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Original Article

Electrocardiogram Assessment in Chough (Pyrrhocorax pyrrhocorax) Following Intranasal Administration of Anesthetics

Majid Taati[1*], Abbas Raisi[2]

Abstract

Objective- The objective of the present study was to define electrocardiographic data following intranasal administration of diazepam, midazolam and xylazine with or without Ketamine in Chough.

Design- To determine the heart effects of anesthetics in intranasal administration, an experimental in vivo study was employed.

Animals- Ten healthy Choughs were examined in the current study

Procedures- After intranasal administration of diazepam, midazolam and xylazine with or without ketamine, electrocardiograms were recorded by a direct writing electrocardiograph. Then the heart rate, durations (seconds - s) and amplitude (millivolts - mv) of the P wave, QRS complex and T wave all measured in the bipolar II derivation

Results- There was a normal sinus rhythm after application of all drugs or combinations. The range of the heart rate of the birds was from 93 to321 beats/min. The P wave was always positive in all recorded leads after administration. During anesthesia or sedation with all drugs, the T wave was positive in leads I, II, III and aVF and negative in leads aVR, and aVL. The amplitude and duration of P, QRS and T waves were changed after intranasal administration of all drugs or combinations.

Conclusion and Clinical Relevance-Based on the electrocardiographic findings it seems that the xylazine is not a suitable drug to induce sedation and anesthesia of choughs via intranasal administration. Therefore, xylazine must be used for birds when its antagonists are accessible.

Keywords- ECG, Anesthesia, Intranasal administration, Chough.

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Introduction

Destruction of the wild animals' habitat and consequent decrease in their population has stimulated studies regarding the acquisition of physiological and clinical data of wild species to help their survival in the nature .[1]Chough (Pyrrhocorax pyrrhocorax) like many wild animals has also suffered from environmental alterations.[2] Anesthesia has been used to reduce stress during handling, capture, transport and surgery.[3] Because of the proper anatomy and physiology of birds that greatly complicates anesthetic risk, anesthetizing a bird should never become a procedure to be taken easily.[4] Monitoring the avian patient during anesthesia is the most critical aspect of the process and appropriate responses to the animal's physiologic state must be performed correctly.[5]

Many advances in avian anesthesia are due to the use of better monitoring techniques. In this regard, studies have shown that electrocardiograms (ECG) can be effectively used to monitor the heart during anesthesia in birds. Moreover, to define the homeostatic balance in wild species, information on the cardiac function is one of the important parameter to be achieved.[6,7] Besides the difficulty involved in delivering a safe and effective volume, the use of injectable anesthetic agents have many disadvantages such as cardiopulmonary depression, prolonged and violent recoveries.[8]

The electrocardiogram is used increasingly in veterinary medicine as a non-invasive and auxiliary diagnostic test.[9-12] It is a useful method to determine the heart rhythm and frequency supplied by the P-QRS-T deflections of the electrocardiogram tracing.[13,14] Since information on wild animal cardiac activity is very important and scarce, the objective of the present study was to define electrocardiographic data for Chough following intranasal

[1]Department of Physiology, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran.
[2] Department of Clinical Sciences, Faculty of Veterinary Medicine, Lorestan University, Khorramabad, Iran.
*Correspondence to: Address all correspondence to Majid Taati (DVM, PhD). E-mail: taati.m@lu.ac.ir

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administration of diazepam, midazolam and xylazine with or withoutketamine.

MATERIALS AND METHODS

Animals

Ten healthy adult domesticated Choughs (Pyrrhocorax pyrrhocorax) of both genders, weighing from 250 to 220gramswere used. The food management consisted of commercial feed and water ad libitum. The experimental protocol was approved by the Committee of Ethics in Animal Experimentation of the Lorestan University.

