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Comparative Study on the Anaesthetic Effect of Tiletamine-zolazepam and Propofol as an Induction Agent for Conventional and Endoscopic Abdominal Surgeries in Domestic Cats

S.A. Chauhan[1], Shubham Pant[1], G.S. Khandekar[1], S.D. Tripathi[1], V.D. Aher[1], T.I. Attar[1], V.G. Nimbalkar[1]

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ABSTRACT

Background: Felines have higher metabolic and heart rates than canines and therefore are considered to be the delicate subjects for anaesthesia and pain management. Major surgeries in felines require balanced anaesthesia with smooth and fast induction, longer duration of action and faster and excitement free recovery.

Methods: The study was conducted on 24 clinical cases of cats, subjected to conventional and endoscopic surgeries for abdominal affections, premedicated with atropine and dexamethasone at the rate of 0.04 and 0.2 mg/kg body weight to assess the anaesthetic effect of tiletamine-zolazepam combination at the rate of 8 mg/kg body weight IM in group A (n=12) and propofol @ 8 mg/kg body weight IV in group B (n=12) respectively as inducing agent to isoflurane maintained anaesthesia.

Result: The mean induction time were 421.9±69.47 seconds (7.03±1.16 minutes) in group A and 56.2±0.43 seconds (0.94±0.01 minute) in group B. In both the groups quality of induction was smooth with rapid loss of all reflexes allowing easy intubation. A significant drop in rectal temperature at 15 min post induction with minimal alterations in heart rate, respiration rate and saturated oxygen level were observed. The mean time of recovery recorded were 75.91±8.1 minutes in group A and 88.2±10.2 minutes in group B. Smooth, rapid and good quality recovery was observed in both the anaesthetic groups; however, propofol-induced transitory hypothermia and shivering, lowered the quality of recovery in group B. All the physiological and hematological parameters were in normal limits.

Key words: Cats, Induction agent, Isoflurane, Propofol, Tiletamine-zolazepam.

INTRODUCTION

Ketamine hydrochloride has always been a popular and promising anaesthetic of choice in cats, because of its minimal depressant effect on the cardiovascular (Child *et al.,* 1972; Haskins *et al.,* 1975) and respiratory systems (Evans *et al.,* 1972). However, Beck *et al.* (1971) expressed presence of laryngeal and pharyngeal reflexes during ketamine anaesthesia resulting in strenuous intubation. Additionally the procurement of ketamine also becomes very difficult due to many government policies further encouraging the use of alternative anaesthetic agents in cats like Propofol and tiletamine-zolazepam.

The combination of tiletamine hydrochloride (a cyclohexamine anesthetic) and zolazepam hydrochloride (a benzodiazepine sedative and muscle relaxant) has been formulated for intramuscular administration. Tiletamine administered intramuscularly to cats produces comparatively safe anaesthesia. The addition of zolazepam produces muscle relaxation and sedation, reduces potentially deleterious side effects and allows a reduction in the dose of tiletamine.

Tiletamine hydrochloride, a congener of phencyclidine approved by FDA since 1982 for anesthetic use in dogs and cats just like ketamine, is recently marketed in India with zolazepam hydrochloride and is considered 3 times potent than ketamine in duration of action. Propofol a non-barbiturate (2,6-diisopropylphenol) is a hypnotic anesthetic agent. Propofol was distinguished by a smooth induction, a quick onset of unconsciousness and a brief duration of effect. For its effect proper intravenous excess is mandatory. Additionally propofol can result in oxidative injury to erythrocytes and can increase the chances of Heinz body formation after 3 days and more severe symptoms can be seen like malaise, anorexia and diarrhea after 5 days. Hence, tiletamine alone is a more effective agent for induction of anaesthesia in cats than other species.

[1]Department of Veterinary Surgery and Radiology, KNP College of Veterinary Science, Maharashtra Animal and Fisheries Sciences University, Satara-412 801, Maharashtra, India.

Corresponding Author: S.A. Chauhan, Department of Veterinary Surgery and Radiology, KNP College of Veterinary Science, Maharashtra Animal and Fisheries Sciences University, Satara-412 801, Maharashtra, India. Email: ssalvekar@gmail.com

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Therefore this study was designed with the objective to compare the effects of tiletamine-zolazepam and propofol @ 8 mg/kg intramuscular and intravenous respectively as inducing agents of anaesthesia maintained with isoflurane in cats.

