Effect of meloxicam coadministration on the anaesthetic potency of thiopental sodium in a chick model

Yaareb J. Mousa and Mahmood B. Mahmood*

Abstract

Few studies have dealt with thiopental sodium-induced anaesthetic action and the effect of combining meloxicam (a high plasma protein-bound) in 10–15 day old chicks. First, the analgesic median effective dose (ED_{50}) was determined as 35.85 mg/kg, IM by up-and-down routine, while the hypnotic ED_{50} value was 34.40 mg/kg, IM in the chick model. A thiopental sodium injection (18, 36 and 72 mg/kg, IM) produces a significant dose-responsive hypnotic effect in chicks, determined by the beginning of the lack of a righting reflex, duration and recovery time. Thiopental sodium and meloxicam (72 and 1 mg/kg, IM) in combination shortened the beginning of hypnosis, and significantly extended its duration, with a significant increase in recovery time from the hypnotic effect when compared to the group receiving only thiopental sodium. The same combination also elicited a significant increase in the analgesic percentage and efficacy, and significant increase in the voltage current estimated via using electrical stimulation to induce the ache feeling. No significant changes were found in the concentrations of serum glutamate pyruvate trans-aminase (GPT), glutamate oxalo-acetate trans-aminase (GOT) with body temperature between the two groups, with the exception of a significant change in respiratory rate. The outcomes of this study support the prospect of using thiopental sodium as an anaesthetic agent for veterinary surgical procedures in the chicks, in combination with meloxicam, to produce worthy, consistent, and proficient anaesthesia.

Key words: *analgesia; chick model; hypnosis; meloxicam; thiopental sodium*

Introduction

Thiopental sodium is an ultra-short anaesthetic agent used to quickly induce general anaesthesia. The mechanism by which thiopental sodium induced anaesthesia results in inhibition of the central nervous system (CNS) is by potentiating activity of the gamma-aminobutyric acid (GABA)

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neurotransmitter (Finkel et al., 2009). Thiopental sodium has a good hypnotic effect with less efficacy in analgesia in comparison to other narcotic agents (Finkel et al., 2009; Flecknell, 2009; White and Trevor, 2009). Meloxicam belongs to the category of non-steroidal anti-inflammatory agents (NSAIDs) and has an pain-relieving, anti-inflammatory and antipyretic activity that works by non-selectively inhibiting the cyclooxygenase enzyme (both COX1 and COX2 isoforms), and this reduces prostaglandin production (Smyth and FitzGerald, 2009; Hilal-Dandan and Brunton, 2014). Due to its analgesic, anti-inflammatory, and antipyretic effects, meloxicam may be used as pre-anaesthetic (premedication) or in conjugation with anaesthetic drugs for enhancing the anaesthetic status in surgical operations like hypnosis and analgesia. Meloxicam is considered a high plasma protein-bound (Turck et al., 1996) that may affect the efficacy of thiopental sodium.

For the above reasons, the aim of this study was to use and authenticate thiopental sodium to induce general anaesthesia in a chick model for the first time, and to determine the likely effect of meloxicam on the anaesthetic property of thiopental sodium for use in veterinary medical field, and to determine its suitability in replacing the usual anaesthesia protocol in animals using a mixture of ketamine and xylazine.

Materials and methods

Chick model and drugs used

Seven to fifteen-day old broiler chicks of both genders were used in all trials with a regular body weight between 120–178 g. They were kept under constant heat lamps at a temperature of 30–37°C. The floor was covered with wood shavings. All chicks had access to drinking water and feed ad libitum. Thiopental sodium (2.5%, Egyptian International Pharmaceutical Industries Co., Egypt) and meloxicam (2%, Intracin Pharmaceuticals Private Ltd., India) were diluted with saline solution (0.9% NaCl) for injection at 10 ml/kg, intramuscularly (IM).

Ethical considerations

This research and the use of the experimental chick model were approved by the Ethics committee of the Veterinary Medicine College, University of Mosul and its Department of Physiology, Biochemistry, and Pharmacology.