Anaesthesia protocols

Each of the birds received seven drug combinations with an interval of one week. Briefly, ketamine (30 mg/kg, Daroupakhsh, Iran), xylazine (8 mg/kg, Daroupakhsh, Iran), diazepam (8mg/kg, Daroupakhsh, Iran), midazolam (8mg/kg, Daroupakhsh, Iran), ketamine –diazepam, ketamine -midazolam and ketamine -xylazine were administered intranasaly using a micropipette (Varipet 4810; Eppendorf, Hamburg, Germany).

In this study, standard bipolar and augmented unipolar leads were recorded. Alligator clip electrodes were attached to the skin at the base of the right and left wings and gastrocnemius muscle of the right and left limbs of the choughs in dorsal recumbence. Electrode gel was rubbed into the skin in the area where the alligator clips were attached to act as a conductive medium agent and thereby decrease the resistance of the skin. Electrocardigorams (ECGs) were recorded by a direct writing electrocardiograph (Kenz 110, Japan).The speed used was 50 mm per second, with voltage calibration of 1 cm for each millivolt (1mV=10mm). Leads I, II, III, aVR, aVL and aVF were recorded. The heart rate, durations (seconds - s) and amplitude (millivolts - mv) of the P wave, QRS complex and T wave all measured in the bi-polar II derivation.[3,15,16]

Experimental results were expressed as mean ± standard deviation (SD). All data were analyzed by one-way analysis of variance to assess statistical significance between experimental groups with the computer program SPSS 16.0 for Windows (SPSS, Inc., Chicago, Illinois, USA) and p value less than 0.05 was considered significant.

RESULTS

All of the choughs´ electrocardiograms during anesthesia with drugs are depicted in Figures 1 to 7. The durations and amplitudes of all waves in lead II are shown in Table 1.

There was a normal sinus rhythm after application of all drugs or combinations (Fig.1-7). The range of the heart rate of the birds was from 93 to 321 beats/min with a mean (±SEM) of 215.7 ± 17.5 beats/min. xylazine and ketamine -diazepam induced the least (93 beats/min) and the greatest (321 beats/min) heart rates, respectively.

The P wave was always positive in all recorded leads after administration of the used anesthetics. The choughs that received ketamine and/or diazepam alone had the least P wave amplitudes (0.08 mv) and the other birds that were implicated with ketamine -xylazine and/or ketamine -diazepam showed the highest P wave amplitudes (0.11 mv). The difference between these minimum and maximum values was significant ($P \leq 0.05$). The least duration of the P wave (0.024 ± 0.002 sec) was showed during the anesthesia with xylazine which is significantly different from the highest one recorded for ketamine -diazepam (0.032±0.001 sec) ($P \leq 0.05$).

Implication of ketamine -xylazine and ketamine -diazepam resulted in the least (0.16 mv) and highest (0.32 mv) amplitudes of QRS waves, respectively. When results compared, significant difference between mean amplitudes of QRS in choughs administered with ketamine -xylazine and ketamine -diazepam was found ($P \leq 0.05$). The range of the mean QRS durations was 0.026-0.067 sec in lead II. The mean value for the QRS durations during the anesthesia with ketamine -xylazine (0.067 sec) was significantly higher than the values evaluated for ketamine -midazolam (0.026 sec) ($P \leq 0.05$).

During anesthesia with all drugs, the T wave was positive in leads I, II, III and aVF and negative in leads aVR, and aVL.

Comparing between the least (0.21 mv) and highest (0.34 mv) mean T wave amplitudes did not show significant difference. Intranasal administration of Ketamine-xylazine and ketamine-diazepam showed the least and highest mean T wave amplitudes, respectively.

Although ketamine-midazolam and ketamine-diazepam combinations induced the lowest mean duration of the T wave (0.046 sec), ketamine alone and ketamine-xylazine combination resulted in the highest values (0.056-0.06 sec). When compared the maximum and minimum values, significant difference ($P \leq 0.05$) between them was obvious.