MATERIALS AND METHODS

As per approval to this study by animal ethical committee of Krantisinh Nana Patil college of veterinary science, Shirwal, Dist Satara with resolution number 02, a total of 24 clinical cases of cats of either sexes, presented with various abdominal affections subjected for conventional and endoscopic surgeries (Table 1) at Veterinary Clinical Complex and Department of Surgery and Radiology of Krantisinh Nana Patil College of Veterinary Science, Shirwal, Mumbai Veterinary College, Mumbai and at private clinics in and around Pune during the year 2020-2021 were selected for this study.

All the cats underwent a thorough clinical and hematological examination to assess their ability to undergo anaesthesia and surgical procedures and details of age, sex, weight, breed were recorded and were randomly divided in two different groups, A and B. As per requirement of the ailment involved the cats were further subjected to radiography and or ultrasonography. Physiological parameters like rectal temperature, heart rate, respiration rate and color of mucus membrane were recorded. After proper restraining a total 2-3 ml of blood was collected from the cephalic or femoral vein prior to administration of anaesthetic drugs. The cats were fasted for 6-8 hours and water was withheld for 4-6 hours before the induction of anaesthesia. The surgical site was scrubbed with 7.5% povidone iodine solution and prepared aseptic with 10% povidone iodine 70% isopropyl alcohol before making an incision.

All the cats were premedicated with atropine sulfate @ 0.04 mg/kg body weight and Dexamethasone @ 0.2 mg/kg body weight subcutaneously, 10 minutes prior to induction of anaesthesia. Induction of anaesthesia was done with Tiletamine- zolezepam combination @ 8 mg/kg of body weight intramuscularly in group A and propofol @ 8 mg/kg of body weight intravenous in group B. The jaw relaxation and gag reflex were assessed by opening the mouth of the cat and pulling the tongue out from the mouth respectively. A laryngoscope with a small blade and proper light source was used for visualization of the epiglottis where 10% lignocaine spray was sprinkled. By pressing the base of the tongue ventrally, an endotracheal tube no 2.5 was inserted into the Rima glottis till it reaches to midway of tracheal bifurcation and secured with the help of bandage. All the cats were preoxygenated for 3 to 5 minutes and then were connected to an inhalant anaesthesia machine having isoflurane vaporizer. The surgical plane was maintained by isoflurane with minimum alveolar concentration ranging from 1-3% as per depth of anaesthesia. Various surgical techniques were done under this anaesthesia *viz*. spaying, castration, c-section, herniorrhaphy, enterotomy, cystotomy, laparoscopic ovariohysterectomy, gastroscopy *etc*. Following completion of the surgery, the dial setting of the vaporizer was switched off in a gradual fashion, followed by emptying of the rebreathing bag. After the reappearance of swallowing reflex, extubation was performed.

Following parameters were studied during the study.

Anaesthetic parameters

Time and quality of induction of anaesthesia, quality and duration of maintenance of anaesthesia, quality of muscle relaxation, quality of recovery from anaesthesia.

Physiological parameters

Rectal temperature, heart rate, respiratory rate, SpO2.

Hematological and biochemical parameters

Complete blood count, differential leucocyte count, Liver function test (SGOT, SGPT), kidney function test (BUN, serum creatinine).

The IBM- SPSS-20 software was used to analyze numerical data gathered in the present study. Descriptive statistics was employed for all the parameters and t test was employed to understand the subgroup difference in continuous variables of Group A and B. Analysis of variance (ANOVA) was performed to evaluate changes in various physiological factors after fixed interval of time in each group separately. All results were considered statistically significant when $P \leq 0.05$.

RESULTS AND DISCUSSION

The mean±S.E time of induction recorded was 421.9±69.47 seconds in group A and 56.2±0.43 seconds in group B (Table 1). Yanmaz *et al.* (2017) reported the time of onset of anaesthesia as 5.88±0.54 minutes in cats with the administration of the 10 mg/kg zolazepam-tiletamine combination intramuscularly. However, Ko *et al.* (2007), Li *et al.* (2015) and Liang *et al.* (2021) reported a reduction in induction times when tiletamine-zolazepam was combined with other anaesthetics like butorphanol, xylazine, ketamine, dexmedetomidine and medetomidine.

