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ORIGINAL ARTICLE

# Histopathological and Serum Enzyme Changes of Propofol Combined with Pre-Anesthetic Agents in Domestic Pigeons (*Columba livia*)

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## Abstract

**Objective-** Because of the several differences between avian and mammalian physiology and anatomy, avian anesthesia requires to be more attentive. The aim of this study was to determine a safe injectable anesthetic agent that had more compatibility with the avian features.

**Design-** Experimental study

**Animals-** Twelve male pigeons

**Procedure-** The pigeons weighing 302±35 g (mean ± SD) were divided into two groups (n=6). In group 1, midazolam (6 mg/kg,-IM) and in group 2, metamizole (500 mg/kg,-IM) were administrated as the pre-anesthetic agents and thereafter, propofol (8 mg/kg,-IV) was injected as the main anesthetic drug in both groups. The serum enzymatic changes were analyzed before and 1 hour after the last injection. Histopathological examinations of the liver and kidneys were also evaluated in terms of possible damages to the tissue.

**Results-** The results of blood biochemistry evaluation in group 1 showed significant changes in the levels of AST and LDH before and after the injections ($p<0.05$). Histopathology results revealed significant changes in liver parameters in both groups. However, these changes were seen more prominent in group 1 ($p<0.05$). Also, none of the drugs of both groups had a negative impact on the kidney tissue ($p>0.05$).

**Conclusion and clinical relevance-** Based on the results, metamizole and propofol combination showed that is safer than midazolam and propofol in terms of blood biochemical and histopathological evaluations and is more compatible with pigeons.

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## 1. Introduction

Based on the unique anatomical features of avian, the best type of anesthesia should provide the least physiological changes, the highest therapeutic index as well as rapid induction and recovery in these animals. Anatomical conditions such as absence of diaphragm in some species, correct positioning during anesthesia for having a better oxygenating, less volume of pectoral muscles in some species such as Anseriformes and Galliformes that can affect ventilation along with the respiratory and cardiovascular evaluations should be considered as the major factors in avian anesthesia.[1] Some of the significant points in the physiology of birds have high sensitivity to $CO_2$ changes that can cause apnea or decreasing in body temperature due to more metabolism during anesthesia and also decrease in glucose level.[2] The most complication that may occur during or subsequent to the anesthesia is relevant to the respiratory and cardiovascular systems. In addition, as cardiac output decrease during anesthesia, in cases with air sac damage, respiratory distress is possible which could be important in inhalation anesthesia.[3]

Although it is possible to carry out both injectable and inhalation protocol according to the animal condition and the existing equipment, inhalation anesthesia has more benefits and safety in birds but the high cost of implementing or its limitation in some surgeries such as respiratory tract, beak, or trachea should be considered. Meanwhile, by damaging to the air sacs or breaking the pneumatic bones during surgery and therefore releasing the anesthetic gas, the health of the operating room staff may fall in danger. Thus, the necessity of using the injectable protocol in these situations is meaningful and the correct choice of the drug and the type of anesthesia should be used.[4]

Sodium metamizole or dipyrone has a mechanism similar to the non-steroidal anti-inflammatory drugs (NSAIDs) and induces its effects by preventing the synthesis of prostaglandin. Metamizole has the ability to pass through the placenta. In combination with phenothiazines, it creates hypothermia and is contraindicated. No cardiovascular complications have been reported but in the prolonged and inappropriate dose, it could cause hypoxia in birds.[5] Benzodiazepines have a rapid onset of action and metabolism in birds. These drugs can have analgesic, anesthetic and muscle relaxant effects. Propofol, chemically named 2,6-diisopropyl phenol, is classified as alkyl phenols. The rapid metabolism, non-irritating to the tissue and pH between 6 to 8.5 are some of the well-known features of propofol. It is used in most of the animals with or without pre-anesthetic and it is also considered as an induction agent in inhalation anesthesia.[6,21] This drug has a very rapid onset of action and must be injected slowly and intravenously. According to the studies, the dose of it in birds varies from 4 mg/kg to 14 mg/kg. It can also be injected as an infusion at a rate of 1 mg/kg/min.[7,8]