Assessment of thiopental sodium ED_{50s} in the chick model

A. Analgesic ED_{50} of thiopental sodium

The hypnotic ED_{50} value of thiopental sodium was estimated according to the up-and-down routine designated by Dixon (1980). The first dose of thiopental sodium was at 40 mg/kg, IM based on an introductory study. The chick model measured independently prior and 15 minutes after thiopental sodium administration treatment using the electro-stimulator device (Harvard apparatus, USA) (presence of distress call point to pain perception in chicks) (Mousa and Mohammad, 2012; Mousa, 2014; Mousa and Al-Zubaidy, 2019), and then the doses of thiopental sodium were lowered or raised by 5 mg depending on the presence or absence of analgesia (decrease or increase in doses was chosen whereby not exceeding 30% of the first dose of thiopental sodium for an accurate outcome).

B. Hypnotic ED_{50} result of thiopental sodium

The value related to hypnotic ED_{50} for thiopental sodium was estimated using the up-and-down manner outlined above (Dixon, 1980). The first dosage of thiopental sodium was 40 mg/kg, IM based on a preliminary trial. Chicks were monitored individually for 4 h for the

presence of hypnosis from thiopental sodium through the lack of a righting reflex, and then doses of thiopental sodium were decreased or increased by 5 mg/kg depending on the presence or absence of hypnosis.

Dose-response of thiopental sodium hypnosis in the chick model

Thiopental sodium hypnosis (lack of a righting reaction) were monitored in three groups of chicks (six chicks/group) injected with thiopental sodium at doses of 18, 36, or 72 mg/kg, IM. These doses were acquired from the ED_{50} values of thiopental sodium from an earlier experiment in chicks (that resemble ED_{25}, ED_{50}, and ED_{100} of thiopental sodium). Chicks were monitored individually to record the beginning of hypnosis, its duration, and the recovery time from hypnosis with a return to normal movement in all groups (Roder et al., 1993; Al-Zubaidy and Mohammad, 2005).

Hypnotic and analgesic efficacy and body indices of thiopental sodium: effect of meloxicam coadministration in the chick model

A. Effect of meloxicam coadministration on thiopental sodium analgesia

The first group received only a thiopental sodium injection (72 mg/kg, IM) whereas the second group received a combination of thiopental sodium and meloxicam (72 and 1 mg/kg, IM). The dosage of thiopental sodium was selected based on the results of the prior two experiments (dose-response and ED_{50} of thiopental sodium) while the dose of meloxicam was selected from another study in chickens (Souza et al., 2017). The voltage current of the electro-stimulator device produces an ache feeling (distress call) that was documented prior to injection and after 15 min of treatment for each chick model. Other documented data were analgesic percentage and delta voltage for all experimental groups.

B. Effect of meloxicam coadministration on thiopental sodium hypnosis

Two groups of chicks (6 chicks/group) were included. The first group receive only a thiopental sodium injection at a dose of 72 mg/kg, IM, while the second group received a combined injection of thiopental sodium and meloxicam at a dose of 72 and 1 mg/kg, IM. The beginning, duration, and recovery from hypnosis to normal motion were documented in both groups for each chick model.

C. Effect of thiopental sodium alone or in combination with meloxicam on respiratory rate and body temperature

Before and thirty minutes after the thiopental sodium injection (72 mg/kg, IM) or the combined injection of thiopental sodium and meloxicam (at 72 and 1 mg/kg, IM), respiratory rate (per minute) was measured at dorsal recumbency for every chick. Body temperature was measured from the cloaca using a digital thermometer for both treated groups (6 chicks per group).

Measurement of serum GPT and GOT concentration in the chick model treated with thiopental sodium or a combination of thiopental sodium and meloxicam

After 4 hours of thiopental sodium injection (72 mg/kg, IM) or thiopental sodium plus meloxicam (72 and 1 mg/kg, IM), blood samples were acquired from the jugular vein from both groups (6 chicks/group). Blood samples were centrifuged (3000 rpm for 15 minutes) in gel tubes to obtain serum, and serum was chilled pending analysis during 24 hours. Serum GPT (Reitman and Frankel, 1957) and GOT (Plummer, 1987) concentrations

were determined (in units/L) with the specified kit (Biolabs, France) using the chemistry analyser device (Genotek, USA).

