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Clinical Evaluation of Intramuscular and Intraosseous Xylazine-Ketamine Anesthesia in Quails (*Coturnix coturnix japonica*)

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Summary: Purpose of this study was to compare the use of intramuscular (IM) and intraosseous (IO) xylazine-ketamine combination by monitoring clinical parameters in quails. The experiment was carried out on twenty clinically healthy mature male quails randomly divided into two groups. The first group (n=10) received the combination of 8 mg/kg Xylazine HCl 50 mg/kg and Ketamine HCl IM and second group (n=10) received: the same combination via IO route. Each quail was monitored for heart rate (HR), respiratory rate (RR), cloacal temperature (CT) and electrocardiography (ECG). The induction and duration time of anesthesia in IO group was significantly shorter than that for IM Group (P<0.05). The HR of IO group was significantly decreased on 15th, 20th and 30th min as compared to the IM group (P<0.05). When statistical differences were compared among different groups, the RR of IO group reduced significantly (P<0.05) on the 3th, 5th, 10th and 15th min than that of the IM group. There were no significant differences observed in the CT values between IO and IM group during the anesthesia. Also, reflexes disappeared in both groups throughout the anesthesia. In conclusion, sufficient anesthesia can be obtained by the use of both the IM and the IO xylazine-ketamine administration. Furthermore, it was determined that IO route can be easily used in clinical practice such as IM anesthesia in quails.

Key Words: Intramuscular, intraosseous, ketamine, quail, xylazine

Bıldırcınlarda *(Coturnix coturnix japonica)* İntramusküler ve İntraosseöz Xylazine-Ketamine Anestezisinin Klinik Olarak Değerlendirilmesi

Özet: Bu çalışmanın amacı bıldırcınlarda xylazine-ketamine kombinasyonunun intramuskuler (IM) ve intraosseal (IO) kullanımını klinik parametreleri izleyerek karşılaştırmaktır. Çalışma, klinik olarak sağlıklı ve yetişkin olan 20 adet erkek bıldırcında rastgele iki gruba ayrılarak yürütüldü. Birinci gruba (n=10) 8 mg/kg Xylazine HCl ve 50 mg/kg Ketamine HCl kombinasyonu IM olarak verildi. İkinci gruba (n=10) ise aynı kombinasyon IO yolla verildi. Her bir hayvan monitörize edilerek kalp atım sayısı (HR) solunum sayısı (RR), cloacal ısı (CT) ve EKG değerleri kayıt edildi. Anestezi indüksiyonu ve anestezi süresi IO grupta IM gruptan önemli derecede daha kısa bulundu (P<0.05). IM grup ile karşılaştırıldığında IO grubun HR değerlerinin 15, 20 ve 30. dakikalarda önemli derecede azaldığı belirlenmiştir (P<0.05). Gruplar arasında RR bakımından istatistiksel değişiklikler karşılaştırıldığında IO grupta 3, 5, 10 ve 15. dakikalarda IM gruba göre bir düşüş ve önemli bir fark bulundu (P<0.05). Anestezi boyunca CT değerlerinde gruplar arasında istatistiksel olarak önemli bir fark gözlenmedi. Ayrıca her iki grupta da anestezi boyunca refleksler değerlendirildi. Sonuç olarak bıldırcınlarda xylazine-ketamine kombinasyonun hem IM hem de IO olarak uygulandığında yeterli bir anestezi elde edilebileceği ve IO yolun klinik pratikte IM yol gibi kolaylıkla kullanılabileceği sonucuna varıldı.

Anahtar Kelimeler: Bıldırcın, intramuskuler, intraosseus, ketamine, xylazine

Introduction

There are many studies (2,6,7,10,11,16,17) that demonstrated the effect of anesthetic agents on metabolic, hemodynamic and cardiovascular parameters in avian veterinary practice. Although several anesthetic agents are often used to induce anesthesia, safe and effective anesthesia methods and administration route of anaesthetic agents are of great importance for small pet birds (12). Among the ways of routine injection, IM or subcutan (SC) routes are preferred routinely in avian species. The advantages of IO injections in order to anesthesia in birds have been reported by researchers in recent years (10,15).

A dissociative anesthetic, ketamine, has been widely applied as an inducer of anesthesia characterized by marked analgesia and amnesia (8,16,17). Ketamine has become a popular and powerful analgesic for short surgical procedures (16). However, it is rarely used alone because of poor muscle relaxation, muscle tremors, myotonic

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contractions, and rough recoveries. For this reason, to neutralize its side effects, ketamine is frequently used together with an α- 2-adrenoceptor agonist depending on the species involved (8). Xylazine HCl, an α- 2- adrenoceptor agonist, is widely used in avian species for its potent sedative, analgesic and myorelaxant properties. Ketamine in combination with xylazine that is a commonly used anesthetic in veterinary practice is also safe and effective for induction of anesthesia in birds. If properly dosed, this combination can be used to induce anesthesia with minimal adverse cardiovascular and respiratory effects (6,9,11,12,14).