Table 1. Heart rate and electrocardiographic values of the six standard leads during anesthesia with drugs in choughs. (mean ± SEM)

parameters / groups	HR	P		QRS		T	
		Amplitude (mv)	Duration (sec)	Amplitude (mv)	Duration (sec)	Amplitude (mv)	Duration (sec)
ketamine	167.4± 11.1 [a]	0.08±0.013 [a]	0.024±0.002 [a]	0.23±0.027 [ab]	0.034±0.003 [ab]	0.246±0.025 [a]	0.056±0.003 [a]
xylazine	93±8.01 [b]	0.09±0.006 [ab]	0.028±0.001 [ab]	0.19±0.024 [b]	0.03±0.002 [ab]	0.23±0.029 [a]	0.052±0.003 [ab]
diazepam	301.8±34.7 [c]	0.08±0.014 [a]	0.026±0.002 [a]	0.24±0.034 [ab]	0.066±0.024 [a]	0.28±0.031 [ab]	0.05±0.004 [b]
midazolam	267.4±34.43 [c]	0.102±0.004 [ab]	0.026±0.003 [a]	0.27±0.034 [ac]	0.032±0.002 [ab]	0.27±0.029 [ab]	0.05±0.003 [b]
Ketamine-xylazin	110±7.851 [ab]	0.11±0.006 [b]	0.025±0.002 [a]	0.16±0.010 [ab]	0.067±0.026 [a]	0.21±0.018 [a]	0.06±0.004 [a]
Ketamine-diazepam	321.6±9.86 [c]	0.11±0.004 [b]	0.032±0.001 [b]	0.32±0.030 [c]	0.034±0.002 [ab]	0.34±0.038 [b]	0.046±0.004 [b]
Ketamine-midazolam	251±16.6 [c]	0.09±0.01[ab]	0.028±0.002 [ab]	0.19±0.022 [ab]	0.026±0.002 [b]	0.27±0.017 [ab]	0.046±0.0027 [b]

Means with different superscripts (a, b, c) within each column are significantly different (P<0.05).

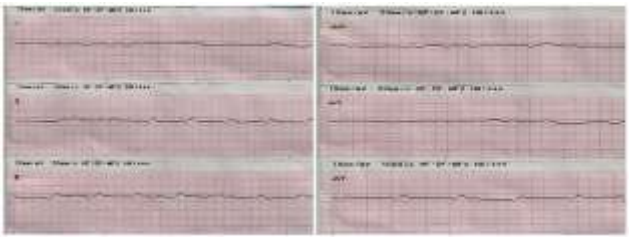

Figure 1. Electrocardiogram of the choughs in six leads after intranasal administration of ketamine (standardization, 1 mill volt = 10 mm; chart speed, 50 mm per second).

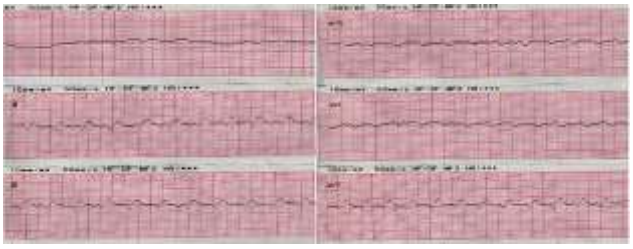

Figure 2. Electrocardiogram of the choughs in six leads after intranasal administration of xylazine (standardization, 1 mill volt = 10 mm; chart speed, 50 mm per second).

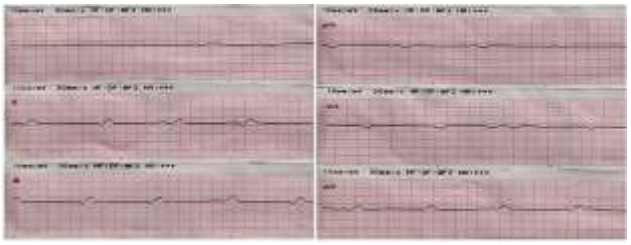

Figure 3. Electrocardiogram of the choughs in six leads after intranasal administration of Diazepam (standardization, 1 mill volt = 10 mm; chart speed, 50 mm per second).