Statistics

Parametric statistical analysis included one-way statistical analysis of minimum significant dissimilarity, whereas paired and unpaired student T-test was used to compare the means of the two groups (Katz, 2006; Petrie and Watson, 2013). Non-parametric data (hypnosis and analgesic percentages) were examined by the Fisher test, and Mann-Whitney test used to analyse the delta voltages (Katz, 2006). The significance level was set at $P<0.05$.

Table 1-A. Analgesic ED_{50} value of thiopental sodium in the chick model

Parameter	Results
Analgesic ED_{50}	35.85 mg/kg, IM
Dosage range	30-40 mg/kg, IM
First dosage	40 mg/kg
Last dosage	35 mg/kg
± in the dosages	5 mg/kg
Overall chick used	6 (XXOOXO)*

*X= analgesia; O= no analgesia

Results

ED_{50s} of thiopental sodium in the chick model

A. Analgesic ED_{50} of thiopental sodium

The analgesic ED_{50} value of thiopental sodium essential to cause analgesia in 50% of chicks was 35.85 mg/kg, IM, which is stated here for the first time in chicken. Table 1-A shows the results from this trial.

B. Hypnotic ED_{50} of thiopental sodium

The ED_{50} value of thiopental sodium that produces hypnosis (lacking of the righting reflex) in 50% of the experimental chick model was 34.40 mg/kg, IM (Table 1-B). Reactions elicited by thiopental sodium hypnosis in chicks during 5 min. were ataxia, recumbency, locked eyelids, defecation, lacking of righting reflex, and quite sleep with normal breathing.

Table 1-B. Hypnotic ED_{50} of thiopental sodium in the chick model

Parameter	Results
Hypnotic ED_{50}	34.40 mg/kg, IM
Dosage range	30-40 mg
First dosage	40 mg/kg
Last dosage	30 mg/kg
± in the dosages	5 mg/kg
Overall chick used	5 (XOXXO)*

*X= hypnosis; O= no hypnosis

Dose-response of hypnosis produced by thiopental sodium in the chick model

In summary, thiopental sodium injections at doses of 18, 36 or 72 mg/kg, IM yielded narcosis in a dose-dependent manner. The beginning of hypnosis (lack of the righting reflex) was rapid through 3-17 min. while the duration of hypnosis was between 21-157 min. Recovery from hypnosis of thiopental sodium persisted for 53-192 min., depending on the dose of thiopental sodium used in this experiment (Table 2).

Effect of meloxicam on the anaesthetic potency of thiopental sodium and body indices in the chick model

A. Coadministration of meloxicam and its effect on analgesia produced by thiopental sodium

The analgesic effect after injection of the thiopental sodium and meloxicam mixture was measured for 15 minutes and showed that there was a significant

Table 2. The dose-response related to hypnosis for various thiopental sodium dosages in the chick model

Thiopental sodium (mg/kg, IM)	Hypnosis		
	Beginning (min.)	Duration (min.)	Recovery (min.)
18	17.60 ± 3.92	21.80 ± 1.83	53.40 ± 7.91
36	5.83 ± 0.87 *	81.33 ± 2.81 *	121.83 ± 11.11 *
72	3.00 ± 0.52 *	157.17 ± 6.77 *,a	192.50 ± 4.87 *,a

Data expressed as Mean ± SE for six chicks per dose group
* significantly different from thiopental sodium (18 mg/kg, IM); $P<0.05$
a significantly different from thiopental sodium (36 mg/kg, IM); $P<0.05$

Table 3-A. Analgesia produced by thiopental sodium with or without meloxicam in the chick model

Treated groups	Analgesia %	Voltage (volt) before injection	Voltage (volt) after injection	Delta Voltage
Thiopental sodium (positive control)	100	7.00 ± 0.45	16.50 ± 0.76 +	9.50 ± 0.56
Thiopental sodium and meloxicam	100	7.00 ± 0.26	24.50 ± 0.22 *,+	17.50 ± 0.43 *

Data expressed as Mean ± SE for six chicks per group
Pain elicited via electro-stimulator was documented prior to and 15 minutes after thiopental sodium treatment (72 mg/kg, IM) with or without meloxicam (1 mg/kg, IM)
* significantly different from thiopental sodium alone ($P<0.05$)
+ significantly different from pre-treatment voltage in the same group ($P<0.05$)

