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Research Article

Assessing Analgesia and Motor Block Scores in Male Dogs: The Impact of Single vs. Repeated Dose Lumbosacral Liposomal Lidocaine

Sena'a M. Hussein[1,2], Raffal A. Omar[3*]

[1]Surgery and Obstetric Department /College of Veterinary Medicine /University of Baghdad/Iraq; [2]Animal Production Department, College of Agriculture, University of Sumer, Dhi Qar, Iraq; [3]Physiology Biochemistry & Pharmacology Department /College of Veterinary Medicine /University of Baghdad/Iraq.

Abstract | In recent medical advancements, there has been growing interest in utilizing liposomes, which are lipid-based vesicles, to enhance the targeted delivery and prolonged release of local anesthetics. The purpose of this study was to assessment the effect of single and repeated lumbosacral injection of liposome carrying lidocaine in comparison with lidocaine hydrochloride. A total of 24 male local breed dogs were divided randomly into the lidocaine group that received 4.5 mg/Kg of 2% lidocaine and liposome group which received the same dose of lidocaine carried by liposome. Pinprick and spinal reflex tests were evaluated each minute for the first five minutes following lumbosacral injection and then every five minutes until the sensory blockade disappeared. Motor activities were constantly monitored and evaluated every 30 seconds. Clinical evaluation of analgesia and motor blocks after injection revealed a complete analgesia and there was no response to deep muscle pricks lasting for (120) / minutes starting after 15 minute from lumbosacral injection while in repeated dose last for (180) / minutes after 15 minutes from injection of liposomal lidocaine. Lidocaine single dose group it lasting for (60) / minutes after 20 minute from lumbosacral injection while and in repeated dose last for (84) / minutes after 20 minutes from injection. Motor score showed a complete muscle relaxation which was strong and lasting for (49) / minutes from 15 minute after lumbosacral injection while in repeated dose last for (101) / minutes from 20 minutes from injection of liposomal lidocaine. Lidocaine single dose concerning complete muscle relaxation score lasted for (25) / minutes from 20 minute after lumbosacral injection . In repeated dose last for (53) / minutes from 20 minutes from injection. Nerve functions scores revealed a significant different injections between liposomal lidocaine groups and lidocaine groups. In motor block after injection, there was no significant differences were observed between the two groups during the study periods. Analgesia after recovery clinical evaluation show significantly different between groups, the motor after recovery recorded in significantly different. The conclusion, Lumbosacral liposomal lidocaine injection demonstrates safety, rapid induction, and excellent analgesia, ensuring smooth recoveries suitable for surgery without complications.

Keywords | Lidocaine hydrochloride, Epidural anesthesia, Bangham method, Epidural nerve block, Analgesia, Dogs.

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***Correspondence** | Raffal A Omar, Physiology Biochemistry & Pharmacology Department /College of Veterinary Medicine /University of Baghdad/Iraq; **Email:** raffal_omar@covm.uobaghdad.edu.iq
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INTRODUCTION

Local anesthetics are essential components of modern medical practice, serving to alleviate pain and discomfort during various medical procedures. Some of the obstacles that prevent the use of general anesthesia in some surgical operations include the expense of the drug, technical expertise, and risk issues (Sabri, 2018). Lidocaine, a commonly employed local anesthetic, has served as a fun-

damental component in the field of pain management for several decades (Bahar and Yoon, 2021). The technology underlying drug delivery systems also improves along with medical research. One such development is the creation of liposome-carrying lidocaine, a revolutionary technique that increases the effectiveness and duration of the numbing effects of lidocaine in comparison to standard lidocaine (Yang et al., 2020). The main distinctions between free lidocaine and lidocaine delivered by liposomes will be discussed in this study of local anesthetics. This section will examine each formulation's pharmacological mechanisms, modes of action, and advantages in clinical contexts. Understanding these differences will help us better grasp how the cutting-edge liposome-based method maximizes lidocaine's potential for reducing pain and broadens the field of medical practice (Ji et al., 2020).