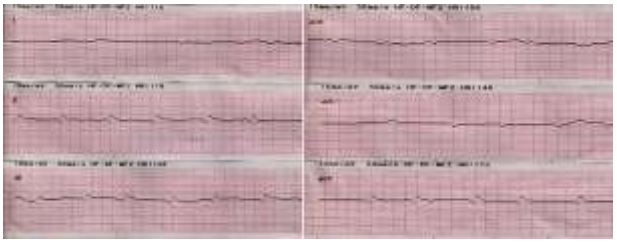

Figure 4. Electrocardiogram of the choughs in six leads after intranasal administration of Midazolam (standardization, 1 mill volt = 10 mm; chart speed, 50 mm per second).

Figure 5. Electrocardiogram of the choughs in six leads after intranasal administration of Ketamine-xylazine (standardization, 1 mill volt = 10 mm; chart speed, 50 mm per second).

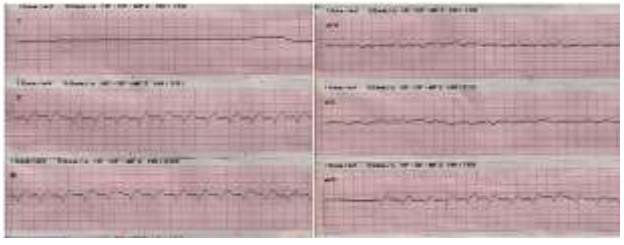

Figure 6. Electrocardiogram of the choughs in six leads after intranasal administration of Ketamine-Diazepam (standardization, 1 mill volt = 10 mm; chart speed, 50 mm per second).

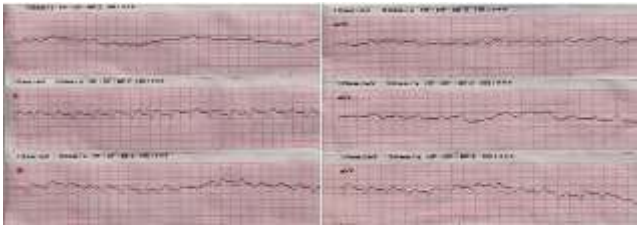

Figure 7. Electrocardiogram of the choughs in six leads after intranasal administration of Ketamine-Midazolam (standardization, 1 mill volt = 10 mm; chart speed, 50 mm per second).

Discussion

Electrocardiography has been used to monitor heart rate and rhythm in anesthetized patients.[15] Because the myocardium is very sensitive to hypoxia, the ECG can serve as a reliable indicator of the oxygenation of the bird's myocardium under anesthesia.[17]To the author's knowledge, this is the first report about the ECG on anesthetized chough.

In our study, all the birds had a normal sinus rhythm following the anesthesia induced by the intranasal administration of xylazine, diazepam, and midazolam alone or combined with ketamine.

The doses of drugs were chosen according to our previous studies on chough.[18] In present study, choughs that received ketamine unexpectedly had significant lower heart rate than birds administered diazepam, midazolam alone or combined with ketamine. Salerno and van Tienhoven (1976) reported a dose dependent fall in heart rates following Ketamine administration in chickens.[19]The fall in heart rate in these birds is contrary to the behavior of ketamine in mammals in which case the drug is known to cause tachycardia.[20] It is believed that the increase in the heart rate in animals anaesthetized by ketamine may be due to the action of this agent in the CNS, which causes an overflow of increased electrical activity in the limbic hypothalamic centers of the autonomic nervous system *via* medullary centers.[21] This discrepancy may be due to the different physiological properties between mammals and birds. It has been suggested that Ketamine hydrochloride, a cyclohexamine, is a suitable anesthetic agent for birds, especially for chemical restraint and moderate analgesia for minor surgical and diagnostic procedures.[22-25] Ketamine alone is not used in birds because of poor muscle relaxation and spontaneous movement, even at high dosages .[26] It is often combined with other drugs to minimize these unwanted side effects. Significant species variation has been shown with ketamine when used in birds. For example, in several raptor species and waterfowl, the ketamine resulted in poor quality chemical restraint and anesthesia.[22]