Table 3-B. Hypnosis from thiopental sodium with or without meloxicam in the chick model

Treated groups	% Hypnosis	Hypnosis		
		Beginning (minute)	Duration (minute)	Recovery (minute)
Thiopental sodium (positive control)	100	4.50 ± 0.34	77.33 ± 5.48	128.67± 14.96
Thiopental sodium and meloxicam	100	1.17 ± 0.17*	153.00 ± 3.35*	197.83 ± 3.70*

Data expressed as Mean ± SE for six chicks per group
Thiopental sodium administered parenterally (72 mg/kg, IM) with or without meloxicam (1 mg/kg, IM)
* significantly different from thiopental sodium alone group ($P<0.05$)

increase in the antinociceptive efficacy in comparison to the group treated solely with thiopental sodium. Meanwhile, there was a significant increase in analgesic efficiency and a significant increase in delta voltage current creating pain in comparison with the group receiving only thiopental sodium (Table 3-A).

B. Meloxicam coadministration and the effect on hypnosis produced by thiopental sodium

The combined mixture of thiopental sodium and meloxicam (72 and 1 mg/kg, IM) significantly shortened the beginning of the hypnotic effect and raised the duration, along with a significant elevation in the recovery time from the hypnosis

Table 3-C. Respiratory rate and body temperature of thiopental sodium with or without meloxicam in the chick model

Groups	Respiratory rate (per min.)		Body temperature (°C)	
	Before 30 min.	After 30 min.	Before 30 min.	After 30 min.
Thiopental sodium alone (positive control)	82.50 ± 0.92	70.17 ± 2.23 $^{+}$	40.53 ± 0.02	37.35± 0.13 $^{+}$
Thiopental sodium and meloxicam	82.17 ± 1.72	57.83 ± 1.08 $^{*,+}$	40.47 ± 0.02	37.28 ± 0.06 $^{+}$

Data expressed as Mean ± SE for six chicks per group
Thiopental sodium was given (72 mg/kg, IM) with or without meloxicam (1 mg/kg, IM)
* significant difference from thiopental sodium alone group at $P<0.05$
$^{+}$ significant difference from the pre-treatment for the same group ($P<0.05$)

when compared with the group receiving thiopental sodium alone (Table 3-B).

C. Effect of thiopental sodium alone or in combination with meloxicam on respiratory rate and body temperature

The findings in Table 3-C show that the respiratory rate and body temperature in chicks under narcosis were significantly inhibited in both groups receiving thiopental sodium alone or in combination with meloxicam in comparison with values before injection. However, the combination of thiopental sodium and meloxicam proved to have a significant deleterious effect on respiration in comparison with the experimental group injected only with thiopental sodium. Narcosis with thiopental sodium is characterized by a deep sleep with persistent leg movements and paddling reflex, whereas narcosis produced by the thiopental sodium-meloxicam coadministration is shallow and results in a quiet sleep with deep breathing.

Serum GPT and GOT concentrations for chicks treated with thiopental sodium alone or thiopental sodium plus meloxicam

Table 4 shows that there were no significant differences in serum GPT and GOT concentrations between the group receiving thiopental sodium alone and those treated with a combination of thiopental sodium and meloxicam.

Table 4. Serum GPT and GOT concentrations for chicks treated with thiopental sodium alone or thiopental sodium plus meloxicam

Treated groups	GPT (U/L)	GOT (U/L)
Thiopental sodium (positive control)	12.33 ± 0.95	222.67 ± 2.06
Thiopental sodium and meloxicam	13.50 ± 0.89	220.50 ± 2.58

Data expressed as Mean ± SE for six chicks per group
Thiopental sodium administered (72 mg/kg, IM) with or without meloxicam (1 mg/kg, IM)