This study was conducted to research if the IO administration of the xylazine-ketamine combination enhances the quality of anesthesia as compared to IM administration for general anesthesia in quails.

Materials and Methods

This study was carried out on 20 adult clinically healthy mature (26 week old) male quails (*Coturnix coturnix japonica*) with 198.07±11.28 g (as Mean±SD) body weight. Quails provided from animal farming department of Kafkas University.

The study was started after the birds were adapted to their environment for a week. They were housed at constant room temperature with a 12-12 h light-dark cycle and fed with a wheat-based diet in accordance with the previous feeding regimen. All experiment were performed in quails deprived of food for 60 min, but allowed free access to water.

Animal research ethics committee of Veterinary Medicine in Kafkas University approved all experiments before studies were conducted (2012/04).

Study Protocols

The birds were divided into two groups on the basis of their exposure route of anesthetics as IM and IO. Quails in the IM group (n=10, BW= 200.7±11.04) was anesthetized with 8 mg/kg xylazine (Rompun® 2%, 50 ml, Bayer, Germany) and 50 mg/kg Ketamine (Ketalar® 10 ml injectable, Pfizer-Turkey) by insulin syringe. Deep pectoral muscle was used for IM injection. Quails in the IO group (n=10, BW=196.7±11.74) received 8 mg/kg xylazine and 50 mg/kg ketamine with insulin syringe. In the IO group, Xylazine-ketamine was diluted at 1:1 ratio with 0.9% NaCl solution. The distal end of the left tibia was chosen for IO administration using 14 to 20 gauge spinal needles depending the bird's size. After aseptic conditions, the knee joint of quails laid on lateral recumbency was positioned at flexion. Needle positioned the tibia tuberosity parallel to the diaphysis was inserted to medulla of tibia. Whether needle was in medullary region was determined with loss of resistance against the needle.

Measurements

Experimental quails were monitored and recorded for HR, RR, CT and ECG at initial, and on the 1, 3, 5, 10, 15, 20, 30, 40 and 50th minutes after injection by a multi-parametric monitor (Veteriner Monitör® MMED6000DP S6-V).

Assessment of the clinical effect of anesthesia

Records of quails in all groups were kept in terms of the induction period, duration of anesthesia and recovery period. Recorded periods were determined by using standard painful stimuli. A superficial (needle used to prick the skin) and deep pin-prick (needle inserted into the muscle) were performed on different body parts. Also, other body reflexes (righting reflex, feather plucking reflex, palpebral reflex, pharyngeal reflex) were recorded.

Statistical analysis

Statistical analyses were performed using the commercial Minitab-16 software program (with Man-Whitney U test and Wilcoxon test followed by Friedman's test). All results were expressed as the Mean ± Standard error of mean (SEM). A P value <0.05 was considered to be statistically significant.

Results

Induction and duration time of anesthesia

The induction time in the IO group (1.03±0.3 min, n=10) was significantly shorter (P<0.05) than that for the IM group (5.62±0.3 min, n=10). On the other hand, the duration time of anesthesia in the IM group (45.60±2.54 min) was significantly longer (P<0.05) than the IO group (39.90±2.23 min).

Heart Rate

Changes in the HR of the experimental groups according to time were shown in the *Table 1*. The HR was not changed in the IM group in relation to baseline values throughout the anesthesia.

However, in the IO group the HR was significantly decreased from the 10th min on to the 40th min when compared to baseline values (P<0.05). The HR returned to baseline values at 50th min. The HR of the IO group significantly decreased on 15th, 20th and 30th min as compared to IM group (P<0.05).

Sinus rhythm was changed as a bradycardia that of arrhythmia obtained from ECG data in all of the quails.

Respiratory Rate

The RR according to time and to the experimental groups was shown in the *Table 1*. While significant decrease in the RR were observed in the IM group on the 20th min (P<0.05), decrease in the IO group were on the 1th to 40th min (P<0.01) as compared to baseline values. When statistical alliterations were compared among the groups, reduction in the RR of the IO group were found to be significant than the IM group on the 3th, 5th, 10th and 15th min (P<0.05).

Cloacal Temperature

Table 1 shows the alteration in the CT according to time and to the experimental groups. There were no significant differences observed in the CT between IO and IM group during the anesthesia. The CT began to significant decrease (P<0.001) on the 10th min both the IM and IO group, and these significant decrease continued during anesthesia.