Local anesthetic involves the temporary suppression of sensory and motor functions in a specific region of the body, with the aim of interrupting the transmission of nerve impulses responsible for pain and other sensations to other areas of the body (Weinstein et al., 2018). The duration of local anesthesia refers to the time this suppression lasts, varying based on factors like anesthetic type, concentration, and administration technique. Onset time denotes the interval between administering anesthetic agents and the onset of sensory and motor blockade. Recovery period is the span after anesthetic administration when the effects wane, and normal sensory, motor functions are restored. These concepts are integral to pin management and medical procedures requiring localized numbing (Almasi et al., 2020). The lumbosacral region, comprising the lower back and sacral area, is a common site for pain management interventions due to its association with conditions like chronic lower back pain and certain neuropathic disorders (Baron et al., 2016). In recent medical advancements, there has been growing interest in utilizing liposomes, which are lipid-based vesicles, to enhance the targeted delivery and prolonged release of local anesthetics like lidocaine. This innovative approach aims to optimize pain (Eesa, 2010; Amin, 2012; Ali, 2013; Abubakar et al., 2015; Omar and Eesa, 2017). While lumbosacral injection analgesia refers to the local anesthetics that block sensory, motor, and autonomic nerves (Jones, 2001; Ismail, 2016; Natalini, 2010). For up to 48 hours after injection, lumbosacral injections anesthesia inhibited the stress response signals represented by drops in cortisol and norepinephrine serum concentrations (Sibanda et al., 2006; Lawal and Adetunji, 2009; O'Hearn and Wright, 2011).

One of the most effective treatments for postoperative pain in veterinary medicine is lumbosacral injections analgesia/anesthesia (Sarotti et al., 2015; Garcia-Pereira, 2018). It is now often used in orthopedic procedures, notably those involving dogs' hind limbs (Hoelzler et al., 2005; Kona-Boun et al., 2006; Steagall et al., 2017). The removal of local anesthetics from neural tissues and their elimination by systemic absorption are required for the resolution of lumbosacral injections anesthesia because there is no reversal agent for these drugs (Park et al., 2009; Al-rubeai et al., 2012; Mhawes et al., 2015). Short-acting local anesthetics are used for lumbosacral injection analgesia; nevertheless, they do not lengthen the duration block in unexpectedly lengthy operation (Rodriguez et al., 2001). On the other hand, prolonged sensory and motor block after lumbosacral injection block following quick surgical procedures increases post-anesthetic care unit time and cost, owner discontent, and may result in postoperative hind limb paralysis and urinary retention (Shoeibi et al., 2007).

Controlling severe local pain during surgical operations might provide a challenge due to the limited duration of action exhibited by local anesthetics (Markman and Philip, 2007; Gordon et al., 2010; Golzari et al., 2014). Prolonging local pain therapy is required to manage the economic value, physical burden on patients and care-givers (Epstein-Barash et al., 2009). Lidocaine has excellent diffusing and penetration properties as well as a rapid action onset, with short duration of analgesia (Hall et al., 2001; Haider and Mahdi, 2013; Khalil, 2019). Therefore, many drugs have been co-administered with lumbosacral injections injection to maximize and extend the duration of analgesia (Harjai et al., 2010; Najm, 2013). The utilization of sophisticated medicine delivery systems that sustain the flow of lidocaine following a lumbosacral injection has the potential to enhance the overall outcome. The objective of this investigation was to develop a liposome-loaded nanostructured lipid carrier capable of providing sustained release of lidocaine for extended periods of anesthesia, whether administered as a single dose or in multiple doses.

MATERIAL AND METHODS

Experimental animals

Twenty four healthy male local breed dogs, (3.167 ± 0.145) years old, weighing (25±0.714), were enrolled in this study. All dogs were housed in individual cages for 15 days for acclimatization, fed commercial food, and given free access to water. The College of Veterinary Medicine at the University of Baghdad's regional council for animal care and use provided ethical approval (number P.G.1364 at 2022/7/3) before starting this study.