Discussion

There are no prior studies dealing with the anaesthetic action profile induced by thiopental sodium and the effect of meloxicam coadministration in the 10-15 day-old chick model. Therefore, this is the first experiment of this kind. The aim of the study was to use and authenticate thiopental sodium in chicks for induction of anaesthesia and to determine the possible valuable

effect of meloxicam on the anaesthetic characterization of thiopental sodium for use in the veterinary field. Thiopental sodium is considered a general anaesthetic that stimulates rapid induction of anaesthesia by increasing the GABA neurotransmitter effect on the $GABA_A$ receptor subtype, causing CNS depression (Finkel et al., 2009; Flecknell, 2009; White and Trevor, 2009). Thiopental sodium has a good hypnotic effect with occasionally less analgesic efficiency (Finkel et al., 2009; White and Trevor, 2009), whereas thiopental sodium is a safe medication of choice for producing anaesthesia since it possesses many benefits, including a familiar mechanism of action, protection from myocardial and cerebral ischemia, decreasing histamine release with a uniquely stable hemodynamic status during anaesthesia (Butera et al., 1980; Atasoy et al., 1993) and was found to induce more efficient anaesthesia than other barbiturates (Shaaban et al., 2018). Furthermore, meloxicam may be preferred for use in the veterinary field to induce balanced anaesthesia categorized by good hypnotic and analgesic effects because its analgesic, antipyretic, and anti-inflammatory effects are the result of COX inhibition (Smyth and FitzGerald, 2009; Hilal-Dandan and Brunton, 2014). The results present here showed the anaesthetic profile of thiopental sodium in the chick model by determining the analgesic and hypnotic ED_{50} values, and by determining the hypnotic dose-response for thiopental sodium. The study results shows that thiopental sodium in combination with meloxicam produce balanced, reliable, and efficient anaesthesia. The thiopental sodium-meloxicam combination maximizes the hypnotic effect and increased analgesic efficacy, and a decrease in the doses of both drugs minimized the side effects when compared with thiopental sodium alone. This is of beneficial importance for the use of this combination in veterinary medicine (Mohammed et al., 2011; Brohi et al., 2019). The likely pharmacokinetic interaction between thiopental sodium and meloxicam may be regarded to the ability of meloxicam to strongly bind with plasma proteins (about 99%) (Turck et al., 1996), which may displace thiopental sodium from its binding sites on plasma proteins and make it more available to act centrally on GABA receptors. The findings of this study revealed that respiratory rate and body temperature in narcotic chicks were significantly inhibited in both groups receiving thiopental sodium alone or in coadministration with meloxicam in comparison with their values prior to injection, while the combination of thiopental sodium and meloxicam had a significant and deleterious effect on the respiratory centre in comparison to the group receiving only thiopental sodium. This is because of the potentiated inhibition caused by the pharmacokinetic interaction between thiopental sodium and meloxicam, which increases its concentration and activity on GABA receptors and exaggerates its deleterious activity on the respiratory and vasomotor centres in the brain, as confirmed in several species (Hikasa et al., 1993; Sumitraa et al., 2004; Dalir-Naghadeh et al., 2006; Abd-Almaseeh, 2008; Ferreira et al., 2013; Ninu et al., 2015; Biswas et al., 2017; Brohi et al., 2019). Serum GPT and GOT concentrations were near their normal values of chicks, as reported elsewhere (Cruz et al., 2018) and there is evidently no significant liver or tissue damages between either thiopental sodium and thiopental sodium plus meloxicam groups in relation to serum GPT and GOT concentrations. This is another reason for using this combination for inducing prolonged and enhanced anaesthesia in the chicks.

Conclusions

The outcomes of this study support the prospect of using thiopental sodium as an anaesthetic agent for veterinary surgical procedures in chickens that may be enhanced when used in combination with meloxicam to produce worthy, consistent, and proficient anaesthesia.