Reflexes

Assessed reflexes disappeared in both groups throughout the anesthesia. Alteration in pin-prick reflex was shown in Figure 1. Also body reflexes such as righting reflex, feather plucking reflex, palpebral reflex and pharyngeal reflex were showed in Figure 2. Because similar responses were shown in body reflexes at the same time intervals, they were presented in same figure.

Discussion

Recently researches (1,5,6,10,11) have recommended different α-2-adrenoceptor agonists such as xylazine, detomidine and medetomidine combination with ketamine HCl a suitable injectable anaesthetic agent for avian species. Also, several investigators (6,11,14,17) have recommended that xylazine-ketamine combinations usually result in rapid and smooth induction, associated with deep analgesia, good muscle relaxation and absence of all reflexes and smooth recovery. A research in Budgerigars by Gandomania at al. (8) reported that induction and recovery time was obtained longer with ketamine-xylazine combination than with sole ketamine or xylazine. Although there were many different studies (4,5,10,11) on the anesthetic drug combination and usable or effective dose, research on route of administration is limited. The preferred route of administration of this combination are commonly IM or intravenous (IV) for birds (2,6).

The choice of administration route is often as important as the anesthetic agent. However, IO administration of injectable anesthetics and sedatives for general anesthesia in birds is restricted. It is suggested that the IO route is superior to intramuscular and comparable to IV administration (3,10,13). Because of the medullary venous channels connect to the systemic circulation, absorption of anesthetic agent has takes less time. When intravenous access is not available or not feasible, IO route is used in urgently situations to provide fluids, medication and anesthetic drug (3,13). In avian species, usually ulna or tibia can be used for this purpose for which the needle is injected through in the bone's medulla or marrow that allows immediate access to the vascular system (10,15). A study by Kamiloglu et al. (10) was reported that the advantage of IO application as the quick induction of anesthesia, shorter recovery time. Also, in our study, the initiation of anesthesia was smooth and rapid; profound analgesia and smooth recovery were obtained; and all reflexes were disappeared within both IM and IO injection of xylazine-ketamine combination. On the other hand, the IO application is advantageous for onset and duration of anesthesia as it is quicker and shorter than the IM usage. However, research (3,10,13,15) reported that haemorrhage and bone fracture may occur during cannula placement. In this study, we did not observe any complication during the IO implementation.

The researches (6,8,11,14) used xylazine-ketamine anesthesia both in birds and other animals has shown that this combination may cause cardiac and respiratory depression by dose-dependent rather than the administration route. Xylazine-ketamine combination can be used to remove the side effects of xylazine on cardiovascular and respiratory system (6). However, the elimination of cardio-respiratory depressive effect of this combination cannot always be possible. Ketamine, a dissociative anesthetic, has a stimula

Table 1. Effect on the HR, RR and CT of IO and IM injection of Xylazine/ketamine combination at different time points

Values	Groups	0 min	1 min	3 min	5 min	10 min	15 min	20 min	30 min	40 min	50 min	Statistical significant (Wilcoxon Test)
HR	IM	357.7±6.5	330.8±20.1	334.3±30.1	323±49.6	323.4±41.0	324.7±38.7	342.3±37.3	318.3±52.7	329±37.2	332.5±31.8	P>0.05
	IO	357.7±3.8^{a}	342.8±22.2^{ab}	329.6±48.7^{abc}	311.9±42.4^{abc}	302.1±42.9^{bc}	293.6±32.9^{bc}	279.6±39.5^{c}	260.8±46.7^{c}	300±42.8^{c}	344.4±35.3^{ab}	P<0.01
Statistical significant (Mann Whitney U Test)		P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P<0.05	P<0.05	P<0.05	P>0.05	P>0.05	
RR	IM	17.1±3.2	15.9±2.9^{b}	15±2.5^{b}	14.6±2.0^{b}	14.6±1.1^{b}	13.8±1.1^{b}	13.4±1.4^{b}	13.9±1.4^{b}	15.6±3.9^{b}	17.1±4.3	P<0.05
	IO	17±3.0^{a}	14.3±2.7^{b}	12.4±1.9^{bc}	11.3±2.1^{c}	11.5±1.0^{c}	11.7±1.2^{c}	12.5±1.4^{bc}	13.4±1.4^{bc}	14.1±1.2^{bc}	17±2.6^{a}	P<0.001
Statistical significant (Mann Whitney U Test)		P>0.05	P>0.05	P<0.05	P<0.05	P<0.05	P<0.05	P>0.05	P>0.05	P>0.05	P>0.05	
CT	IM	41.4±0.6^{a}	41.1±0.7^{a}	40.6±0.8^{a}	40.1±1.1^{ab}	39.1±1.2^{b}	38.9±1.0^{b}	38.4±0.9^{bc}	37.5±1.4^{c}	36.9±1.1^{c}	36.2±1.4^{c}	P<0.001
	IO	41.1±0.8^{a}	41.1±0.6^{a}	40±0.3^{ab}	40.1±1.2^{ab}	39.3±1.9^{b}	38.1±1.1^{bc}	37.9±0.8^{c}	37.6±0.8^{cd}	36.8±1^{cd}	36.1±1.3^{d}	P<0.001
Statistical significant (Mann Whitney U Test)		P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	