Ketamine is generally used in conjunction with other drugs such as diazepam or xylazine to improve the quality of the anesthesia by providing more muscle relaxation or increased analgesia.[22] In previous study we showed that intranasal use of xylazine, diazepam, and midazolam alone or combined with ketamine provides reliable sedation in chough.[18]In this experiment, diazepam - ketamine given to choughs resulted in significant enhanced heart rate when compared with ketamine, xylazine or diazepam - ketamine combination. Maiti et al also reported that the heart rate of white leghorn cockerels that received diazepam – ketamine was significantly higher than the values for birds were anaesthetized by midazolam or xylazine with ketamine.[21]

The least heart rate in the present study was pronounced during the anesthesia with xylazine. Depression of the heart rate after intravenous administration of xylazine-ketamine in the anaesthetized chickens has been reported .[21]Xylazine is a non-narcotic, sedative, muscle relaxant and analgesic alpha-2-adrenergic agonists that have been used in wide range of wild and domestic animals and birds.[27-30] This agent can cause cardiopulmonary effects such as second-degree heart block, bradyarrhythmias and increased sensitivity to catecholamine-induced cardiac arrhythmias.[4] Its cardiopulmonary depressive effects are not compensated by the effects of ketamine.[31] Severalmechanisms contribute to the xylazine-induced bradycardia such as decreased sympatheticactivity, inhibition ofnoradrenaline release from sympatheticnerve terminals, direct depression of cardiacpacemaker and conduction tissue,increased vagal tone and direct increasein the release of acetylcholine from parasympatheticnerves in the heart.[32] When used in combination with ketamine, thesedative and analgesic effects of xylazine are increased.[4]

Our results showed that the heart rate following intranasal administration of diazepam and midazolam in choughs was very near to those with ketamine-diazepam and ketamine-midazolam. Like other benzodiazepines, midazolam and diazepam act on the benzodiazepine binding site of GABAAreceptors. When bound they enhance the binding of GABA to the GABAA receptor whichin turn results in inhibition of central nervous system.[33] Midazolam with the least cardiopulmonary effects is slightly more potent thandiazepam.[8] Intramuscular injection of midazolamhas caused no

significant changes in cardiopulmonary function in Canada geese, pigeons and quail .[29,34,35]

We observed that the P wave was constantly positive during the anesthesia with all agent or combinations. It has been documented that the P wave morphology may vary in the ECG of healthy birds, which is a possible physiologic variation.[36,37] Moreover, different morphologies (biphasic, inverted and etc) in P wave have been described in healthy domestic fowls.[38]Negative P waves may be seen in the ketamine-xylazine induced anesthesia. For example, a negative P wave on lead II in a red-tailed hawk during the anesthesia with ketamine-xylazine has been shown.[39]

The mean amplitude of the P wave in choughs anesthetized by ketamine-xylazine and ketamine-diazepam was 0.11mv, which is significant higher than values obtained following administration of ketamine and/or diazepam.One of the effects of anesthesia on heart function could be the smaller P waves.[15,36,40] The mean duration of the P wave was 0.024- 0.032 sec which is comparable with the value described by Espino et al., who had utilized isoflurane for anesthetizing the buzzards in his study.[15] An increase in duration of the P wave has been suggested in biatrial enlargement and birds infected by influenza virus.[41]

In agree with studies on many avian species (15,37,39,40,42,43,44,45,46-53), our findings showed that the QRS polarity was negative in leads I, II, III, and aVF after anesthesia induced by all drugs and combinations. Themaximum (0.32 mv) and minimum (0.16 mv) amplitudes of the QRS were observed in choughs anesthetized with ketamine-diazepam and ketamine-xylazine, respectively.An increased voltage in QRS complexesmay be indicative of heart muscle hypertrophy and developed ascites in birds. [15,47]