References

1. ABD-ALMASEEH, Z. T. (2008): Comparative Anesthetic Protocols: Propofol and Thiopental in Xylazine Premedicated Donkeys. J. Anim. Vet. Adv. 7, 1563-1567.
2. AL-ZUBAIDY, M. H. I., F. K. MOHAMMAD (2005): Metoclopramide induced central nervous system depression in the chicken. BMC Vet. Res. 1, 6-10.
3. BISWAS, D. S., M. HASAN, S. MALLICK, N. S. JUYENA, M. SHORIOTULLAH and M. R. ALAM (2017): Clinical and haematological changes upon administration of Xylazine-Ketamine and Xylazine-Thiopentone anaesthetic combinations in ewes. Bang. Vet. 34, 9-19.
4. BROHI, R. D., A. B. KALHORO, A. B. KACHIWAL, I. B. KALHORO, D. H. KALHORO, S. AHMED, F. A. KHAN, H. S. TALPUR, Z. REHMAN and D. BHATTARIA (2019): Effect of Propofol and Thiopentone Sodium in Sheep Sedated with Xylazine Hydrochloride. Pak. J. Zool. 51, 1-7.
5. BUTERA, S. T., H. E. GARNER, J. N. MOORE and J. F. AMEND (1980): Xylazine/sodium thiopental combination for short-term anesthesia in the horse. Vet. Med. Small. Anim. Clin. 75, 765-770.
6. CRUZ, C. E., E. R. FREITAS, N. M. BRAZ, R. P. R. SALLES and I. N. G. Da SILVA (2018): Blood parameters and enzymatic and oxidative activity in the liver of chickens fed with calcium anacardate. Rev. Ciên. Agron. 49, 343-352.
7. DALIR-NAGHADEH. B., F. SARRAFZADEH-REZAEI, L. MOBARAKI and G. SADEGHI-HASHJIN (2006): A comparison between the effects of xylazine-ketamine and xylazine-thiopental combinations on cardiac rhythm in dogs. Iran. J. Vet. Surg. 1, 73-81.
8. DIXON, W. J. (1980): Efficient analysis of experimental observations. Annu. Rev. Pharmacol. Toxicol. 20, 441-462.
9. FERREIRA, T. H., R. J. BROSNAN, Y. SHILO-BENJAMINI, S. B. MOORE and S. R. HOLLINGSWORTH (2013): Effects of ketamine, propofol, or thiopental administration on intraocular pressure and qualities of induction of and recovery from anesthesia in horses. Am. J. Vet. Res. 74, 1070-1077.
10. FINKEL, R., M. A. CLARK, L. X. CUBEDDU, R. A. HARVEY and P. C. CHAMPE (2009): Lippincott's illustrated reviews: Pharmacology. Philadelphia: Williams and Wilkins.
11. FLECKNEL, P. (2009): Laboratory animal anesthesia. Elsevier Inc.
12. HIKASA, Y., M. KUBOTA, K. TAKASE, T. KAKUTA and S. OGASAWARA (1993): Effects of thiopental, ketamine, diazepam, xylazine, and nitrous oxide on EEG spike activity and convulsive behavior during enflurane anesthesia in atropinized cats. Effect of increasing inhalant concentrations. Vet. Surg. 22, 311-317.
13. HILAL-DANDAN, R. and L. L. BRUNTON (2014): Goodman and Gilman's Manual of Pharmacology and Therapeutics. New York: McGraw-Hill Companies Inc.
14. KATZ, M. H. (2006): Multivariable analysis: A practical guide for clinicians and public health researchers. New York: Cambridge University Press.
15. MOHAMMED, A. A., M. A. M. SAYED and M. A. ABDELNABI (2011): A New Protocol of Anesthesia Using Thiopental, Diazepam and Xylazine in White New Zealand Rabbits. Aust. J. Basic App. Sci. 5, 1296-1300.
16. MOUSA, Y. J. (2014): Anaesthetic properties of ketamine in chicks stressed with hydrogen peroxide. Vet. Med. 59, 369-375.
17. MOUSA, Y. J. and F. K. MOHAMMAD (2012): The analgesic efficacy of xylazine and dipyrone in hydrogen peroxide-induced oxidative stress in chicks. Iraqi J. Vet. Sci. 26, 69-76.
18. MOUSA, Y. J. and M. H. I. AL-ZUBAIDY (2019): Anesthetic efficacy of ketamine, ketamine-tramadol and ketamine-ketorolac in the chicks. Iran. J. Vet. Res. 20, 33-38.
19. NINU, A. R., R. TAYAL, A. KUMAR, S. M. BEHL and S. K. CHAWLAH (2015): Comparison of thiopentone and ketamine as induction and maintenance agents in buffaloes undergoing diaphragmatic herniorrhaphy. J. App. Anim. Res. 43, 462-467.
20. PETRIE, A. and P. WATSON (2013): Statistics for Veterinary and Animal Sciences. Oxford: Blackwell Science.
21. REITMAN, S. and S. FRANKEL (1957): A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruric transaminase. Am. J. Clin. Path. 28, 56-63.
22. RODER, J. D., H. R. AMOUZADEH, S. SANGIAH, G. BURROUS and C. W. QUALLIS Jr (1993): Effects of hepatic P-450 enzyme inhibitors and inducers on the duration of xylazine+ketamine anesthesia in broiler chickens and mice. Vet. Hum. Toxicol. 35, 116-118.
23. SHAABAN, M. F., M. M. KASSEM, M. H. EL KAMMAR and S. A. KORTTTUM (2018): Clinical Evaluation of Intravenous Propofol Alone or in Combination With Diazepam, Ketamine HCl and Thiopental Sodium to Induce General Anaesthesia in Dogs. Alex. J. Vet. Sci. 57, 106-114.
24. SMYTH, E. M. and G. A. FITZGERALD (2009): Basic and clinical pharmacology. 11th ed. New York: McGrew-Hill Co Inc. Pp. 313-329.