The quality of induction was graded as excellent in 58% of cats and good in 42% of cats in group A. In propofol anaesthesia 75% of cats exhibited struggling during the intravenous injection with a brief period of apnoea and coughing during intubation. Hence the overall quality in group B was graded as good (Grade B). The altered quality of induction in group B could be attributed to the stretch method of restraining required for cats for intravenous administration of propofol. The longer duration required for induction in group A could be attributed to the drug's pharmacokinetics pertaining to the intramuscular injection route. Therefore, considering the ease of administration of medications in the case of cats and the comfort of the animal with respect to handling and environment, intramuscular injection of Tiletamine-zolazepam combination @ 8 mg/kg could be recommended as an excellent inducing agent providing quick rapid and smooth induction of anaesthesia in cats allowing easy intubation Fig 1.

The effect of an inducing agent over skeletal muscle relaxation was based on a modified scale score given by Li *et al.* (2013) which from 0 to 3, where score 0 being resistant to anaesthetic and 3 representing the most profound relaxation of muscles. The mean±S.E score for muscle relaxation was 2.6±0.14 in group A and 2.4±0.14 in group B with the cat exhibiting profound jaw relaxation and easy intubation. Higher score could be attributed to the combined

Table 1: Details of each cat with respect to approximate age (years), weight (kilograms), sex, breed, type of affection and recovery time in group A and B.

Animal no.	Breed	Age (yrs)	Sex	Weight (kgs)	Surgical affection	Procedure	Time of induction (Sec)	Duration of recovery (Min.)
Group A- Anaesthesia induced by Tiletamine-Zolazepam Combination								
ZC1	ND	1.5	M	2.5	Bilateral abdominal hernia	Herniorrhaphy	630	85
ZC2	ND	2	M	3.5	Evisceration of intestine	Herniorrhaphy	546	92
ZC3	Persian	1	F	3.5	Spaying	Ovariohysterectomy	75	52
ZC4	ND	1	M	1.6	Intestinal obstruction due to fecolith	Enterotomy	420	154
ZC5	ND	11	F	2	Uterine mass	Tumor removal with ovariohysterectomy	240	70
ZC6	Persian	1.5	F	3.9	Abdominal laceration	Suturing of wound	180	62
ZE1	ND	1.2	F	2	Spaying	Ovariohysterectomy	718	50
ZE2	ND	2	F	2.4	Spaying	Ovariohysterectomy	722	80
ZE3	ND	1.5	F	2.2	Gastritis	Gastroscopy	600	72
ZE4	ND	2	F	3	Spaying	Ovariohysterectomy	250	64
ZE5	ND	1.6	F	2.5	GI foreign body	Gastroscopy	580	52
Mean±S.E		2.4±0.79		2.67±0.70			421.9±69.47	75.91±8.1
Group B- Anaesthesia induced by Propofol								
PC1	ND	1.6	M	2.2	Abdominal hernia	Herniorrhaphy	55	145
PC2	ND	2.5	F	2	Evisceration of intestine	Herniorrhaphy	58	130
PC3	ND	2	F	1.8	Dystocia	Ovariohysterectomy	56	95
PC4	Persian	1.8	M	3.5	Urolithiasis	Cystostomy	57	75
PC5	ND	2	F	2.1	Spaying	Ovariohysterectomy	55	70
PC6	ND	1.5	F	2.4	Spaying	Ovariohysterectomy	56	82
PE1	ND	2.5	F	3.2	Gastritis	Gastroscopy	56	40
PE2	ND	1.5	F	2.8	Spaying	Ovariohysterectomy	58	52
PE3	ND	1.2	F	2.6	Spaying	Ovariohysterectomy	59	68
PE4	ND	2	F	2.4	Gastritis	Gastroscopy	54	150
PE5	ND	1.8	F	2.4	Spaying	Ovariohysterectomy	55	80
PE6	ND	2.5	F	2.6	Spaying	Ovariohysterectomy	56	72
Mean±S.E		1.9 ±0.12		2.5±0.14			56.2± 0.43	88.2±10.2

M- Male, F- Female.