Based on the different effects of anesthetic drugs on the liver and kidneys, necropsy can be a reliable diagnostic method for investigating the possible side effects on these organs. Nonetheless, non-invasive methods such as the evaluation of blood biochemical parameters can also be helpful. Serum parameters such as total protein, lactate dehydrogenase, alkaline phosphatase and aspartate aminotransferase can provide valuable information on liver damage. The aim of this study was to determine an injectable anesthetic agent with the least adverse effects along with most safety in pigeons by evaluating blood biochemical and histopathological effects of midazolam-propofol and metamizole-propofol particularly when using of inhalation protocols are contraindicated.

## 2. Materials and Methods

This experimental study was carried out under the supervision of the Ethics Committee of the Faculty of Veterinary Science, Science and Research Branch of Tehran, Islamic Azad University (license No. 5478). In this study, 12 male pigeons aged 1 to 2 years old with a weight of 302 ± 35 grams were used. Prior to this experiment, all birds were kept in the same condition and also were

avoided to intake food for four hours and water for one hour. The health status of all pigeons was controlled in terms of heart rhythm, respiration and mucous membrane color. The pigeons were divided into the two groups (n=6). In the first group, Midazolam (Dormicum, Caspian Tamin, Iran) with a dose of 6mg/kg as a pre-anesthetic were injected intramuscularly in pectoral muscle. After 5 minutes, 8 mg/kg of propofol (Provine, Claris, India) was injected intravenously in the brachial vein. In the second group, 500 mg/kg of metamizole (Novasoul, Apomedia, Austria) were administrated intramuscularly and after five minutes propofol was injected the same as the first group.

### *Biochemical assessment scale*

The blood samples were collected 1 ml before the birds were anesthetized (baseline) and at 1 hour after last injection by IV catheter (gauge No. 26) placed into the brachial vein.[32] Then the sample of each one of the birds transferred into the lithium heparin tubes (BD Vacutainer). On each tube, group number, date and time of the sampling were recorded. Then they were centrifuged (Eppendorf centrifuge 5810 R, Hamburg, Germany) at a speed of 1300 rpm for six minutes.[37] After separation of plasma, the samples were placed immediately in an autoanalyzer machine (BT-1500 Biotechnica instruments, Rome, Italy). The required laboratory kits were all made by Bionic Co. (USA). Then blood biochemical parameters include alkaline phosphatase (ALP), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), total protein (TP) and glucose (GLU) were measured and recorded.

### *Histopathological assessment scale*

In order to histopathological examinations, after being reassured for complete recovery, all birds were euthanized by cervical dislocation method 24 hours after completion of the experiment.[9] Tissue samples that were collected from liver and kidneys, fixed in 10% buffered neutral formalin, cut into 5 µm in thickness and then stained by hematoxylin-eosin (H&E) staining method. Based on the grade of damages to the kidneys and liver tissue, qualitative data turned into quantitative according to the guidelines presented in Table 1. [10,11]

***Table 1.*** Histopathological scoring scale for liver and kidneys.

| Tissue | Parameter | Evaluation criteria | Score |
|---|---|---|---|
| **Liver** | Vacuolar Degeneration | Less than 5% | 1 |
| | | 5 to 33% | 2 |
| | | 33 to 66% | 3 |
| | | More than 66% | 4 |
| | Necrosis | Lack of necrosis | 1 |
| | | 1 to 3 necrotic cell/s | 2 |
| | | 3 to 6 necrotic cells | 3 |
| | | More than 6 necrotic cells | 4 |
| | Inflammation and increased kupffer cells | Lack of inflammation | 1 |
| | | Mild | 2 |
| | | Moderate | 3 |
| | | Severe | 4 |
| **Kidney** | Granular or Hyaline casts | Lack of casts | 1 |
| | | Mild | 2 |
| | | Moderate | 3 |
| | | Severe | 4 |
| | Necrosis | Lack of necrosis | 1 |
| | | 1 to 3 necrotic cell/s | 2 |
| | | 3 to 6 necrotic cells | 3 |
| | | More than 6 necrotic cells | 4 |
| | Interstitial nephritis | Lack of inflammation | 1 |
| | | Mild | 2 |
| | | Moderate | 3 |
| | | Severe | 4 |

