EVALUATION OF ANAESTHETIC ACTIVITY OF FENTANYL, XYLAZINE AND KETAMINE IN DOMESTICATED PIGEONS

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ABSTRACT

The present study was designed to investigate the sedative anaesthetic activity of a combination of Xylazine (X), Fentanyl (F) and Ketamine (K) in local domestic pigeons. Twelve pigeons of either sex were used. The combination of (X) and (K) were administered as pre-medication to induce sedation. Fiften minutes, after (X+F) administration, (K) was injected. All drugs were injected into the pectoral muscles. The anaesthetic effect of these drugs was reversed by injection of Yohambine (Y) and Naloxone (N) combination subcutaneously. The sedative and anesthetic activity of the (X+F-K) combination and, alterations in heart rate (RR), Respiratory rate (RR) and cloacal temperature (CT) were investigated at 10 minute before (X+F) injection, 10 and 15 minute after (X+F) administration, 5, 15, 25, 35, 45 and 55 minutes, after (K) injection and at 1, 5, 15, 25, 35, 45 and 60 minutes after (Y+N) injection.

The HR, RR and CT of pigeon decreased within 10 minute after (X+F) injection and remained lower until its improvement after (Y-N) injection. The drugs combination used in this study produced a satisfactory general anaesthesia in ten of the twelve pigeons. The (Y-N) combination was an effective reverse that provide safe recovery from this anaesthetic protocol in pigeons.

INTRODUCTION

In recent years, the application of anaesthesia in avian species has gained importance in clinics. Anaesthesia procedures for avian species are different from those in domestic mammalian species as there are some physiological differences, among avian species should be taken in to consideration when choosing an anaesthetic drug (1).

Among avian species, pigeons are one of the most famous domesticated birds, and have become important in veterinary practice in Iraq because of their increasing popularity as pet.

Despite the inhalant anaesthesia is preferred for birds (2), but it required expensive equipment. The using of injectable anaesthetic agent may have the advantage of increased speed of induction of anaesthesia, the need for minimal equipment and low cost (3). Therefore, there are increasing interests towards using of injectable anaesthetic agent in veterinary practice particularly in pigeons.

Scrutiny of published articles showed that pigeons sensitivity to anaesthetics is questionable and also there is only few publications concerning anaesthetic management in pigeons laking appropriate information about the species- specific effects of anaesthetic agents in these birds. Therefore, developing safe and effective anaesthesia protocol has often been challenging in pigeons.

There is a need to perform a new study in domesticated pigeons aim to:

1- Evaluate the use of a combination of Xylazine (X), alpha$_2$- adrenoceptor agonist, Fentanyl (F), Opioid agonist, and Ketamine (K), general anaesthetic, in pigeons for anaesthetic purposes.
2- Investigate the effect of that combination on heart rate and respiratory rate.

3- We assumed to find the effectiveness of Yohambine (Y), alpha- adrenoceptor antagonist, and Nalaxone (N), Opioid antagonist, combination to reverse (XF and K) induced anaesthesia in pigeons.

MATERIALS AND METHODS

Animals and husbandry:

This study was performed on twelve local domestic healthy pigeons of either sex weighting 230-265 g with mean of 250 ± 3.052. All pigeons were adapted to the new and aquiet environment for at least (15) days. Water and feeding with wheat were allowed prior to the experiment.

Anaesthetic protocol:

Injectable solutions were used through an insulin injector (27 GX ½; 1 ml; medical ject, S. A. R.). Each of the pigeons was injected in deep left pectoral muscle with combination of Xylazine (X) (Seton, 20 mg/ml, Laboratories Calier, Barcelona, spain) at dose of 4 mg/kg. BW. Im and Fentanyl (F) (Fentanyl- Janssen, 0.05 mg/ml, Jassen pharmaceutica) at dose of 0.03 mg/kg. BW. Im together after mixing in a single insulin injector as premeditation. Fifteen minutes after (X-F) administration, Ketamine (K) (Tekam, 50 mg/ml; Hikma pharmaceuticals, Aman, Jordan) was injected as anaesthesia agent at a dose of 20 mg/kg. BW. Im to deep right pectoral muscle. In order to reverse the anaesthetic effect of the previous drugs, Yohambine (Y) (Reverzine, 10 mg/ml, Parnell laboratories, Alexandria, Australia) and Naloxone (N) (Naloxone- merk, 0.4 mg/ml, Merk, Germany) combination was used at dose of Y/N (13/1 mg/kg. BW. S/C) at (55) minutes after injection of (K).

