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[1]University of Kafkas
Faculty of Veterinary Medicine
Department of Surgery
Kars / Turkey

[2]University of Kafkas
Faculty of Veterinary Medicine
Department of Physiology
Kars / Turkey.

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[*]**Corresponding author**
Email:sadikyayla@gmail.com
Telefon: 0(474) 242 6800

Comparision of Intravenous and Intraosseous Administration of Propofol-Ketamine Combination for Anesthesia in Quails (*Coturnix coturnix japonica*)[#]

Sadık YAYLA*[1], Nadide KAMİLOĞLU[2], Alkan KAMİLOĞLU[1], İsa ÖZAYDIN[1]

SUMMARY

This experiment was conducted to compare the use of intraosseous (IO) and intravenous (IV) propofol-ketamine combination on clinical and cardio-respiratory parameters. The experiment was carried out on twenty clinically healthy mature male quails (*Coturnix coturnix japonica*). Quails divided into two groups. The first group (n=10) received 10 mg/kg Propofol-30 mg/kg Ketamine IV and second group (n=10) received 10 mg/kg Propofol-30 mg/kg IO. Each quail were monitored for heart rate, respiratory rate, cloacal temperature and electrocardiography. While the duration time of anesthesia in IV group was significantly shorter than IO group ($p<0.05$), no significant differences were recorded as regard the onset of anaesthesia in two groups. There were no significant differences obtained in heart rate (HR), respiratory rate (RR) and cloacal temperature (CT) between groups in recorded time points during anesthesia. Intraosseous administration of propofol-ketamine combination was seen as an alternative route to intravenous way, for it was shown similar changes in both IV and IO group in terms of clinical and physiological parameters. Moreover, use of propofol-ketamine combination for induction and maintenance of anesthesia was safe and reliable anesthetic combination that can be effectively used for quails.

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Bıldırcınlarda (*Coturnix coturnix japonica*) Anestezi için Propofol-Ketamine Kombinasyonunun İntravenöz ve İntraosseöz Uygulanmasının Karşılaştırılması

ÖZET

Bu çalışmada propofol-ketamin kombinasyonunun intravenöz (IV) ve intraosseal (IO) yolla uygulamasıyla klinik ve kardiyo-respiratorik parametreler üzerine olan etkileri karşılaştırılmıştır. Çalışma klinik olarak sağlıklı bulunan 20 adet erkek, olgun bıldırcın (*Coturnix coturnix japonica*) üzerinde yürütülmüştür. Bıldırcınlar iki gruba ayrılarak birinci gruba (n=10) 10 mg/kg Propofol-30 mg/kg Ketamin IV olarak uygulanırken ikinci gruba (n=10) ise 10 mg/kg Propofol-30 mg/kg Ketamin IO uygulandı. Her bir bıldırcın monitörize edilerek kalp atım sayısı (HR), solunum sayısı (RR), kloakal ısı (CT) ve elektrokardiyogramları (ECG) alınarak izlendi. Anestezi süresi IV grubunda IO gruptan önemli derecede daha kısa bulunurken ($p<0.05$), anestezinin başlangıç süresi açısından bir fark bulunmadı. Ayrıca gruplar arasında HR, RR, CT bakımından istatistiksel olarak anlamlı bir fark yoktu. Sonuç olarak propofol-ketamin kombinasyonunun IO yolla uygulanması IV yola bir alternatif olarak düşünülebilir. Çünkü klinik ve fizyolojik parametreler bakımından hem IV hem de IO gruptaki bulgular benzerlik gösterdi. Ayrıca, anesteziye giriş ve anestezi süresince propofol-ketamin kombinasyonu kullanımı kanatlı hayvanlar için bir model olarak düşünülen bıldırcınlarda da etkin bir biçimde kullanılabilecek bir anestezik kombinasyonu olarak düşünülebilir.

INTRODUCTION

Propofol, as a week analgesic, has been used to ensure prompt recovery and minimal side effect, patient comfort, safety and immobility before anesthesia. Also, it tends to depress hemodynamic parameters and dose dependant respiratory depression. On the other hand, it has the advantages of functioning as an antiemetic, and an anticonvulsant and amnestic agent (Langan et al 2000, Machin et al 2000, Mendes and Selmi 2003, Miller et al 2005, Morse et al 2003). Ketamine, a dissociative anesthetic, is one of the most preferred injektable anesthetic agents that provide excellent analgesia and amnesia (Azizpour and Hassani 2012, Brickman et al 1992, Mortero et al 2001, Yayla et al 2012). Despite its obvious advantages over other agents, the use of ketamine alone causes significant adverse effect include poor muscle relaxation, muscle tremors, myotonic contractions, and rough recoveries. Therefore, to mitigate its side effects, ketamine is also recommended for use in combination with propofol (Mortero et al 2001, Tomatir et al 2004, Umar et al 2006, Yayla et al 2012).