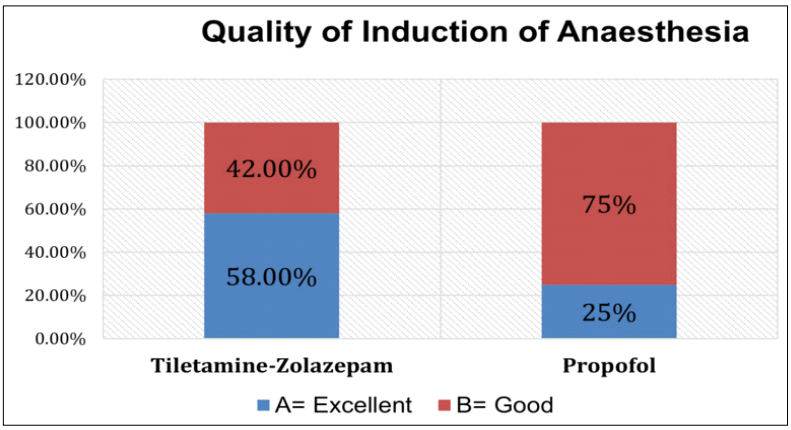

Fig 1: Quality of induction in tiletamine-zolazepam and propofol anesthesia.

effect of a dissociative agent and benzodiazepine where tiletamine produces dissociation, analgesia, immobilization and general anaesthesia, whereas zolazepam produces anxiolysis and muscle relaxation (Landry *et al*. 2020). Group B cats demonstrated muscle relaxation below par with group A which might be due to the low induction dose of propofol alone without preanaesthetic.

The quality of maintenance was assessed by the absence of reflexes, presence of muscle relaxation and degree of pain experienced by the animal while handling the organs during the surgery. The surgical plane of anaesthesia was satisfactorily achieved with complete loss of all the reflexes and excellent muscle relaxation during the maintenance period in both the groups. Pain appeared to be wholly abolished and could be deduced from no movement or vocalization and stable physiological parameters throughout the surgery. The time duration observed for complete recovery was 75.91±8.1 minutes in group A and 88.25±10.2 minutes in group B (Table 1).

Quality of recovery was graded between excellent, good, fair and poor depending on the signs like calmness, vocalization, hyper excitability, vomiting, *etc*. In group A, Smooth, rapid and struggle-free recovery without any vocalization ranging between good to excellent was observed in 83% of the cats. Recovery was also found prompt in 17% of cats; however, there was struggling along with vocalization and hyperesthesia (Fig 2). Thus, a wide

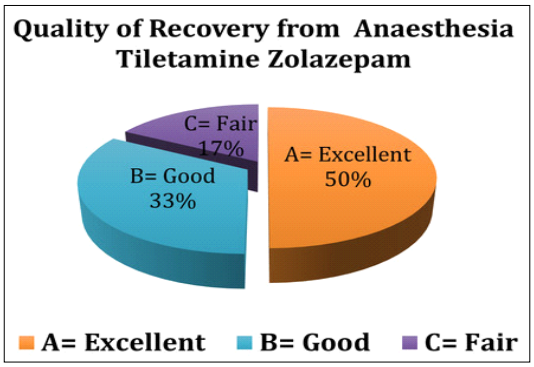

Fig 2: Quality of recovery in tiletamine-zolazepam anesthesia.

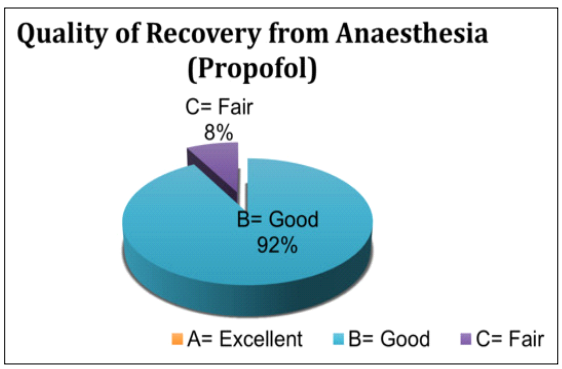

Fig 3: Quality of recovery in propofol anesthesia in cat.

Table 2: Mean±S.E haematological and biochemical parameters of both the groups.