Parameters:

At (10) minutes before injection of pre-medication; (10 and 15) minutes after injection of pre-medication; (5, 15, 25, 35, 45 and 55) minutes after injection of (K) during anaesthesia, and (1, 5, 15, 25, 35, 45 and 60) minutes after the injection of antagonist (Y-N) combination, the following parameters were measured:

1- Heart rate (HR, beats/minute): by using of stethoscope.
2- Respiratory rate (RR, breath/minute): by counting the thoracic excursions as described by Valvede et al (4).
3- Clocal temperature (CT): was determined by a thermometer placed in to the cloacae.
4- The sedative and anesthetic effects of the drug combination during the anesthesia protocols were assessed according to the criteria suggested by Metehan et al., (5) explained as below:

First degree of anesthesia: Able to stand up, partly responsive to environmental objects and walk voluntarily when stimulated.

- Second degree of anesthesia: unable to stand up and tend to stay in lateral recumbency. Partial response to needle pricks stimuli and hardly responsive to environmental stimuli.
- Third degree of anesthesia: Inability to restore body posture, hardly has foot withdrawal response against need prick- Good muscle relaxation.
- Fourth degree of anesthesia: Deep general anesthesia, no reflexes available including pedal, palbabral and corneal. Complete closure of third eyelids. Perfect muscle relaxation (condition of no head or wing control when raised up, and they tend to fell down spontaneously). No response to any pain reflexes.

RESULTS

Mean HR decreased (10) and (15) minutes following (X-F) administration and remained consistently below baseline, However it increased following (K) administration for (55) minutes untile administration of (Y-N). Immediately after (Y-N) administration, mean HR increased sharply until (25) minute and then decreased to value lower than base line (Table 1).

Mean RR was significantly ($P<0.01$) decreased (10 and 15) minute, following (X-F) injection, but, returned to baseline (5) and (15) minutes after (K) injection and then was significantly ($P<0.01$) below the baseline value and decreased again.

(Y-N) administration significantly ($P<0.01$) increased the RR from value obtained at (55) minutes anaesthesia, and, whereas measurement of data at (5), (15), (25) and (35) after antagonist administration were not significantly different from value obtained at baseline (Table 1).

CT decreased significantly from baseline at all time of experiment. However; it was not significant ($P<0.01$) from baseline at (60) minutes after injection of (Y-N) and returned to normal value (Table 1).

Table (1): Heart and respiratory rates and cloacal temperature (mean ± SE) for eleven pigeons anaesthetized with Xylazine, Fentanyl and Ketamine and reversed by Yohambine and Naloxone combination.

Periods	Time (min)	HR (beats/min)	RR(breath/min)	CT (°C)
Baseline value	0	286.416± 4.266	57.166± 3.116	40.958± 0.189
Pre- Medication	10	87.583± 4.309*	27.666± 2.788*	38± 0.275*
	15	82.25± 3.373*	24.166± 2.211*	37.833±0.284*
Anesthesia	5	132.833± 12.15*	51.166± 3.708	37.083±0.287*
	15	122.5± 11.326*	42.833± 4.220	36.158±0.331*
	25	99.583± 5.755*	41.416± 4.510*	34.041±0.298*
	35	87.166± 4.463*	39.25± 4.281*	33.125±0.308*
	45	70.583± 4.101*	36.750± 2.719*	32.291±0.474*
	55	64.083± 3.804*	31.333± 3.018*	31.5± 0.480*
Reverse	1	130.916±11.835*	56.416± 3.051	31.791±0.419*
	5	291.5± 13.849	69.25± 4.571	33.833±0.381*
	15	305.25± 11.158	72.166± 5.696	35.25± 0.424*
	25	301.916± 19.831	96.083± 6.163*	36.75± 0.424*
	35	252.083± 10.828	94.166± 4.784*	37.666± 0.607*
	45	244.166± 9.090*	80.666± 5.206*	38.375± 0.276*
	60	172.083± 5.546*	75.583± 4.452*	39.791± 0.217

HR, heart rate; RR, respiratory rate; CT, cloacal temperature. Measurement area were compare with baseline value by performing t-test.
Figures represent mean ± Standard error.
*** Significantly ($P<0.01$) different from baseline value.**

The sedative and anaesthetic effects after drug administration are summarized in table (2). The administration of (X-F) induced moderate sedation. At (5) minutes after (K) administration most pigeons go to deep anaesthesia. The drug combination of (F, X-K) produced a satisfactory general anaesthesia for ten of the eleven pigeons. Two pigeons had third degree of anaesthesia.

The effect of (Y-N) combination as a reverse on recovery was observed after (5) minutes of reverse administration. The complete recovery time at which they stand to walk, aranged from (164-302) minutes at mean 195.583± 13.104.