Combination of propofol and ketamine has been use successfully in a variety of surgical interventions obtained short-term anesthesia in mammalian species (Langan et al 2000, Sakai et al 2000, Tomatir et al 2004, Umar et al 2006). This combination has been favored because of the opposing hemodynamic and respiratory effect of each drug. It was reported that propofol-ketamine combination was safe and effective for surgical procedures and believed to result in less toxicity than either drug alone. Cardiopulmonary effect of each are opposing in action, thus theoretically balancing each other when use together. Also, researchers suggest that using propofol-ketamine combination might enhance hemodynamic stability and decrease respiratory depression (David and Shipp 2011, Mortero et al 2001, Tomatir et al 2004).

As propofol is an intravenous agent, use of propofol-ketamine combination has been preferred via intravenously in studies (Machin et al 2000, Mendes and Selmi 2003, Miller et al 2005, Morse et al 2003, Mortero et al 2001) to produce anesthesia. However, intravenous administration of anesthetics are generally difficult to implement, intramuscular, subcutan or intraosseal (Azizpour and Hassani 2012, Durrani et al 2012, Eyarefe et al 2012, Kamiloglu et al 2008, Machin et al 2000, Valverde et al 1993) route is preferred way to induce anesthesia in birds. An alternative route to intravenous administration, intraosseous infusion (IO) is used to provide fluids, medication and anesthetic when intravenous input is not feasible. When intravascular input cannot be obtained, intraosseous input is usually the next approach. Besides, in recent years, the advantages of intraosseous injections have been reported by researchers (Kamiloglu et al 2008, Valverde et al 1993) in order to anesthesia in birds. But, studies regarding their use together for general anesthesia are limited in birds.

The objective of this study was to compare the use of propofol-ketamine combination via intraosseous and intravenous route and the chance on heart rate, respiratory depression and body temperature in quails.

MATERIALS AND METHODS

Twenty healthy mature (26 week old) male quails (*Coturnix coturnix japonica*) provided from animal farming department of Kafkas University were used with 201.9±8.78 g (as Mean±SD) body weight. The birds were adapted to their environment for a week before the study was started. Also, birds were withold in a clean and stress-free environment at a temperature of 25ºC with a 12-12 h light-dark cycle. All experiment were performed in quails deprived of food for 60 min, but allowed free access to water.

Study Protocols

The birds were categorized as two groups with intravenous (IV) and intraosseal (IO).

IV Group (n=10, BW= 202.8±9.22) was given combination of 10 mg/kg propofol (Propofol® %1, 20 ml ampul, Fresenious Kabi-Germany) and 30 mg/kg Ketamine (Ketalar® 10 ml injectable, Pfizer-Turkey) by insulin syringe to cutaneous ulnar vein. IO Group (n=10, BW=201.0±8.72) was administered 10 mg/kg propofol and 30 mg/kg Ketamine combination with insulin syringe to distal end of the left tibia. In both groups, propofol-ketamine was diluted 1:1 ratio with 0.9 % NaCl solution.

Depending the bird's size, 14 to 20 gauge spinal needles was used for intraosseous administration. The knee joint of quails laid on lateral recumbency was positioned at flexion under aseptic conditions. Needle has been inserted to medulla of tibia that parallel to the diaphysis defined as radiological. Loss of resistance against the needle proved that needle was in medullary region.

Measurements

Heart rate (HR), respiratory rate (RR), cloacal temperature (CT) and ECG were recorded for each quail before drug administration and at the

1, 3, 5, 10, 15, 20, 30, 40 and 50th minutes after injection. A multi-parametric monitor (Veterinary Monitor® MMED6000DP S6-V, MVM-Hamburg, Germany) was used for these measurements.

Assessment of the clinical effect of anaesthesia

Depth of anesthesia was assessed by monitoring response to standard painful stimuli as pin-prick and sensory function as righting reflex, feather plucking reflex, palpebral reflex, pharyngeal reflex and eyelid status.

Records of quails in all groups were kept in terms of the induction period, duration of anaesthesia and recovery period.

Tested stimuli and sensory function after anesthetic application for each quails observed as follows respectively;

Onset of anaesthesia was described as unconsciousness from administration to the stages of anaesthesia. Also, duration of anaesthesia was idendified from loss of consciousness to reappearance of sensory function. Standard painful stimuli used for this reason, performed in two ways as superficial (needle used to prick the skin) and deep pin-prick (needle inserted into the muscle). Needle was applied to muscle in different body parts such as neck, pectoral, wings and legs. Also, other body reflexes (righting reflex, feather plucking reflex, pharyngeal reflex) were recorded. In addition, eyelids scored as 0 for closed, 1 for half-opened and 2 for opened.