Parameters	Hb		PCV		TEC		TLC		AST		ALT		BUN		CRET	
Groups	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Pre-Op	12.7 ±0.6	12.76 ±0.76	38.61 ±1.89	37.55 ±2.38	7.45 ±0.6	8.5 ±0.63	10.65 ±0.74	12.58 ±1.37	35.13 ±3.7	29.07 ±2.71	54.24 ±6.25	66.89 ±3.62	28.67 ±2.35	23.64 ±1.02	1.30 ±0.1	1.33 ±0.1
Operative	11.34 ±0.4	11.51 ±0.69	34.95 ±1.52	35 ±2.17	6.51 ±0.4	6.75 ±0.46	8.26 ±0.82	7.24 ±0.82	31.13 ±3.27	35.73 ±2.92	52.03 ±5.84	66.30 ±2.30	24.36 ±3.25	35.94 ±1.16	1.20 ±0.08	1.76 ± 0.10
Post-Op	12.11 ±0.47	11.1 ±0.47	36.77 ±1.33	33.39 ±1.21	6.72 ±0.47	6.85 ±0.34	7.97 ±0.93	7.04 ±1.07	32.22 ±3.19	31.15 ±2.13	52.25 ±6.07	66.57 ±2.62	25.36 ±2.32	22.64 ±1.43	1.24 ±0.1	1.46 ±0.08

range in quality of recovery was observed which might be attributed to individual-level variation between each animal, pertaining to breed, age, sex, feeding habits and type of affection. Most of the cats (92%) in group B showed smooth but prolonged recovery. Vocalization and struggling were not seen; however, a drop in body temperature was noted in each animal during recovery. In contrast, a few cats (8%) of this group struggled to maintain a position with prominent vocalization during recovery (Fig 3). The quality of induction, Muscle relaxation and recovery in various stages had been depicted in the Fig 4 (A to F).

Hematological parameters like CBC, LFT and KFT were studied before and during anaesthesia and after 24 hours of recovery (Table 2). The mean±S.E values of hemoglobin (Hb) and pack cell volume were 12.7±0.67 gm % and 38.61±1.89% in group A and 12.76±0.76 gm % and 37.55± 2.38% in group B respectively. There was a non-significant reduction in both the values during a surgical procedure might be due to anaesthesia-induced pooling of circulating blood cells in the spleen and other secondary reservoirs as discussed by Steffey *et al.* (1977) and Stephen (1986) in T-Z anaesthesia in cats. Postoperatively, in both the groups, the values returned to the baseline and were within normal physiological limits. These findings were in conjunction with Li *et al*. (2012) in tiletamine-zolazepam. The mean±S.E total erythrocyte count before anaesthesia was 7.45±0.62 million/mm^3 and 8.5±0.63 million/mm^3 in both the groups respectively.

A non-significant decrease in the total leucocyte count was observed in both the groups during anaesthesia and recovery. The reduction in total leucocyte count could be due to the pooling of circulating blood cells in the spleen and other secondary reservoirs, as Li *et al.* (2012) mentioned. Spada *et al*. (2015) found a non-significant decrease in total leucocyte count with tiletamine-zolazepam However, all the values during the study were in the normal physiological range. There was a nonsignificant decrease in the mean values of granulocytes (neutrophils, eosinophils

Fig 4: Induction of anaesthesia in cats with Propofol (A) and Tiletamine-zolazepam (B) followed by different stages of recovery in tiletamine-zolazepam (C), (E) and Propofol (D) (F).

Table 3: Mean±S.E physiological parameters of both the groups.