### *Statistical analysis*

In this study, all statistical analyses were performed by SPSS version 22. Biochemical data were analyzed by the Wilcoxon test. Kruskal-Wallis test was used to analyze histopathological changes and also to compare the results between two groups. The significance rate was considered as $p<0.05$.

## 3. Results

### *Biochemical assessment results*

In group 1, ALP increased while GLU and TP decreased but these changes were not significant ($p>0.05$). Also, AST

and LDH were significantly increased in this group ($p$<0.05). In group 2, an insignificant increase in case of ALP, AST and LDH and insignificant decrease in GLU and TP were recorded ($p$>0.05) (Table 2).

### *Histopathology assessment results*

#### *Liver tissue*

The liver histopathological changes were included severe vacuolar degeneration and mild coagulative necrosis in both groups. Also, mild to moderate inflammation and kupffer cells aggregation was recorded in group 1 while this parameter was seen as a mild level in group 2. There were significant differences in terms of necrosis and increased kupffer cells between two groups ($p$<0.05), while the differences of vacuolar degeneration were not significant ($p$>0.05) (Figures 1 and 2) (Table 3).

#### *Kidney tissue*

Microscopic findings of renal tissue showed no changes in both groups. The entire structure of tissue such as tubules were seen normal and obviously detectable (Figure 3 and 4) (Table 3).

## 4. Discussion

In birds, both inhalation or injection anesthesia can be used. Inhalation anesthesia is a safe and effective protocol which benefits from quick recovery and measuring the level of anesthesia. Although not only use of this type of anesthesia requires advanced equipment, there is also the risk of exposure of the operating room personnel to anesthetic gases, which can be a health hazardous [13,14,15], but also it is not operational in some clinical conditions such as surgeries of beak, oropharynx or trachea.[16] Therefore, in these cases, injectable protocols will be selective methods and are most commonly used in birds.[17] Previous studies have suggested the use of pre-anesthetic drugs with propofol to reduce the dose and, more importantly, to reduce side effects.[18,19] In the present study, in order to determine a compound which has more compatibility with the bird's body condition accompanied with less pathological and enzymatic changes, propofol dose was adjusted through the use of pre-anesthetic drugs. Metamizole and midazolam were used in groups 1 and 2 respectively and their effects in composition with propofol on blood biochemistry parameters and liver and kidney tissue were studied.

***Table 2.*** Results (mean ± SD) of biochemistry evaluation at prior to the anesthesia (Pre) and one hour after anesthesia (Post)

| Parameter | Reference range[12] | Group | Pre | Post | *p*-value |
|---|---|---|---|---|---|
| **ALP (U/L)** | 160-780 | 1 | 189.55 ± 279.33 | 192.970 ±313.33 | 0.083 |
| | | 2 | 104.823 ± 336 | 110.217 ± 348 | |
| **AST (U/L)** | 45-123 | 1 | 20.954 ±85.33 | 20.855 ± 128.33 | 0.046 * |
| | | 2 | 22.512 ±88 | 21.701 ±101.66 | |
| **GLU (mg/dl)** | 232-369 | 1 | 36.526 ± 304.83 | 15.845 ± 289.66 | 0.345 |
| | | 2 | 26.053 ±292 | 27.092 ±282.16 | |
| **LDH (U/L)** | 30-205 | 1 | 42.625 ± 143.66 | 50.305 ± 228.83 | 0.028 * |
| | | 2 | 64.264 ± 112.66 | 59.948 ± 157.16 | |
| **TP (g/dl)** | 2.1-3.5 | 1 | 0.611 ± 2.83 | 0.515 ±2.95 | 0.416 |
| | | 2 | 0.307 ± 2.78 | 0.511 ±2.85 | |

(*) significant if $p$<0.05.

