RESEARCH ARTICLE

Exploring Anaesthesia Options in Chickens: Zoletil vs. Midazolam-Ketamine vs. Dexmedetomidine-Ketamine

Manasi Debbarma[1], Hitesh Bayan[1]*, Bedanga Konwar[1], Kalyan Sarma[2]

Abstract

Various anaesthetics and sedatives have been used for balanced anaesthesia in birds. Careful selection and appropriate dosage are required due to potential anatomical, physiological, and metabolic variations. This study was aimed to evaluate the effects of zoletil, midazolam-ketamine, and dexmedetomidine-ketamine in chickens. Eighteen chickens were divided into three equal groups and received one of the anaesthetic combinations by intramuscular injections: Group A: zoletil @ 15 mg/kg; Group B: midazolam @ 0.5 mg/kg and ketamine @ 40 mg/kg and Group C: dexmedetomidine @ 5 µg/kg and ketamine @ 20 mg/kg. Clinical and physiological parameters were evaluated. Group A had faster sedation time and shorter anaesthesia duration. Group A and C had moderate sedation but rough recovery, while Group B had heavy sedation and smooth recovery. Group B had shortest recovery time. Weak pedal and abolished palpebral reflex with closed eyelids were observed in all groups. Heart rate and respiration rate decreased significantly at 30 min in all groups. Cloacal temperature decreased significantly in Group A and C at 30 min, then non-significantly at 60 min, while non-significant fluctuations were observed in Group B. Midazolam-ketamine showed better anaesthetic outcome than zoletil or dexmedetomidine-ketamine in chickens.

Key words: Chickens, Dexmedetomidine, Ketamine, Midazolam, Zoletil.

Ind J Vet Sci and Biotech (2024): 10.48165/ijvsbt.20.4.25

Introduction

Anaesthesia is essential for safe and effective handling of birds for any clinical examination or surgical procedure while minimizing stress, trauma or discomfort. The use of anaesthetic drugs to captured birds enhances their probabilities of surviving a medical or surgical procedure (Coles, 1997).

Zoletil is a non-opioid, non-barbiturate injectable anaesthetic which is a combination of equal concentrations of tiletamine and zolazepam in 1:1 ratio. Ketamine is a dissociative anaesthetic used to induce and maintain general anaesthesia. Ketamine when administered alone in birds produced rough recoveries, myotonic contractions, opisthotonus and inadequate muscle relaxation (Valverde *et al.,* 1993). To enhance the efficacy and counteract the negative effects of ketamine, an alpha-2 adrenergic agonists or benzodiazepines are combined for general anaesthesia (Azizpour and Hassani, 2012). Midazolam is a water soluble and short acting benzodiazepine with sedative, muscle-relaxing, anxiolytic, amnestic and appetite-stimulating properties in birds (Araghi *et al.,* 2016). Dexmedetomidine is an alpha-2 adrenoceptor agonist and active sterioisomer of the racemic mixture medetomidine commonly used as sedative and tranquilizer in veterinary practice. The use of anaesthetics in birds presents challenges due to the dearth of studies in this area and the wide range of species that remained unstudied (Paula *et al*., 2013). The aim of this research was therefore to study the effects of zoletil, midazolam-ketamine and dexmedetomidine-ketamine in chickens.

[1]Department of Veterinary Surgery and Radiology, College of Veterinary Sciences & Animal Husbandry, Central Agricultural University, Aizawl-796015, Mizoram , India

[2]Department of Veterinary Medicine, College of Veterinary Sciences & Animal Husbandry, Central Agricultural University, Aizawl-796015, Mizoram, India

Corresponding Author: Hitesh Bayan, Department of Veterinary Surgery and Radiology, College of Veterinary Sciences & Animal Husbandry, Central Agricultural University, Aizawl, Mizoram, India. e-mail: hbayan@gmail.com

How to cite this article: Debbarma, M., Bayan, H., Konwar, B., & Sarma, K. (2024). Exploring Anaesthesia Options in Chickens: Zoletil vs. Midazolam-Ketamine vs. Dexmedetomidine-Ketamine. Ind J Vet Sci and Biotech. 20(4), 119-123.