Neurological examination

This includes the examination of the front legs, back legs, tail, and anus during a neurologic examination (Paluš, 2014; Almasi et al., 2020). It includes the following supportive parameters:

Pinprick examination

Based on its ability to distinguish between sharp and dull feelings it serves as a stand-in marker for spinothalamic tract function. Pinprick sensation is rated on a 3-point ordinal scale (absent, impaired, and normal). Inability to distinguish between sharp and dull sensations is indicated by absence of sensation (pinprick score = 0). (Pinprick score: 1) importantly, feeling might differ from the reference area in both directions. Sensations are considered normal (pinprick score = 2) if they are regarded to be similar to those in the reference location. Light touch sensations were categorized as light touch score = 2 (Haefeli et al., 2014) and pinprick score = 3 when there will no sensation after inserting the needle deep in the subcutaneous tissue Table 1. Both lidocaine hydrochloride and Liposomal loaded lidocaine (Liposomal Lidocaine), at the single and repeated doses used for lumbosacral injections in the present study, produced sensitivity to needle-prick stimulation of the skin of hand legs and perineal region in dogs. The needle prick analgesia test was efficient were blocked after lumbosacral injections of the drugs, and produced complete analgesia after lumbosacral injections.

Table 1: Scoring the degree of analgesia and motor block modified from (Ismail, 2018)

Score	"Degree of analgesia"
0	No analgesia
1	Mild analgesia (weak or depressed response)
2	Moderate analgesia (no response to superficial skin pricks)
3	Complete analgesia (no response to deep muscle pricks)

Spinal reflex

To evaluate the function of the spinal reflex; pedal and withdrawal reflexes were used Table 2. These reflexes were performed by pinching a toe in which a positive response were seen when dogs flexes the hip, stifle, and hock (Khante et al., 2019).

Table 2: Score of muscle relaxation modified from (Khante *et al.*, 2019).

Score	Spinal reflex	Description
1	Absent	Rigidity in muscle of hind limb
2	Mild (only superficial)	Partial relaxation of hind limb muscle
3	Strong (superficial and deep)	Complete relaxation

Surgical technique

The dogs were fasted for six hours before the lumbosacral injection. The lumbosacral region was clipped and shaved, washed with tap water and soap, then disinfected with 70% ethyl alcohol in order to prepare it aseptically for an aseptic lumbosacral site. There is a depression that resembles the lumbo-sacral space at the intervertebral it, and a 22G 90 mm (90 millimeters = 9 cm) spinal needle was placed into it (Grubb and Lobprise, 2012).

The hanging drop test and lack of resistance during the injection served as evidence that the needle had been inserted correctly into the lumbosacral injections area. Each animal in each group received a calculated dose of 4.5 mg/kg .B. W. (Valverde, 2008), which was slowly administered lumbosacral injection (Figure 1). The animals were kept in a calm, quiet place until they made a complete recovery and returned to their normal gait under close observation.

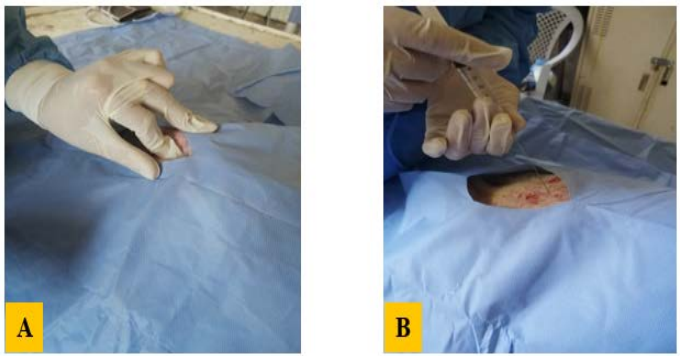

Figure 1: Surgical technique, A. location of anesthetics area, B. injection of the anesthetic agent

Statistical Analysis

The Statistical Analysis System- (SAS, 2012). Program was used to detect the effect of difference factors in study parameters. Least significant difference –LSD test (Analysis of Variation-ANOVA) or T-test was used to significant compare between means in this study.

RESULTS

Clinical evaluation

The clinical assessment of analgesia and motor blocks, measured in minutes, yielded significant findings. In the single-dose liposomal lidocaine group, complete analgesia, characterized by an absence of response to deep muscle pricks, persisted for 120 minutes. This analgesic effect began 15 minutes after lumbosacral injection. In the repeated-dose liposomal lidocaine group, analgesia extended even further, lasting for 180 minutes and commencing 15 minutes after injection. On the other hand, the lidocaine single-dose group exhibited a shorter duration of analgesia, with a 60-minute effect, starting 20 minutes after lumbosacral injection. In the lidocaine repeated-dose group, the duration of analgesia was 84 minutes, also beginning 20 minutes after injection.