Table (2) The sedative and anesthetic effect of drugs combination

Pigeon number	Base-line 0 min	Pre.10 min	Pre. 5 min	An. 5 min	An. 15 min	An. 25 min	An. 35 min	An. 45 min	An. 55 min	Rev. 1 min	Rev. 5 min	Rev. 15 min	Rev.25 min	Rev.35 min	Rev. 45 min	Rev.60 min	Recovery time
1	0	1	1	4	4	4	4	4	4	4	2	2	2	2	2	1	202
2	0	1	2	4	4	4	4	4	4	4	3	2	2	1	1	1	168
3	0	1	1	4	4	4	4	4	4	4	2	2	2	2	1	1	178
4	0	1	2	4	4	4	4	4	4	4	2	2	2	2	1	1	270
5	0	1	2	3	3	3	3	3	3	3	3	2	2	2	2	1	165
6	0	1	1	4	4	4	4	4	4	4	2	2	2	1	1	1	212
7	0	1	2	4	4	4	4	4	4	4	2	2	2	2	2	1	170
8	0	1	1	4	4	4	4	4	4	4	2	2	2	2	1	1	182
9	0	1	1	4	4	4	4	4	4	4	2	2	2	2	2	1	302
10	0	1	1	3	3	3	3	3	3	3	2	2	2	1	1	1	164
11	0	1	2	4	4	4	4	4	4	4	2	2	2	2	2	1	170
12	0	1	1	4	4	4	4	4	4	4	3	2	2	1	1	1	164
																	195.583± 13.104

Baseline values before administration of drugs, Pre: premedication (after injection of Xylazine- Fentanyl); An: anesthesia (ketamine), Rev: Revering of anaesthesia by Yohambine- Naloxone.

1- first degree of anaesthesia. 2- second degree of anaesthesia. 3- third degree of anaesthesia. 4- Fourth degree of anaesthesia

DISCUSSION

The healthy recovery of all pigeons from (X-F-K) (anaesthetic combination) after its reverse with (Y-N) (reversing combination) showed that this anaesthetic protocol was fairly effective and safe for pigeons.

The present study demonstrated that the drug combination, which was used, permitted to record the pharmacological effects of the alpha-2 adrenoceptor agonist and opioid agonist together and then compare the changes induced by injection of (K) after (15) minutes and (Y-N) combination after (70) minutes.

A decreased in HR was recorded for all pigeons during the premedication and anaesthesia. Bradycardia, which may be attributable to adminished sympathetic tone and increase systemic vascular resistance, which leads to hypertension resulted in a reflex barroreceptor- mediated physiological bradycardia, which is the characteristic pharmacological response to alpha-2 adrenoceptor agonist (6).

Furthermore, the administration of opioid agent, Butorphanol, caused decreased in heart rate when it used in African grey parrots and cockatoos (7 and 8). The decreased HR induced in the pigeons of this study might be the result of (X) administration as it has an alpha-2 adrenoceptor agonist effect and (F) binding Mu and Kappa receptors.

Directly after few minutes of its injection, Ketamine temporarily counter balanced the Brady cardiac effect resulted from premidication is may be due to (K) stimulate central sympathetic outflow, which in turn, causes stimulation of the heart (9). Generally, HR decreased gradually after (K) administration. (10) reported decrease in HR in cynomolgus mammals after using (K) and (K+ medetomidine) similarly, but the bradycardia in the present study, most probably, contribute to final negative chromotropic effect of drugs combination on the pigeon's heart.

Opioid causes respiratory depression (9) and sedation with alpha-2 adrenoceptor associated with respiratory depression (11) and it worth while inquiring the degree of respiratory depression produced with any alpha-2 adrenoceptor agonist will be increased when the agonist is given with other sedative (6). Therefore, the RR at present study was declined in all pigeons immediately after the injection of premedication, this decreased was partially counteract after few minutes of (K) injection, but returned to be declined until injection of reversing combination (Y-N).

Cloacal temperature decreased gradually after injection of premedication and anaesthesia since birds especially pigeons lose heat rapidly during anaesthesia (12). The decreased temperature gradually elevated after injection (Y-N) to each near the normal value at (60) minutes after (Y-N) injection and stayed for relatively longer time before it returned to normal value. The reason for the dramatic decrease in body temperature in pigeons remain unknown (5).