With all anesthetic agents and combinations utilized here, the T wave was positive in all leads except in leads aVR and aVL. The mean duration (0.046-0.6 sec) and amplitude (0.21-0.34 mv) of the T wave were almost the same as values for buzzard which anesthetized with isoflorane.[15] Elevated and peaked T waves can be observed in shocked raptors and after electrocution as a result of hyperkalemia.[48] The same T patternhas been demonstrated as a sign of hyperkalemia in ducks.[49] If anesthesia is too deep, the T-waves will become smaller and eventually disappear. As the depth further increases, the R-waves will increase in magnitude and S-waves will decrease.[50] When we compare our results with reports about other wild birds like buzzard, it will be able to note that the amplitude and duration of T waves and QRS complex was not very weak.[15] Based on the electrocardiographic findings that mentioned above and complementary data from our previous study on choughs, it is obvious that the anesthesia with drugs used in this study is not deep. Although we did not record the ECG deflections in conscious choughs, our findings may be used as the first reference values for the ECG parameters in chough. Recording an ECG in undomesticated animals can be a problematic procedure and it may be a source of interferences.[15] It has been demonstrated that anesthesia may alter only slightly the values of the ECG.[15] Previously, electrocardiographic reference values for wild birds like buzzard and African grey parrots have been established on anesthetized birds.[15,43] To choose the best drug for anesthesia in wild animals many parameters must be investigated. Based on the electrocardiographic findings it seems that the xylazine is not a suitable drug to induce sedation and anesthesia of choughs via intranasal administration. Therefore, xylazine must be used for birds when its antagonists such as atipamezole and yohimbine are easily accessible.

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Conflicts of interest

None

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چکیده

اندازه گیری اکتروکاردیوگرافی درکلاغ نوک قرمز(Pyrrhocoraxpyrrhocorax) پس از تزریق داخل بینی داروهای بیهوشی

مجید طاعتی[۱*]، عباس رییسی[۲]

[۱] گروه فیزیولوژی، دانشکده دامپزشکی، دانشگاه لرستان، خرم‌آباد، ایران
[۲] گروه علوم درمانگاهی، دانشکده دامپزشکی، دانشگاه لرستان، خرم‌آباد، ایران

هدف- هدف از مطالعه حاضر تعیین داده های الکتروکاردیوگرافی در کلاغ نوک قرمز به دنبال تزریق داخل بینی داروهای دیازپام، میدازولام و زایلازین در ترکیب با کتامین یا بدون آن می باشد.

طرح مطالعه- مطالعه تجربی در شرایط زنده

حیوانات- ده کلاغ سالم در این مطالعه استفاده گردید.

روش کار- پس از تزریق داخل بینی داروهای دیازپام، میدازولام و زایلازین در ترکیب با کتامین یا بدون آن ،الکتروکاردیوگرام ها توسط دستگاه الکتروکاردیوگرافی ثبت شد .سپس ضربان قلب، طول (ثانویه) و دامنه (میلی وولت - مگاوات) موجهای P ، QRS و Tاندازه گیری شد.

نتایج- پس از استفاده از تمام داروها یا ترکیبات، ریتم طبیعی سینوسی ایجاد شد . ضربان قلب پرندگان از ۹۳ تا ۳۲۱ (ضربان / دقیقه)بود. پس از تزریق در همه داروها، موج P مثبت بود. در زمان بیهوشی یا آرام بخشی توسط تمام داروها، موج T درلیدهای I، II، III و aVF منفی و در لیدهای aVR و aVL مثبت بود. دامنه و طول امواج P، QRS و T بعد از تزریق داخل بینی داروها یا ترکیبات آنها تغییر یافت.

نتیجه گیری و کاربرد بالینی- بر اساس یافته های الکتروکاردیوگرام، به نظر می رسد که زایلازین یک داروی مناسب برای آرام بخشی و بیهوشی از طریق تزریق داخل بینی در کلاغ نیست. بنابراین، هنگامی که آنتاگونیستهای آن قابل دسترس باشند، باید از زیلازین برای پرندگان استفاده شود.

کلمات کلیدی-الکتروکاردیوگرافی، بیهوشی، تزریق داخل بینی، کلاغ