$^{a, b, c, d}$: The differences between the means of time carrying various letters in the same line are significant

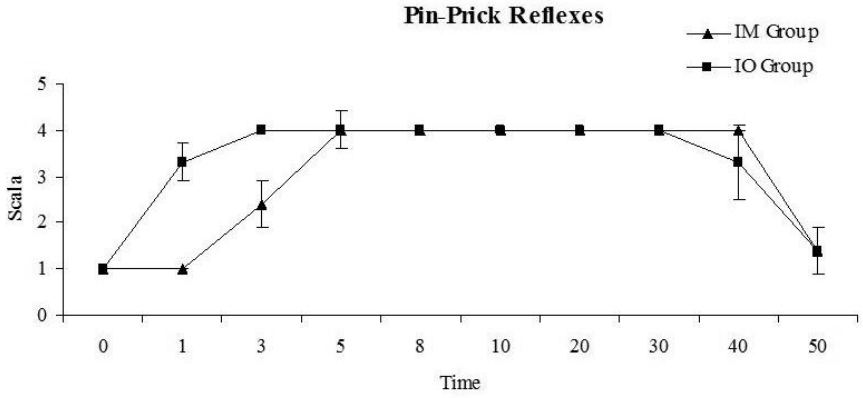

Figure 1. Alteration in pin-prick reflexes induced by IM and IO administration of xylazine/ketamine combination. Median analgesic scores in response to a standard noxious stimuli (pin-prick reflex). 1; no analgesia, 2; mild analgesia, 3; moderate analgesia and 4; complete analgesia.

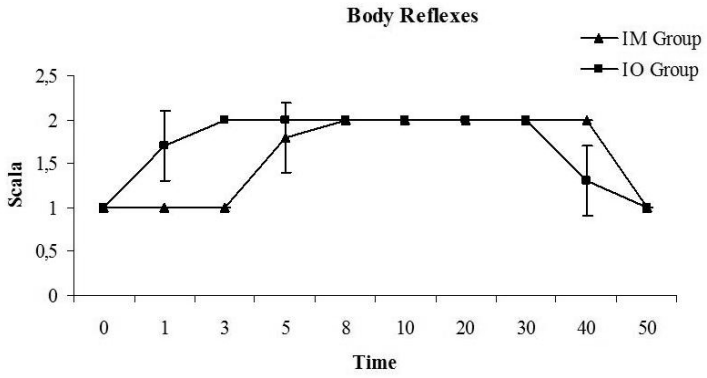

Figure 2. Analgesia scores based on body reflex such as righting reflex, feather plucking reflex, palpebral reflex, pharyngeal reflex. 1; no analgesia, 2; complete analgesia.

tory effect on cardiovascular activity and does not depress respiration (6). An α2-adrenoceptor agonist, xylazine, connect to the pre-and postsynaptic α2-adrenoceptor, leads to changes in the intrinsic membrane and inhibit the release of norepinephrine. Thus, increase in parasympathetic activity and a decrease in peripheral sympathetic activity can cause decline in heart rate as bradycardia, and blood pressure as hypotension. Also, it is known that xylazine has a depressive effect on the respiratory system (6,14). Research in domestic pigeon (5,6,12) and quails (4) also showed that an α2-adrenoceptor agonist and ketamine combination lead to decrease in heart and respiratory rate and body temperature. Moreover, a study in pigeon by Duranni et al. (6) reported that xylazine-ketamine combination creates hypothermia, respiratory depression and bradycardia by IM usage of this combination. In our study, general anesthesia was achieved with sufficient muscle relaxation, without tremors and convulsion, smooth and fast recovery by the use of ketamine xylazine combination both in the IM group and the IO group in quails. But, it was found in the present study that the xylazine-ketamine anesthesia led to cardio-respiratory depression as bradycardia, decreased respiratory rate and hypothermia, quails in both groups. However, the researches related to anesthesia reported that decrease in body temperature was associated with

a slow down in the metabolism rather than the anesthetic agents used (6,14).

In conclusion, if a quick and convenient way of anesthesia for urgent operation is desired IO route can be used as an alternative way. Moreover, using the ketamine-xylazine combination considered as a viable choice that resulted in a sufficient and appropriate anesthesia in quails.

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