The dose required of (X) and (K) for pigeons in this study and previously reported dosage of (X-K) (2-6 mg/kg. Bw Im- 3o mg/kg. BW Im)(12) for birds seems to higher than dosage reported for other animals as it have been reported by (13) who use (X-K) at dosage of (1 mg/kg. Bw iv-1 mg/kg. Bw iv) as a combination in horse. Other information is available on use of X (2.2 mg/kg. Bw. Im) and K (1 mg/kg. Bw. Im) in cat (14). This variance in dosage requirement may, most probably, contribute to higher metabolic rate of pigeons (14).

Birds up to 1 Kg Bw. have high metabolic rates, so they need supply of food and the fatal hypoglycemia and Ketosis are often occurred in birds around 60 g Bw. as a result of starvation for 6-8 houre (15). All that make birds and particularly pigeons in this study consider as unsafe subject for anaesthesia, therefore the effect of anaesthesia should be reversed in order to overcome the problems which may be life threatining in pigeons.

In the present study, (Y-N) combination were used to reverse the sedative and cardiopulmonary inhibitory effect of (X-K-F) combination. The enhancement in HR, RR and CT after injection of reversing combination can be contribute to the injection of (Y-N). Its worth while inquiring that our preliminary studies showed that using of (X-F-K) combination only induced along recovery period of sedation with a sever decrease in RR. In parallel to this study there is some notions in literature showed using of (Y) is an effective reversal agent for (X/K) anaesthesia in raptors and budgerigars (16) and (17), also (N) was used in combination with flumazenil and atipamezole to reverse the anaesthetic effect produced by midazolam/ medetomidine/ Fentanyl combination in rabbits (18).

The route of reversal (antagonist) administration should be also discussed. To obtain a safe reversal of anaesthesia, the administration of the antagonist via the subcutaneous route is preferred. Unlike the intravenous or intrapertonial route the subcutaneous route offers the advantage of much slower antagonist uptake in to the circulation combined with a depot effect leading to smooth reversal of anaesthesia within few minutes. This reduces the risk of re-sedation, which is particularly high in case of lipophilic anaesthetics, which are stored primarily in muscle and to a much lesser degree in fat tissue of the animal and then released in to the circulation over an extended period of time post- anaesthesia (19) and (20).

The (X-F-K) combination produced a profound anaesthesia in ten pigeons, analgesia was adequate and muscle relaxation was complete in all pigeons. However, only two pigeons showed a third degree of anaesthesia and required an additional dose of (K). Using of anaesthetic combination in the present study which can be antagonized by specific antagonist, and every agent in this combination potentiate each others action, lower individual dose requirements, and that lead to a fairly reliable more safely anaesthesia in pigeons.

تقييم الفعالية التخديرية للفنتانيل، الزيلازين والكيتامين في الحمام المستأنس

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الخلاصة

صممت هذه الدراسة لتقييم الفعل التسديري– التخديري للتوليفة الدوائية المؤلفة من الزيلازين+ الفنتانيل– الكيتامين في الحمام المحلي المُستأنس. أجريت هذه الدراسة على (12) حمامة مؤلفة من كلا الجنسين، أستخدم مزيج الزيلازين+ الفنتانيل كعلاج قبل التخدير لغرض إحداث التسدير،و بعد ذلك بخمسة عشرة دقيقة حقن الكيتامين حقنت جميع الأدوية في منطقة العضلة الصدرية، عكس الفعل التخديري لهذه التوليفية الدوائية بواسطة خلال حقن مزيج اليوهامبين والنالكسون تحت الجلد.

قييم الفعل التسديري– التخديري لتوليفة الزيلازين+ الفنتانيل– كيتامين الدوائية، التغيرات في عدد نبضات القلب، معدل التنفس ودرجة حرارة المجمع خلال (10) دقائق قبل حقن الزيلازين+ الفنتانيل، خلال (10)، (15) دقيقة بعد حقن الزيلازين+ الفنتانيل، خلال (5)، (15)، (25)، (35)، (45) و (55) دقيقة بعد حقن الكيتامين وخلال (1)، (5)، (15)، (25)، (35)، (45) و (60) دقيقة بعد حقن مزيج اليوهامبين والنالكسون. لوحظ أن انخفاض معدل نبضات القلب والتنفس ودرجة حرارة المجمع في الحمام خلال (10) دقائق من حقن الزيلازين+ الفنتانيل الى حين تحسنها جميعاً بعد حقن مزيج اليوهامبين والنالكسون. أن أستخدام هذه التوليفة الدوائية وفر درجة عالية من التخدير العام في (10) من أصل

(12) من الحمامات المستخدمة في التجربة، كما وأن استخدام مزيج اليوهامبين والنالكسون كان مؤثراً في عكس مفعول التخدير وتوفير افاقة أمنة في الحمامات التي خضعت للتخدير في هذه الدراسة.

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