Source of support: Nil

Conflict of interest: The authors declare no conflict of interest.

Submitted 10/04/2024 **Accepted** 30/04/2024 **Published** 10/07/2024

Materials and Methods

Experimental Birds

One year old male White Leghorn chickens weighing 1-2 kg with average body weight of 1.5 kg were used. All the chickens were kept in uniform environmental condition. The chickens were housed in pairs in cages in a quiet room to avoid possible stress-inducing factors during the study and fed a commercial diet. The chickens had free access to food

and water. The chickens were adapted for one week before the study and the experiment was carried out in an operation theatre having temperature controlled environment. The chickens were fasted for 3-6 h and routine clinical examinations were carried out prior to the anaesthetic trial.

Anaesthetic Protocol

The study was conducted in the Department of Veterinary Surgery and Radiology on 18 White Leghorn chickens. The chickens were randomly divided into three groups, *viz*., Group-A, B and C, comprising six chickens in each. The chickens in Group A were injected with zoletil @ 15 mg/kg b wt, intramuscularly; Group B were injected with mixture of midazolam @ 0.5 mg/kg and ketamine @ 40 mg/kg b.wt,, intramuscularly, and Group C were injected with dexmedetomidine @ 5 µg/kg and ketamine @ 20 mg/kg b wt, combination, intramuscularly.

Evaluation of Action of Drugs

Clinical parameters, the time for sedation (time from administration of the anaesthetic agent to the loss of consciousness), the duration of anaesthesia (time interval from loss of consciousness to reappearance of sensation), recovery time (elapsed from administration of anaesthetics to the time when the birds walk unassisted) were assessed. In addition, level of sedation achieved was scored using the subjective scoring method as described by Pollock *et al.* (2001). Muscle relaxation was assessed in the muscles of the neck, wings and legs. The degree to which the bird's hind limbs could be flexed, their necks could be extended, and their wings could be pulled easily was measured as the degree of muscle relaxation. Level of muscle relaxation achieved was scored as 0-Weak relaxation, 1-Moderate relaxation, 2-Excellent relaxation. Pedal reflex was evaluated by using a towel clamp on the skin web between digits 2 and 3 as 0-Weak reflex, 1-Moderate reflex, 2-Excellent reflex. Palpebral reflex was observed by tapping the eyelids with a sterile cotton tip swab. Presence or lack of the reflexes were indicated as + or -, respectively. Closed, half open and opened eyelids were indicated as -, +, ++, respectively. Quality of recovery was assessed depending on the severity of excitability, such as wing flapping and ataxia which were scored from 0 to 1.

Physiological parameters like heart rate (auscultated using stesthoscope), and respiration rate (by observing the abdominal wall excursion) were recorded, and cloacal temperature was recorded using digital thermometer. They were observed at 0 min - baseline, 30 and 60 min post-anaesthetics.

Statistical Analysis

General Linear Model of one way and two way ANOVA based on Fisher's Least Significant Difference method and DNMRT were used to determine the significant difference among time points for different treatment groups as well as among treatment groups for different time points using statistical package SPSS version 27.0. Non-parametric Kruskal Walis test was used to determine the significant difference among treatment groups for ranking observations. Results were presented as mean ± SE and differences were considered significant when $p<0.05$.

Results and Discussion

Clinical Parameters

The time for sedation recorded was significantly lower ($p\leq0.01$) in Group A than Group B, and Group C, however there was no significant difference between group B and group C (Table 1). Significantly lower sedation time required in Group A might be due to the effect of tiletamine which is more potent than ketamine (Salve *et al.,* 2022).