***Table 3.*** Results of histopathological changes of the liver and kidney in both groups

| Tissue | Parameter | Group | Mean ± SD, n=18 | *p*-value |
|---|---|---|---|---|
| **Liver** | Vacuolar degeneration | 1 | 3.66 ± 0.816 | 0.053 |
| | | 2 | 3.33 ± 0.816 | |
| | Necrosis | 1 | 1.83 ± 0.408 | 0.043 * |
| | | 2 | 1.33 ± 0.632 | |
| | Inf. Incr. K | 1 | 2.66 ± 0.516 | 0.024 * |
| | | 2 | 1.83 ± 0.408 | |
| **kidney** | Granular or hyaline casts | 1 | 1 ± 0 | 1 |
| | | 2 | 1 ± 0 | |
| | Necrosis | 1 | 1 ± 0 | 1 |
| | | 2 | 1 ± 0 | |
| | Interstitial nephritis | 1 | 1.16±0.408 | 0.588 |
| | | 2 | 1.16±0.408 | |

Inf. Incr. K: inflammation and increased kupffer cells. (*) significant if $p<0.05$.

Although there are few studies on metamizole in birds, this drug is used as a pre-anesthetic in different animals. In addition, due to the fact that metamizole has a strong anti-fever and anti-inflammatory effects, theoretically, it has the advantage of initiating the effect of analgesia and muscle relaxation immediately after injection.[20] The active substance is sodium metamizole and its mechanism is similar to the non-steroidal anti-inflammatory drugs (NSAIDs). According to some studies, it balances ALT in the liver and makes AST to be increased due to the high synthesis of adenosine and high energy production. In serological studies, this drug does not significantly change hemoglobin and renal factors and does not conduct any toxic effects on the normal function of the liver and kidneys at the appropriate dose and for a short time. Metabolism of metamizole is in the liver and excreted via the kidneys.[21]

Benzodiazepines act on GABA receptors and have a half-life of about one hour, a rapid onset of action and metabolism in birds. Long-term use of these drugs has a devastating effect on the kidney and can interfere with the function of the cardiovascular system. Benzodiazepines are water soluble and are used both intravenously and intramuscularly. These drugs can have better effects if they use with opioids as pre-anesthetics.[22]

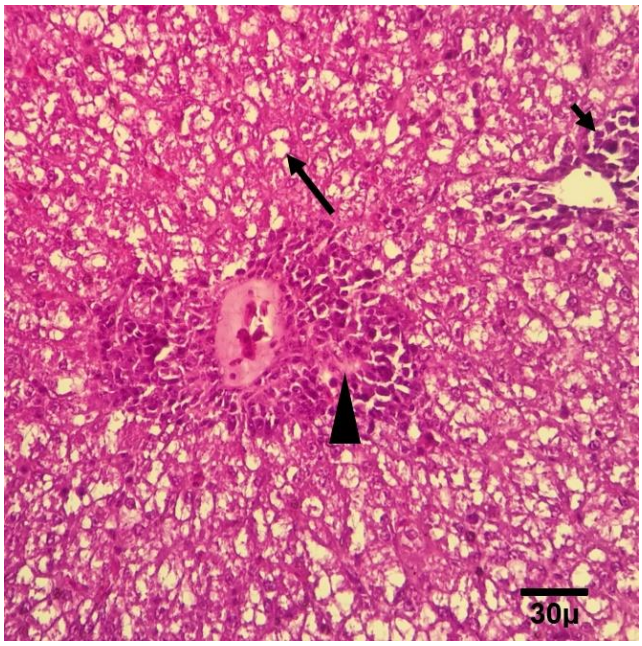


***Figure 1.*** Liver of group 1; Severe vacuolar degeneration (long arrow), mild coagulative necrosis (arrowhead) along with mild to moderate inflammatory cells infiltration (top arrow), (H&E).