Table 3: Analgesia block (time/min.) after injection between liposomal lidocaine groups and lidocaine groups.

Time/minutes Group	0	5	10	15	20	25	30	35	40	45	50	55	60	65	70
liposomal lidocaine Single dose	-	+	+ +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
liposomal lidocaine repeated dose	-	+	+ +	+ +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
Lidocaine single Dose	-	+	+	+ +	+ + +	+ + +	+ + +	+ +	+	+	+	+	+	+	+
Lidocaine repeated dose	-	+	+	+ +	+ + +	+ + +	+	+ + +	+ + +	++	+	+	+	+	+

Table 4: Spinal reflex (time/min.) after injection between liposomal lidocaine groups and lidocaine groups.

Minutes Group	0	5	10	15	20	25	30	35	40	45	50	55	60	65	70
liposomal lidocaine Single dose	-	+	+ +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
liposomal lidocaine repeated dose	-	+	+ +	+ +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
Lidocaine single Dose	-	+	+	+ +	+ + +	+ + +	+ + +	+ +	+	+	+	+	+	+	+
Lidocaine repeated dose	-	+	+	+ +	+ + +	+ + +	+ + +	+ + +	+ + +	++	+	+	+	+	+

-: No analgesia
+: Mild analgesia
+ +: Moderate analgesia
+++: Excellent analgesia

Regarding motor scores, there was complete muscle relaxation, lasting for 49 minutes, observed 15 minutes after lumbosacral injection in the single-dose liposomal lidocaine group. In the repeated-dose liposomal lidocaine group, this effect was more prolonged, lasting for 101 minutes, starting 20 minutes after injection. In the lidocaine single-dose group, complete muscle relaxation was evident for 25 minutes, beginning 20 minutes after lumbosacral injection. In the lidocaine repeated-dose group, the effect persisted for 53 minutes; also commencing 20 minutes after injection. The analysis of nerve function scores indicated significant differences (P≤0.05) between the liposomal lidocaine groups and the lidocaine groups, particularly in the context of analgesia. However, in the motor block duration (time/min.) after injection, there were no significant differences (P≤0.05) observed between the two groups throughout the study periods.Upon evaluating the results of analgesia duration (time/min.) after recovery in the clinical assessment, significant differences (P≤0.05) emerged between the groups. Conversely, the motor block duration (time/min.) after recovery also exhibited significant differences (P≤0.05). Figures 2, 3.4, and 5, as well as Tables 3 and 4.

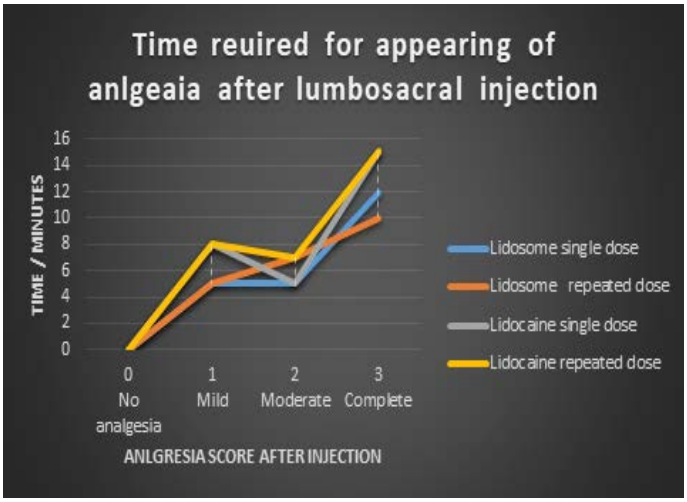

Figure 2: Score of analgesia block (time/min.) after injection between lidosomaine groups and lidocaine groups