The duration of anaesthesia observed between Groups A, B and C were statistically different ($p\leq0.01$) and the longest duration of anaesthesia was observed in Group C followed by Group B and A. Significantly shorter duration of anaesthesia observed in Group A might be due to the rapid metabolism of zolazepam than tiletamine in birds (Nicolau *et al*., 1999) and dexmedetomidine being a potent, non-narcotic, sedative and alpha-2-adrenergic agonist when combined with ketamine produces CNS depression (Patil *et al*., 2018), which prolonged the duration of anaesthesia. Similar duration of anaesthesia was observed by Yayla *et al.* (2018) using midazolam-ketamine in quails, and dexmetomidine-ketamine in broiler chickens by Patil *et al.* (2018).

A significantly ($p\leq0.01$) shorter recovery time was recorded in Group B as compared to Group A and C. The recovery time between Group A and C did not vary significantly although the value was higher in Group C than Group A (Table 1). The recovery time is dose-dependent, with higher doses of dissociative anaesthetics resulting in longer recovery times (Salve *et al*., 2022). The prolonged recovery time in Group C may be due to the synergistic effect of ketamine and dexmedetomidine, which can cause central nervous system depression (Patil *et al*., 2018).

Table 1: Time for sedation, duration of sedation and recovery time recorded (min) in different group of chickens (Mean ± SD)

Group	Time for sedation (min)	Duration of anaesthesia (min)	Recovery time (min)
A	2.85 ± 0.23^{A}	20.50 ± 1.38^{A}	166.33 ± 3.38^{A}
B	3.83 ± 0.33^{B}	26.33 ± 2.01^{B}	115.17 ± 6.68^{B}
C	3.98 ± 0.05^{B}	43.50 ± 1.52^{C}	175.00 ± 3.89^{A}
P value	0.008**	0.001**	0.001**

**p≤0.01 = significant at 1%. Values in the same column with different superscripts differ significantly.

Chickens in Group A and C displayed moderate sedation levels, while Group B displayed heavy sedation. Group A

showed moderate muscle relaxation, Group B showed excellent muscle relaxation, while Group C showed weak to moderate relaxation during the anaesthetic trial (Table 2). Pedal and palpebral reflexes were all absent with closed eyelids in all the groups. Chickens in Group A and C exhibited excitability, whereas Group B did not show any excitability.

Table 2: Quality of sedation, quality of muscle relaxation and quality of recovery obtained in different group of chickens (Mean ± SD)

Group	A	B	C	P value
Quality of sedation	3.17±0.17^{a}	4.00±0.00^{b}	3.33±0.211^{ab}	0.012*
Quality of muscle relaxation	1.00±0.00^{a}	2.00±0.00^{b}	0.67±0.21^{a}	0.001**
Quality of recovery	1.00±0.00^{a}	0.33±0.21^{b}	1.00±0.00^{a}	0.008**

*p≤0.05 = significant at 5%, **p≤0.01 = significant at 1%, NS = Non-significant. Values in the same row with different superscripts differ significantly.

A heavy to moderate sedation observed in the anaesthetised chickens of Group A and C, and heavy sedation in Group B were similar to the observations noted by Durrani *et al*. (2005, 2008). The anaesthetic agents might have acted synergistically to produce deep anaesthesia in the chickens and midazolam being potent in birds with water solubility might have attributed to the heavy sedation of the chickens (Vesal and Eskandari, 2006).

Chickens in Group A showed moderate muscle relaxation, possibly due to tiletamine co-administered with zolazepam, which induced inhibition of internuncial neurons at the spinal level (Salve *et al*., 2022). In Group B, excellent muscle relaxation observed was possibly due to sedative properties of drugs used (Abbas *et al*., 2018). In Group C, weak to moderate muscle relaxation observed was possibly due to ketamine, which lacks skeletal muscle relaxation (Durrani *et al*., 2009).