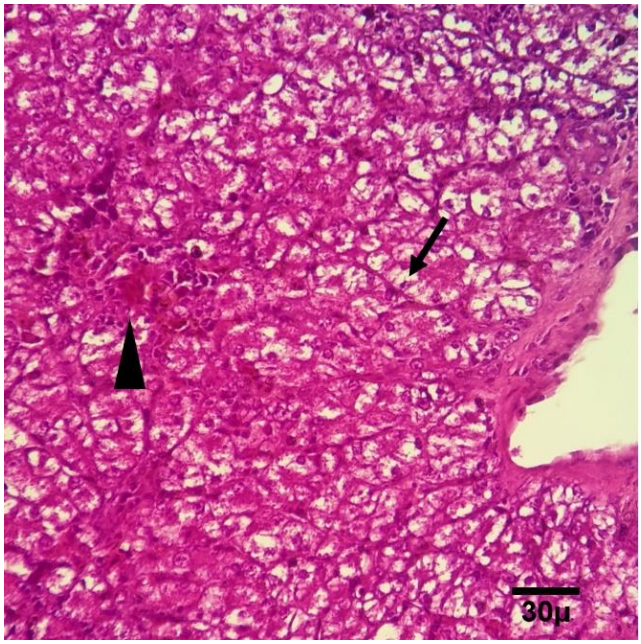


***Figure 2.*** Liver of group 2; Severe vacuolar degeneration (arrow), mild leukocytes infiltration and coagulative necrosis (arrowhead) (H&E).

Propofol is an analgesic and anesthetic drug in humans, animals and various species of birds.[23] This drug is classified as an alkyl-phenol and has a rapid metabolism. Its half-life is short and according to various studies is between 1 and 12 minutes. This drug exacerbates the inhibitory effect of GABA and also strengthens the

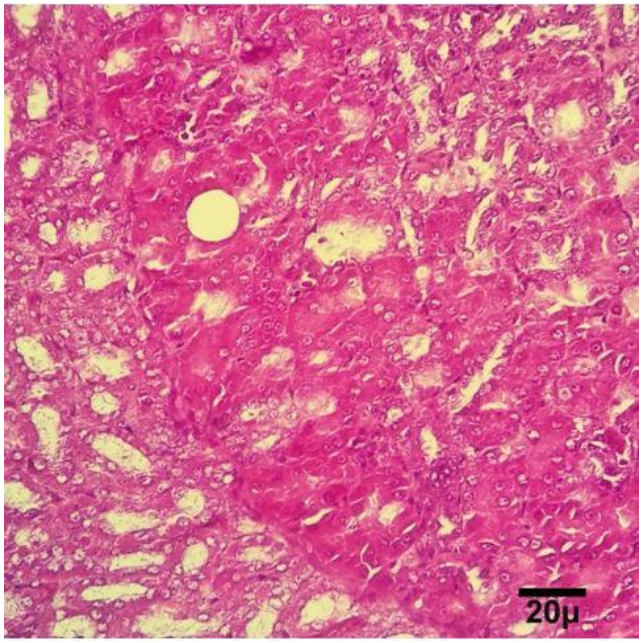


***Figure 3.*** Kidney of group 1; Normal tissue including tubules and the interstitium without inflammation or necrosis (H&E).

