$ 28	237 232 $\pm$ 22	228 227 $\pm$ 29
RBC(10^6 /ul)	3.4 3.3 $\pm$ 0.6	2.7 ^{a*} 2.5 $\pm$ 0.5	2.1 ^{a*} 2.4 $\pm$ 0.8	3.6 3.5 $\pm$ 0.2	3.5 ^b 3.3 $\pm$ 0.3	3.4 ^b 3.3 $\pm$ 0.2
HGB(g/dL)	21 19.8 $\pm$ 5.1	20 ^a 18.8 $\pm$ 4	19.8 20.9 $\pm$ 6.3	24.9 24.2 $\pm$ 2	23.9 ^b 22.8 $\pm$ 2.3	23.2 22.5 $\pm$ 2
HCT(%)	50.3 48.3 $\pm$ 9	45.5 ^a 42.9 $\pm$ 8	39.7 42.6 $\pm$ 13	58.4 57.3 $\pm$ 4	54.3 ^b 52.4 $\pm$ 4	53.1 52 $\pm$ 3
AST(U/L)	98 92 $\pm$ 24	90 102 $\pm$ 35	116 105 $\pm$ 34	81 84 $\pm$ 24	105* 109 $\pm$ 33	107* 109 $\pm$ 40
ALT(U/L)	15 14 $\pm$ 3	14 19 $\pm$ 12	18 20 $\pm$ 9	15 14 $\pm$ 4	19 20 $\pm$ 5	22 20 $\pm$ 4
GLU(mg/dL)	351 344 $\pm$ 43	333 345 $\pm$ 28	369 370 $\pm$ 30	358 367 $\pm$ 42	329 337 $\pm$ 38	313 348 $\pm$ 57

BUTISO: butorphanol + isoflurane; MEDISO: medetomidine + isoflurane; Pm: parameter; Gr: group; T0: pre-injection baseline; PRE10: 10 min after preanesthetic administration; ISO30: 30 min after isoflurane administration. WBC: white blood cell; RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GLU: glucose. Values within the same row marked with an asterisk (*) indicate statistically significant differences compared to T0 ($P < 0.05$). Values within the same row with different superscript letters (^{a-b}) indicate statistically significant differences between groups ($P < 0.05$).

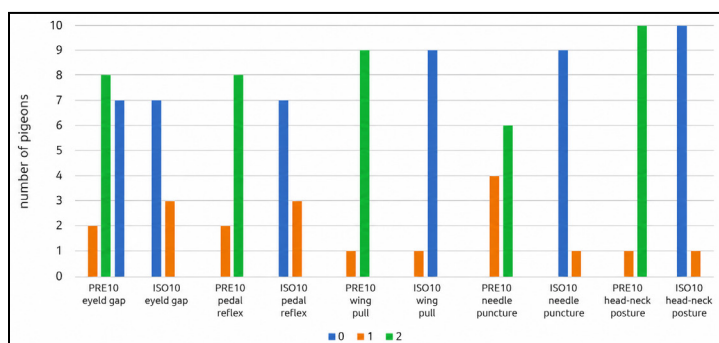


FIGURE 1. Reflex responses of pigeons administered butorphanol + isoflurane (BUTISO) at different time intervals. The number of pigeons that responded to the different reflexes is shown. eyelid spacing, pedal reflex, wing pulling reflex, response to needle picking, and head and neck posture. 0: No response to stimuli; 1: very little and partial response to stimuli; 2: vivid and responsive to stimuli.

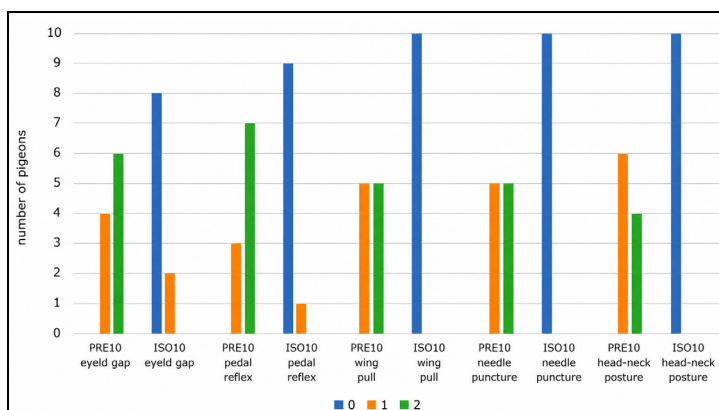


FIGURE 2. Reflex responses of pigeons administered medetomidine + isoflurane (MEDISO) at different time intervals. The number of pigeons that responded to the different reflexes is shown. eyelid spacing, pedal reflex, wing pulling reflex, response to needle picking, and head and neck posture. 0: No response to stimuli; 1: very little and partial response to stimuli; 2: vivid and responsive to stimuli

This difference may be related to the potent central sedative and analgesic effects of MED as an $\alpha 2$ -adrenergic agonist, whereas BUT provides only moderate sedation through opioid receptor activity. These pharmacological differences likely explain the greater reflex depression observed in the MEDISO group. Similar findings have been reported in previous avian studies, where preanesthetic agents improved induction quality and reduced reflex activity during ISO anesthesia [26, 27, 28].

CONCLUSION

The combinations of BUTISO and MEDISO may be considered for use in minimally invasive and surgical procedures requiring anesthesia in avian species. However, based on the observed cardiopulmonary responses, the BUTISO protocol may be preferable in birds with underlying cardiopulmonary or systemic conditions, as it was associated with comparatively more stable physiological parameters.

Conflicts of interest

There are no conflicts of interest to declare, as confirmed by the authors.

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Ethical Statement

The present study was conducted following the approval of animal experimentation by the Harran University Local Ethics Committee (HRU HADYEK; Decision number: 2022/003/05, 01-06).

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