25. SOUZA, M. J., J. B. BERGMAN, M. S. WHITE, K. I. GORDON, L. E. GERHARDT and S. K. COX (2017): Pharmacokinetics and egg residues after oral administration of a single dose of meloxicam in domestic chickens (Gallus domesticus). Am. J. Vet. Res. 78, 965-968.
26. SUMITRAA, M., P. MANKANDANA, K. V. KUPPU RAOB, M. NAYEEMC, B. M. MANOHARD and R. PUVANKRISHNAN (2004): Cardiorespiratory effects of diazepam-ketamine, xylazine-ketamine and thiopentone anesthesia in male Wistar rats-A comparative analysis. Life Sci. 75, 1887-1896.
27. TURCK, D., W. ROTH and U. BUSCH (1996): A review of the clinical pharmacokinetics of meloxicam. Brit. J. Rheumatol. 35, 13-16.
28. WHITE, P. F. and A. J. TREVOR (2009): Basic and clinical pharmacology. New York: McGrew-Hill Co Inc.

Učinak zajedničke primjene meloksikama na anestetsko djelovanje natrijevog tiopentala na modelu pilića

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Malo se studija bavi anestetskim djelovanjem induciranim natrijevim tiopentalom i učinkom kombiniranja s meloksikamom (visoki stupanj vezivanja na proteine u plazmi) u pilića starih 10-15 dana. Srednje učinkovita analgetska doza (ED50) ustvrđena je kao 35,85 mg/kg intramuskularno gore-dolje rutinom, dok je hipnotička ED50 vrijednost bila 34,40 mg/kg, intramuskularno na modelu pilića. Injekcija natrijevog pentanola (18, 36 i 72 mg/kg, intramuskularno) stvara značajni hipnotički učinak ovisno o dozi u pilića određivanjem početka izostanka refleksa uspravljanja i tranja u vremenu oporavka. Kombinacija natrijevog tiopentanola i meloksikama (72 i 1 mg/kg, intramuskularno), skratila je početak hipnoze, značajno produljila njezino trajanje uz značajno produljenje vremena oporavka od hipnotičkog učinka u usporedbi sa skupinom koja je primala samo natrijev tiopentanol. U isto vrijeme ista je kombinacija izazvala značajan porast analgetskog postotka i učinkovitosti uz značajan porast napona struje procijenjen uporabom električne simulacije za induciranje osjeta boli. Uočeno je da nema značajne promjene koncentracija glutamat-piruvat transaminaze (GPT) i glutamat-oksaloacetat transaminaze (GOT) u krvi s tjelesnom temperaturom, osim značajne promjene respiratorne frekvencije između dvije navedene skupine. Rezultati ove studije govore u prilog uporabe natrijevog tiopentanola kao anestetskog sredstva za veterinarske kirurške postupke u pilića čiji se učinci mogu pojačati uporabom meloksikama u svrhu postizanja dobre, dosljedne i učinkovite anestezije.

Ključne riječi: *analgezija, model pilića, hipnoza, meloksikam, natrijev tiopentanol*