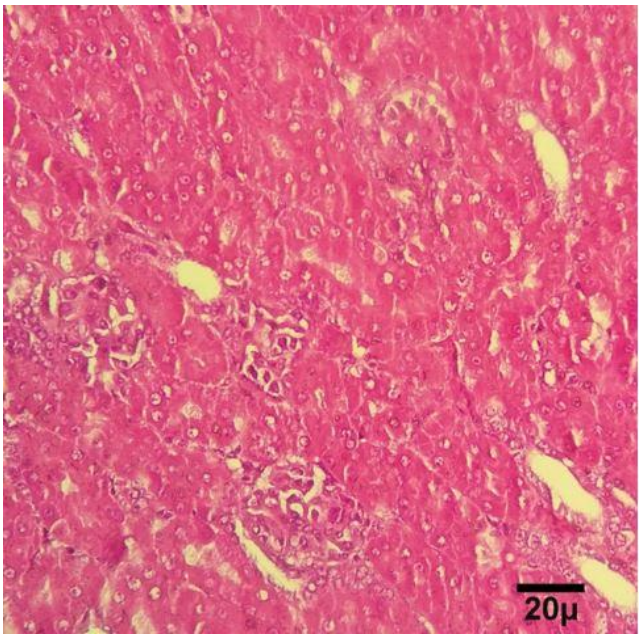


***Figure 4.*** Kidney of group 2; Normal tissue including tubules and the interstitium without inflammation or necrosis (H&E)**.**

glycinergic neuronal transfer in the central nervous system and the spinal cord to create a sedative, analgesic and anesthetic condition. Its metabolism is in the liver and is excreted through the kidneys. Given that propofol can increase liver blood flow, its distribution in other tissues, such as lungs, can be important. This drug has a fast recovery and there is no residual or accumulation in the body. Although propofol has the least effect on blood pressure, it reduces the amount of ventilation, and the most common side effects are on the respiratory system which includes apnea, bradypnea, and respiratory depression. In some rare cases, bradycardia and low blood pressure have been reported.[7] Biochemical and hematological parameters can provide valuable information about controlling and evaluating the disease process, assessing the immune status, and in addition to various environmental, nutritional and pathological effects. There are few studies on the biochemical and histopathological effects of propofol in different species of birds. In this study, blood samples were taken before anesthesia and one hour after the last injection to determine the serological effects of the drugs in each of the groups. The biochemical parameters evaluated in this study included ALP, AST, LDH, glucose and total protein. Alkaline phosphatase isozymes in birds and mammals have been identified in the cell membrane of the liver, kidneys, intestine and bone. The amount of alkaline phosphatase in adult birds is higher than that of chickens. Due to increased cellular activity in cases without cell damage, the level of this enzyme increases in serum. In addition, its rate does not increase with simple damage to hepatocytes. In the present study, ALP increased in both groups after anesthesia. Most of the changes were seen in group 1. Although, these changes were not statistically significant. In a study that evaluated the toxicity of metamizole in chickens, ALP levels were significantly increased.[24] While Priscilla *et al*.[25] reported that ALP levels decreased during anesthesia by isoflurane in American kestrels. The results of the study performed by Al-Sobail *et al*.[26] showed that there was no significant change in ALP levels in ostriches under anesthesia with ketamine, xylazine, and isoflurane. Regarding the increase in serum protein levels as it has been reported in laying hens, reproductive activities should be differentiated from dehydration and underlying inflammatory diseases. The reduction in total protein indicates the body's need for colloid supplements and it needs to look for its underlying cause such as nephropathy,