Statistical analysis

Data are presented as mean ± standard deviation (SD). The ANOVA method for One-way analysis of Variance and Post Hoc Tukey was used two detect significant differences within groups. Paired-t test was carried in parametric analysis to measures differences between groups.

RESULTS

Onset and duration time of anesthesia

No significantly differences were recorded as regard the onset of anaesthesia in IV Group (1.6±0.4 min) and I0 Group (1.84±0.3 min). On the other hand, the duration time of anesthesia in IV group (38.4±1.9 min) was significantly shorter ($p<0.05$) than IO Group (40.7±2.1 min).

Heart rate

Figure 1. A. was shown the changes in HR of both groups according to time. HR was decreased significantly in both groups as compared to baseline values until 40th min ($p<0.01$). However observed decrease in HR was not important as clinically (Figure 1.A.). There were no significant differences obtained between groups in recorded time points during anesthesia. Also sinus rhythm obtained from ECG data was not altered in all the quails.

Respiratory Rate

No significant differences were detected in RR between groups during anesthesia. However, a significant decrease in the RR were observed in the IV Group ($p<0.01$) on the 3th min, while a decrease in the IO Group ($p<0.05$) were recorded from the 3th to 5th min when compared to baseline values (Figure 1.B.). There were no significant differences within the groups except this time intervals.

Cloacal Temperature

No significant differences were observed in the CT between IV and IO group during anesthesia as shown in Figure 1.C. It was obtained significant decrease ($p<0.001$) in CT of IV group from the 3th to 50th min as compared to initial value. Also, significant reduce ($p<0.001$) in CT of IO groups were started at 5th min and continued to 50th min.

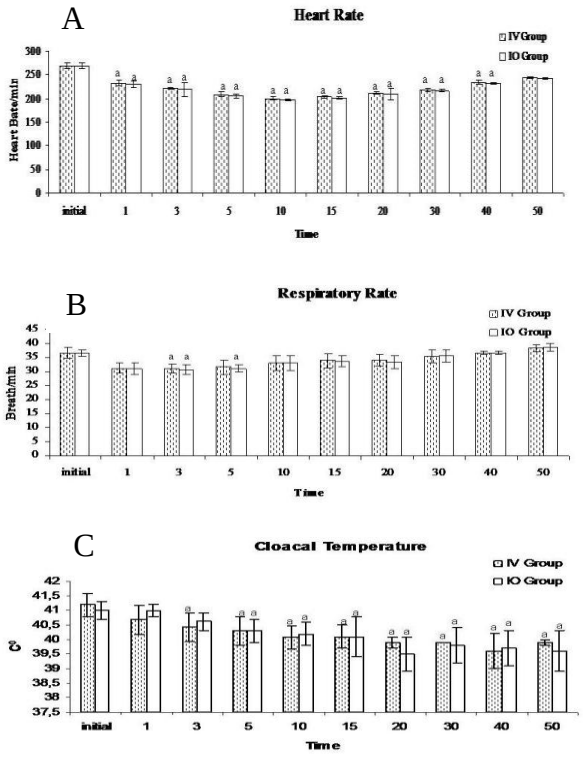

Figure 1. Alterations in some physiological values; **A;** HR, **B;** RR and **C;** CT.

No statistically significant difference was found between the groups in point of HR, RR and CR.; a: Denotes significant chances from initial values within group (a: $p<0.05$).

Reflexes

Alterations in the observed reflexes during experiment were shown in Figure 2. There were no significant differences in eyelid status between groups. The eyelids of quails used ketamine-propofol combination were completely closed at 1th min in two groups. Also, there were no significant differences in palpebral reflexes, righting reflex, feather plucking reflex in both groups. Muscle relaxation following the administration of the ketamine-propofol combination was pronounced in both groups.

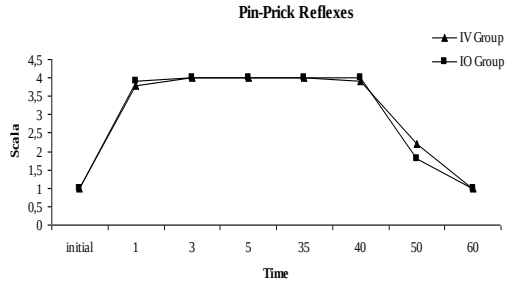

Figure 2. Changes in pin-prick reflexes induced by IV and IO administration of propofol/ketamine combination. Median analgesic scores in response to a standard noxious stimuli (pin-prick reflex). 1; Severe reaction 2; moderate reaction, 3; stay in lateral recumbency and unable to stand up, 4; deep anesthesia and no reaction.