Abolished pedal reflexes were found in all three groups, with moderate reflexes in one chicken from Group B and C. Visceral analgesia from ketamine and alpha-2-adrenergic agonists may have combined to produce profound analgesia. Palpebral reflexes were absent in all groups, indicating adequate depth of anaesthesia (Durrani *et al*., 2005). Chickens also had closed eyelids (Gandomani *et al*., 2011), possibly due to deep anaesthesia produced by the anaesthetic agents.

In Group A, zoletil caused shivering and tremors, instead of inhibiting the adverse effects of tiletamine, the combination of zolazepam actually weakened the negative effects. It might be due to the rapid metabolism of zolazepam than tiletamine in birds (Nicolau *et al.,* 1999). In Group B, four chickens revealed no excitability, whereas two exhibited excitability during recovery. Similar findings were reported by Varner *et al*. (2004), Gandomani *et al*. (2011) and Raisi *et al*. (2019). The low dosage of ketamine and the concurrent administration of sedatives might be the cause of the decrease in side effects during the recovery phase (Abbas *et al*., 2018). In Group C, excitability such as wing flapping and torticollis were observed, possibly due to increased sedation induced by dexmedetomide. These findings suggest that the combination of zolazepam and tiletamine may have weakened the negative effects. This might be associated with an increased degree of sedation induced by dexmedetomide in chickens (Patil *et al*., 2018).

Physiological Parameters

The heart rate decreased significantly in Groups A, B and C at 30 min, with significant increase at 60 min in Group A and C, but non-significant increase in Group B towards the baseline

Table 3: Heart rate, respiration rate and cloacal temperature recorded in different group of chickens at different time intervals post-induction (Mean ± SD)

Parameters	Group	0 min	30 min	60 min	P value
Heart rate	A	200.33±3.02^{a}	164.00±3.11^{bA}	181.83±3.68^{cA}	0.001**
	B	204.17±2.10^{a}	191.00±2.28^{bB}	196.00±2.32^{bB}	0.003**
	C	199.33±2.35^{a}	152.67±3.95^{bC}	171.50±3.74^{cC}	0.001**
	P Value	0.383^{NS}	0.001**	0.001**	
Respiration rate	A	20.83±0.40^{a}	18.67±0.56^{bA}	17.83±0.70^{bA}	0.006**
	B	22.17±0.95^{a}	19.00±0.26^{bA}	20.00±0.00^{bB}	0.004**
	C	22.83±0.87^{a}	16.17±0.31^{bB}	14.33±0.33^{cC}	0.001**
	P Value	0.214^{NS}	0.001**	0.001**	
Cloacal temp (°C)	A	41.57±0.14^{a}	40.42±0.30^{b}	39.85±0.15^{b}	0.001**
	B	41.62±0.12	40.62±0.37	40.82±0.48	0.149^{NS}
	C	41.71±0.13^{a}	41.00±0.23^{b}	40.42±0.26^{b}	0.003**
	P Value	0.754^{NS}	0.405^{NS}	0.141^{NS}	

*p≤0.05 = significant at 5%, **p≤0.01 = significant at 1%, p>0.05= non-significant (NS). Values in the same row and the same column with different superscripts *i.e.* small font and capital font, respectively, differ significantly.

values. All the groups revealed a significantly decreased respiration rate at 30 min and then in Group A, it decreased non-significantly and in Group C, it decreased significantly, whereas in Group B, it increased non-significantly at 60 min observation towards the baseline values. The cloacal temperature in Group A and C decreased significantly at 30 min and thereafter decreased non-significantly. However, non-significant fluctuation in cloacal temperature was recorded in Group B (Table 3).

The observations recorded on heart rates in different groups aligned with the reports of Sandmeier (2000), Durrani *et al.* (2009) and Sani and Onifade (2012). Cardiac depression occurs due to multiple mechanisms, including decreased sympathetic outflow, inhibition of noradrenaline release, cardiac pacemaker depression, increased vagal tone, and acetylcholine release (Vasan *et al.,* 2006).