intestinal diseases, or hepatic impairment. Unlike mammalian, spleen in birds does not play an important role in protein degeneration.[14] Therefore, degeneration of protein in an organ other than the spleen may indicate a decrease in albumin and globulin in anesthetized birds. The results of this study showed that total protein decreased in both groups after anesthesia. This decrease was higher in group 2 but the level of these changes was not significant. The AST enzyme has activity in the liver, heart, skeletal muscle, brain and kidneys and moreover, is not a specific enzyme for hepatocellular damage but it has a high sensitivity to detecting these damage caused by ethylene glycol in pigeons. The enzyme level in liver damage, muscle and vitamin E and selenium deficiency may also increase.[27] If the increment of AST is accompanied by an increase in the creatine kinase, it will indicate muscle damage. The results of this study showed that AST increased in both groups after anesthesia. These changes were significantly higher in group 1. Given that all the birds were examined prior to the study and no muscle damage was observed, this could indicate that hepatocyte damage caused by the combination of midazolam and propofol. Clinicopathologic effects of carprofen on birds were evaluated in a study by Tawina *et al*.[28] in which AST and ALT levels increased significantly. The activity of the LDH is in the muscles, myocardium, liver, bone, kidneys and red blood cells. The reasons to increase enzyme levels are also hemolysis, liver necrosis and muscle damage. In avian, the increase or decrease in the level of this enzyme happens more rapid than the changes in AST. When the level of creatine phosphokinase is normal, increased levels of LDH can be a cause of liver damage. A reduction in LDH can be also seen in cases with severe liver damage. In a study by Michelle *et al*.[29], a significant increase in LDH was observed after anesthesia with halothane, which was the cause of the muscle damage that produced in domestic broiler chickens. In another study in monkeys, levels of LDH and CPK were increased by using isoflurane, ketamine and propofol. [30] The results of the present study represent an increase of LDH in both groups after anesthesia. However, the highest changes were related to group 1. Considering that no damage to the muscles and other organs was detected, it could be an indication of the short-term effects of the drugs used in this group on the liver. The level of normal blood glucose in most birds is between 200 and 450 mg/dl, and blood glucose less than 200 mg/dl is considered as hypoglycemia. Hyperglycemia occurs at the time of mating, stress, peritonitis and pancreatitis and hypoglycemia happens at the time of liver damage, fasting state and systemic diseases. Birds with diabetes usually have a blood glucose level higher than 700 mg/dl. A definitive diagnosis of diabetes is possible by measuring its blood glucose and rejecting the causes of transient hyperglycemia, such as stress or diet. In a study on ostriches, glucose concentration increased significantly after ketamine injection.[26] Hyperglycemic effects of $\alpha_2$ agonist drugs such as xylazine, which can increase the glucose-insulin ratio by stimulating glucose production in the liver, are known in birds. The cause of hyperglycemia during anesthesia can also be due to decreased plasma insulin production due to the effect of xylazine on the pancreas, which prevents insulin secretion without affecting the secretion of glucagon. In a study in red-tailed hawks, glucose level did not change significantly during anesthesia when ketamine used [31] while in the study of isoflurane effects on American kestrels, this drug significantly increased glucose level.[25] Same results were achieved in anesthesia with sevoflurane and isoflurane in crested serpent eagles. In the other study, blood glucose was significantly increased one hour after anesthesia due to the suppression of insulin secretion by the effect of isoflurane.[32] The results of the present study on glucose revealed an insignificant decrease in both groups after anesthesia in compare with awake status. This could indicate that all the drugs didn't have any impact on blood glucose. These results are consistent with the results of the studies that were carried out in the administration of carprofen[28] and halothane.[29] In the evaluation of

histopathologic results, all the combinations induced some hepatocellular changes. Sever vacuolar degeneration was seen in both groups while these changes were more prominent by midazolam and propofol. The coagulative necrosis and aggregation of kupffer cells were also seen in both groups but with more severity in group 1. Although components of both groups were induced hepatocellular damages but the effects of the drugs in group 2 were less than group 1. Also, it is thought that significant increase in AST an LDH level can be relevant to midazolam-propofol effects on liver tissue. Mulcahy *et al*.[33] reported histopathologic effects of propofol, bupivacaine and ketoprofen combination in Spectacled eiders and the results of kidney examination revealed a severe renal tubular necrosis with histopathologic changes more consistent with exposure to a nephrotoxin than with dehydration. Moreover, necrotic epithelium or contained proteinaceous casts were lined in renal tubules. Continuous infusion of propofol at large doses in rabbits could induce focal liver necrosis and acute tubular necrosis of the kidney while incipient inflammation of both liver and kidney were observed with sevoflurane.[34] Wallin *et al*.[35] have reported non-consistent pathologic or gross lesions with sevoflurane and halothane in the liver but just a vacuolization of parenchymal cells. Results of the pathologic effects of chloral hydrate, pentobarbitone, and urethane have been reported by Field *et al*.[36] which none of these agents had no remarkable histopathological changes in any of the abdominal organs. In the present study, histopathologic findings of the kidney showed that none of the drug combination used in both groups have any adverse effects on this tissue. Same result was achieved in a study in poultry that metamizole did not have any toxic effect on kidneys.[35] However, in the study of Lotfi *et al*., a mild necrosis of the renal tissue was reported in birds that were anesthetized with ketamine and metamizole.[37] Based on the results of present study, effects of both combinations on hepatic cells should be considered. However, metamizole-propofol posed less changes and more safety in compare with midazolam-propofol on serum enzymes and liver and kidney tissue in pigeons.