DISCUSSION

The combination of ketamine and propofol has been used with success in anestesiology for many years. But only recently it has begun to spread into veterinary practice (Langan et al 2000, Machin et al 2000, Umar et al 2006). Although used combining propofol with ketamine has been considered as an alternative to other traditional forms of sedation and general anesthesia, there are rare reports about using of this combination in birds. It was reported that propofol in combination medetomidine-ketamine provided rapid induction and smooth recovery in ostriches for anesthesia (Langan et al 2000) and, recommended for use in combination rather than propofol's use alone. The technique of combining propofol with ketamine has been termed dissociative sedation and may be considered as an alternative to other more traditional forms of conscious sedation or general anesthesia (Morse et al 2003). On the other hand, in a report of ducks shown that if propofol anesthesia was used alone that offers several advantages such as lover anesthetic cost, easily portable and ambient temperature dose not alter physical characteristics of the drug (Machin et al 2000). In our study, rapid induction and smooth recovery was obtained using propofol and ketamine combination both IV and IO application during experiments. Also, no significant differences were recorded as regard the onset of anaesthesia. However, the duration of anesthesia with ketamine and propofol in IO group was longer than IV group. Behind, Paul-Murphy et al (1999) observed that the average surgical time needed for bird species was 15 min. Therefore gained anesthesia duration with this combination both IO and IV route provides enough time for surgical procedures.

Intravenous route has been preferred in the studies for both propofol and propofol-ketamine combination (Machin et al 2000, Mendes and Selmi 2003, Miller et al 2005, Morse et al 2003, Mortero et al 2001). But, it is difficult to implement IV injection to avian species, due to rupture of blood vessels that will occur during the path of the needle entry (Kamiloglu et al 2008, Machin et al 2000, Valverde et al 1993). On the other hand, IO administration of anesthetic is preferred when intravenous access is difficult. Successful IO cannulation is unaffected by the circulatory status and the route is being used as a rapid, reliable method in critical condition (Brickman et al 1992, Kamiloglu et al 2008, Moore et al 1989, Tobias and Ross 2010, Valverde et al 1993). Thus, IO route may be as affective as IV route and an alternative implication as a create desired anesthesia. Despite some complication such as haemorrhage and bone fracture during cannula placement, well known of bird's anatomical configuration may be prevent mentioned side effects during IO application. In this study, there were not any described complications during IO enforcement (Kamiloglu et al 2008, Tobias and Ross 2010, Valverde et al 1993).

Contrary to previous reports (David and Shipp 2011, Langan et al 2000, Miller et al 2005) no bradycardia developed as a complication during our study despite unimportant decrease in HR in both groups. Ketamine induced tachycardia and propofol induced bradycardia were shown to offset with ketamine propofol combination and provides relatively good hemodynamic stability with only a mild decrease in cardiovascular parameters (Sakai et al 2000). Hence, use a mixture of propofol with ketamine has been demonstrated to be chemically compatible for expected result of cardiovascular dynamics (Langan et al 2000).

Increased RR in birds (Langan et al 2000) and decreased RR in horses and cats (Mendes and Selmi 2003, Umar et al 2006) is reported in the studies using propofol alone. Also, short-time apnea was reported that commonly associated with IV administration propofol in avian studies (Langan et

al 2000). In the present study, there were not any sign of apnea and RR were not remarkably changed with the use of propofol ketamine combination both IV and IO groups.

Hypo- and hyperthermia can contribute to complication and postoperative physiological and behavioral chance. Therefore, changes in body temperature during anesthesia are minimized by selecting the appropriate anesthetic combinations (English et al 1991, Langan et al 2000, Yayla and Kiliç 2010). Researches have shown that (Langan et al 2000, Machin et al 2000, Miller et al 2005, Tomatir et al 2004) the combination of propofol-ketamine suitable for moderate decrease in body temperature. However, in this study ketamine propofol anesthesia resulted in a significant decline in terms of CT in both groups. Thermoregulation during anesthesia and heat loss may be largely depending on respiratory and cardiovascular depression (English et al 1991).

In conclusion, without more substantial cardiovascular and respiratory depression using propofol ketamine combination both IV and IO route would be clinically acceptable and compares favorable with other techniques in quails. At the dose used in the study propofol and ketamine combination seems to be an effective IV and IO anesthetic agents to induce and maintain anesthesia in quails. Also, propofol in combination with ketamine provided rapid induction and resulted in smooth recovery.

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