The findings on respiration rate concurred with the observations of Gandomani *et al*. (2011), Durrani *et al*. (2008) and Patil *et al*. (2018). This decline was expected during anaesthesia, and in birds, ketamine induces respiratory depression (Rehman *et al*., 2020). The depression may be related to deeper hypnosis caused by midazolam additive effects on anaesthetic combinations (Ajadi *et al*., 2009), and the use of dexmedetomidine and ketamine may cause profound respiratory depression due to the direct depressive effect of alpha-2 agonist drugs on respiratory centers (Vasan *et al*., 2006).

The trend of cloacal temperature was similar to the findings of Varner *et al*. (2004), Sani and Onifade (2012) and Yayla *et al*. (2018). This reduction may be due to the additive effect of sedatives or anaesthetic agents (Vasan *et al*., 2006), which inhibit thermoregulatory centers, reducing heat production and basal metabolism (Gandomani *et al.,* 2011).

Conclusion

Zoletil, midazolam-ketamine and dexmedetomidine-ketamine did not have any significant harmful effects on clinical and physiological parameters in chickens, except significantly prolonged recovery time and excitement during recovery with zoletil and dexmedetomidine-ketamine. Based on the present findings, midazolam-ketamine combination was found to provide satisfactory anaesthesia suitable for short duration surgical procedures

Acknowledgement

The authors acknowledge the Competent Authority, Central Agricultural University, Mizoram, India, for financially supporting the research work.

References

Abbas, S.W., Ali, M.N., Abbas, G., Safwan, H.M., Sajid, M., & Mehmood, M. (2018). Comparative effectiveness of general anesthesia in doves using a combination of ketamine and diazepam. *Advanced Zoology and Botany, 6*(4), 95-100.

Ajadi, R.A., Kasali, O.B., Makinde, A.F., Adeleye, A.I., Oyewusi, J.A., & Akintunde, O.G. (2009). Effects of midazolam on ketamine-xylazineanesthesia in guinea fowl (*Numida meleagris galeata*). *Journal of Avian Medicine & Surgery, 23*(3), 199-204.

Araghi, M., Azizi, S.,Vesal, N., & Dalir-Naghade, B. (2016). Evaluation of the sedative effects of diazepam, midazolam and xylazine after intranasal administration in juvenile ostriches (*Struthioca melus*). *Journal of Avian Medicine & Surgery, 30*(3), 221-226.

Azizpour, A., & Hassani, Y. (2012). Clinical evaluation of general anaesthesia in pigeons using a combination of ketamine and diazepam. *Journal of South African Veterinary Association, 83(1),* 1-4.

Coles, B.H. (1997). Anaesthesia. In: *Avian Medicine and Surgery*. 2nd edn., Oxford, England, Blackwell Science, pp. 125-147.

Durrani, U.F., Ashraf, M., & Khalid, A. (2005). Comparative efficacy of detomidine and detomidine-ketamine cocktail in quails. *Pakistan Veterinary Journal, 25*(4), 197.

Durrani, U.F., Ashraf, M., & Khan, M.A. (2009). A comparison of the clinical effects associated with xylazine, ketamine, and a xylazine-ketamine cocktail in pigeons (*Columba livia*). *Turkish Journal of Veterinary & Animal Science, 33*(5), 413-417.

Durrani, U.F., Khan, M., & Ahmad, S.S. (2008). Comparative efficacy (sedative and anaesthetic) of detomidine, ketamine and detomidine-ketamine cocktail in pigeons (*Columba livia*). *Pakistan Veterinary Journal, 28*(3), 115-118.

Gandomani, M.J., Ghashghaii, A., Tamadon, A., Attaran, H.R., Behzadi, M.A., & Javdani, Z. (2011). Comparison of anaesthetic effects of ketamine-xylazine and ketamine-diazepam combination in budgerigar. *Veterinary Scan, 6*(1), 81-81.