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## Conflict of interest

None.

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## چکیده

# تغییرات هیستوپاتولوژی و آنزیم‌های سرم به‌وسیله پروپوفول در ترکیب با داروهای پیش‌بیهوشی در کبوتر اهلی

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**هدف**- به دلیل تفاوت‌های زیاد فیزیولوژیک و آناتومیک بین پرندگان و پستانداران، بیهوشی در پرندگان نیاز به توجه بیشتری دارد. هدف این مطالعه تعیین یک ترکیب بیهوشی تزریقی ایمن که سازگاری بیشتری با بدن پرندگان داشته باشد در نظر گرفته شد.

**طرح مطالعه**- مطالعه تجربی

**حیوانات**- ۱۲ قطعه کبوتر بومی نر

**روش کار**- کبوترها با وزن ۳۰۲±۳۵ گرم در دو گروه شش‌تایی طبقه‌بندی شدند. در گروه اول، میدازولام (۶ میلی‌گرم/کیلوگرم، داخل عضلانی) و در گروه دوم، متامیزول (۵۰۰ ۶ میلی‌گرم/کیلوگرم، داخل عضلانی) به‌عنوان داروی پیش‌بیهوشی تزریق گردیدند و پس‌ازآن، پروپوفول (۸ ۶ میلی‌گرم/کیلوگرم، داخل وریدی) به‌عنوان داروی بیهوشی اصلی در هر دو گروه تزریق شد. تغییرات آنزیم‌های سرمی خون در قبل از انجام بیهوشی و یک ساعت پس از آخرین تزریق مورد ارزیابی قرار گرفت. همچنین آزمایش‌های هیستوپاتولوژی به جهت بررسی آسیب‌های احتمالی به بافت کبد و کلیه انجام شد.

**نتایج**- نتایج آزمایش‌های سرولوژی تغییرات معناداری در مقادیر آسپارتات آمینو ترانسفراز و لاکتات دهیدروژناز در قبل و بعد از آخرین تزریق را در گروه ۱ نشان داد ($p<۰/۰۵$). نتایج بررسی‌های هیستوپاتولوژی تغییرات معناداری را در هر دو گروه در خصوص پارامترهای کبدی نشان داد، اگرچه این تغییرات به‌طور بارزتری در گروه ۱ دیده شدند ($p<۰/۰۵$). همچنین هیچ‌کدام از ترکیبات دارویی دو گروه، اثرات منفی بر بافت کلیه نگذاشته بودند ($p>۰/۰۵$).

**نتیجه‌گیری و کاربرد بالینی**- بر اساس نتایج مطالعه، ترکیب متامیزول و پروپوفول در موارد بررسی‌های بیوشیمیایی خون و هیستوپاتولوژیکی از ترکیب میدازولام و پروپوفول ایمن‌تر است و سازگاری بیشتری با کبوترها دارد.

**واژه‌های کلیدی**: متامیزول، پروپوفول، میدازولام، بیهوشی کبوتر، آسیب‌شناسی