Parameters	Heart rate (Beats per minute)		Temperature (°F)		Respiratory rate (Breaths per minute)		Oxygen saturation level (Percentage)	
Groups	A	B	A	B	A	B	A	B
Baseline	189.83±6.07^{a}	191.16±7.38^{a}	100.64±0.35^{a}	100.68±0.19^{a}	29.16±1.78^{a}	27.41±1.37^{a}	-	-
15 mins.	180.75±7.98^{ab}	174.75±7.94^{ab}	100.10±0.37^{ab}	99.95±0.55^{ab}	23.83±1.85^{b}	17.33±1.20^{a}	95.16±1.03	93.75±0.90
30 mins.	160.58±6.19^{bc}	156.167±7.78^{bc}	98.61±0.55^{bc}	99.22±0.23^{bc}	18.83±1.64^{b}	16.66±1.09^{b}	96.33±0.98	92.91±0.91
45 mins	145.75±5.54^{c}	151.53±5.79^{bc}	97.76±0.6^{c}	98.5±0.28^{c}	18.83±1.07^{b}	15.750 ±0.84^{b}	95.75±1.13	92.91±0.97
60 mins	137.25±4.21^{c}	139.58±4.57^{c}	97.06±0.58^{c}	97.49±0.35^{d}	20.08±1.09^{b}	16.16±0.64^{b}	94.33±1.06	92.83±0.61
After 24 hrs	154.16±6.07^{c}	134.33±4.11^{c}	100.56±0.14^{a}	100.66±0.14^{a}	21.08 ±0.874^{b}	24.66±1.20^{b}	-	-
F cal.	11.03**	11.17**	10.91**	27.38**	7.66**	21.40**	0.51 ^{NS}	0.43 ^{NS}

NS: Non-significant, **: Significant at 1% level (p<0.01). Mean±S.E bearing different superscripts (in small letters) differ significantly within the columns.

and basophils) were observed during the depth of anaesthesia until recovery. This could be associated with hemodilution and reduction in the level of bacteremia after antibiotic administration.

A substantial rise in monocyte count was observed during the surgery. The rise in agranulocyte count could be due to the stress-induced release of catecholamine, as mentioned by Lamont (2002). It is known that agranulocytosis indicates chronic or long-standing inflammation, which usually supersedes the neutrophilic phase. The agranulocytosis found in this study could be attributed to the pre-existing increase in the count of the cats having chronic affections like fecoliths, uterine tumor, uroliths and intestinal obstruction, as in cases of the cats ZC4, ZC5 and ZC2, respectively.

During this study, no significant variation was observed in the values of aspartate transaminase (AST) in both the groups (Table 2). All the values were in the normal physiological range whereas mean Alanine transaminase (ALT) values during the operative and post-operative phase showed a significant decrease, however within the biological limit. The alteration in the values might be due to the low concentration of glucuronyl transferase in the feline liver, as discussed by Branson and Booth (1995). A highly significant increase in serum creatinine value was noted during anaesthesia between-group B. There was a substantial difference in blood urea nitrogen between groups A and B during the operative phase. This significant increase in BUN and creatinine level in blood would be due to a decrease in glomerular filtration rate (Wright, 1965). All the values ranged in the normal physiological limits.

Amongst the physiological parameters studied before anaesthesia, the mean heart rate, Temperature and respiratory rate in groups A and B recorded were 189.83±6.07 and 191.16±7.38 beats/min, 100.64±0.35 and 100.68±0.19°F and 29.16±1.78 and 27.41±1.37 breaths per min respectively, which were considered as the baseline vlues. A non significant decrease was observed in the duration of anaesthesia in all three parameters which returned to the baseline values at 24 hours after the surgery. The SPO2 values also remained stable in the duration of anaesthesia and were in normal physiological limits. (Table 3).

CONCLUSION

Anaesthesia in cats has always been challenging for veterinarians and ketamine hydrochloride has only been the choice of anaesthetic in cats for many decades. Felines being a very flexible animal can injure the handlers with claws and sharp teeth and therefore necessitates a skilled handler and a quick method of administration of anaesthesia. Tiletamine-zolazepam eliminates the stress of restraint due its ability to produce rapid, steady, excitement-free induction intramuscularly as well as intravenously with minimal effects on respiratory and cardiovascular parameters it provides optimum quality of muscle relaxation, the complete recovery was smooth rapid and struggle free. As compared to this propofol has better muscle relaxation and very smooth recovery however it requires an intravenous route for induction, which can be difficult in furious subjects. Therefore, it could be concluded that the tiletamine-zolazepam combination is recommended as a drug of choice for induction of anaesthesia in cats without premedication with other sedatives requiring minimal restraint for all types of abdominal affections. Moreover, a longer duration of anaesthesia could be maintained effectively with inhalation anaesthesia.

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Department of Veterinary Surgery and Radiology, Mumbai Veterinary Collage, Parel.

Conflict of interest

All authors declare that they have no conflict of interest.

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