Nicolau, A.A., Souza Spinosa, H.D., Maiorka, P.C., & Guerra, J.L. (1999). Evaluation of tiletamine-zolazepam as an anesthetic in quail (*Coturnix coturnix japonica*). *Journal of American Association of Laboratory Animal Science, 38*(1), 73-75.

Patil, M., Desai, D., & Ningadalli, B. (2018). Xylazine-ketamine and dexmedetomidine- ketamine combination comparison in 30 days old broilers. *International Journal of Livestock Research*, *8*(3), 118-127.

Paula, V.V., Otsuki, D.A., Auler, J.O.C., Nunes, T.L., Ambrósio, A.M., & Fantoni, D.T. (2013). The effect of premedication with ketamine, alone or with diazepam, on anaesthesia with sevoflurane in parrots (*Amazona aestiva*). *BMC Veterinary Research*, *9*(1), 1-9.

Pollock, C.G., Schumacher, J., Orosz, S.E., & Ramsay, E.C. (2001). Sedative effects of medetomidine in pigeons (*Columba livia*). *Journal Avian Medicine & Surgery, 15*(2), 95-100.

Raisi, A., Norouzian, H., & Rostami, M. (2019). Influence of tramadol on anaesthesia times, analgesia and electrocardiogram associated with injection anaesthesia in common buzzards (*Buteo buteo*). *Veterinary Research Forum*, *10,* 51-57.

Rehman, M.U., Aslam, S., Iqbal, N.,Durrani, U.F., Hussain, N., Luqman, Z., & Jawad, H. (2020). Comparative efficacy of injectable and inhalation anesthesia in pigeons. *Advances in Animal & Veterinary Science*, *8,* 1203-1210.

Salve, P.D., Thorat, M.G., Raulkar, R.V., Hatzade, R.I., Ingawale, M.V., Pawar, M.B., & Jadhav, A.G. (2022). Clinical efficacy of

tiletamine-zolazepam and ketamine-diazepam combination on quality of anesthesia for ovariohysterectomy in dog. *Acta Scientifica Vet Scientifica*, *4*(2), 51-56.

Sandmeier, P. (2000). Evaluation of medetomidine for short-term immobilization of domestic pigeons (*Columba livia*) and Amazon parrots (*Amazona* species). *Journal Avian Medicine & Surgery, 14,* 8-14.

Sani, I.M., & Onifade, K.I. (2012). Medetomidine elicit variable effects on sedative indices, haematological and physiological parameters in domestic pigeons (*Columba livia*). *African Journal of Pharmacy & Pharmacology*, *6,* 235-240.

Valverde, A., Bienzle, D., Smith, D.A., Dyson, D.H., & Valliant, A.E. (1993). Intraosseous cannulation and drug administration for induction of anesthesia in chickens. *Veterinary Surgery, 22*(3), 240-244.

Varner, J., Clifton, K.R., Bs, S.P., Broderson, J.R., & Wyatt, R.D. (2004). Lack of efficacy of injectable ketamine with xylazine or diazepam for anaesthesia in chickens. *Laboratory Animals*, *33*(5), 36-39.

Vasan, P., Tiwary, R., Maiti, S.K., & Dutta, A. (2006). Xylazine, diazepam and midazolam premedicated ketamine anaesthesia in White Leghorn cockerels for typhlectomy. *Journal of South African Veterinary Association, 77*(1), 12-18.

Vesal, N., & Eskandari, M.H. (2006). Sedative effects of midazolam and xylazine with or without ketamine and detomidine alone following intranasal administration in ring-necked parakeets. *Journal of American Veterinary Medical Association, 228*(3), 383-388.

Yayla, S., Kilic, E., Aydin, U., Donmez, I., Ermutlu, C.S., Baran, V., & Yildiz, U. (2018). Comparative evaluation of intramuscular, intranasal, oral and intraosseal administration of midazolam, ketamine combination in quail (*Coturnix coturnix japonica*). *Dicle Üniv. Vet. Fak. Derg., 11*(2), 60-63.