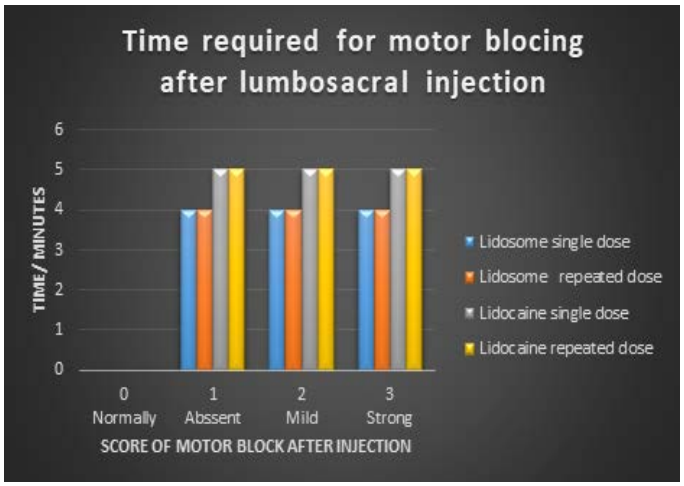

Figure 3: Score of motor block (time/min.) after injection between Liposomal Lidocaine groups and lidocaine groups.

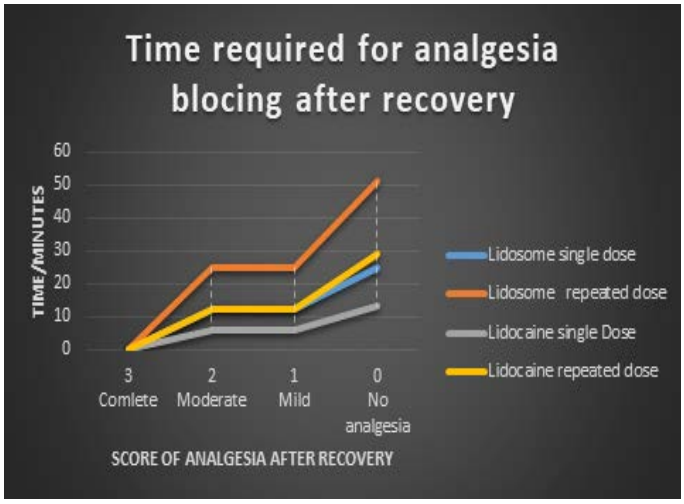

Figure 4: Score of analgesia block (time/min.) after recovery between Liposomal Lidocaine groups and lidocaine groups.

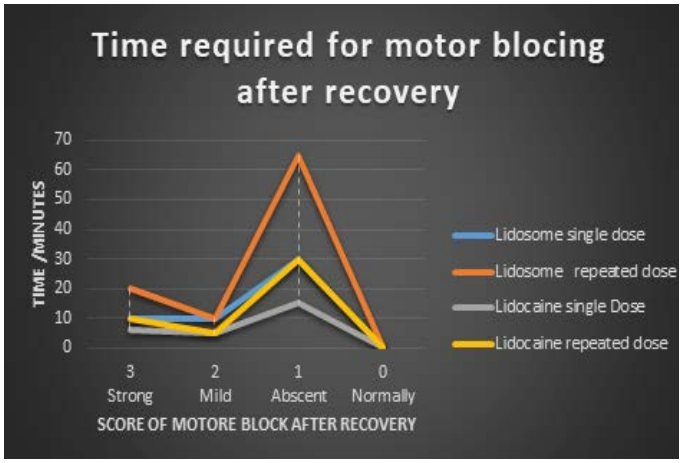

Figure 5: Score of motor block (time/min.) after recovery between Liposomal Lidocaine groups and lidocaine groups.

DISCUSSION

Sensory blockade was monitored by observing aversive reactions to pinprick stimulus, while motor activities were continuously recorded and assessed every 30 seconds till reaching the motor blockade peak intensity then every five minutes were evaluated which modified from (Almasi et al., 2020; Salem et al., 2022). The score used to assess analgesia and motor block was made that modified from (Ghazy and Atiba, 2020). That refers to the absence of sensation during a pin prick and depends on the local dose of anesthetic drug to provide a suitable time during the anesthetic procedure.

The findings of this study indicate that the administration of lidocaine hydrochloride and liposomal lidocaine (referred to as Liposomal Lidocaine) via lumbosacral injections results in prolonged sensory and motor blockade, as well as muscular relaxation in the targeted areas. These effects were observed to be more pronounced when compared to other local anesthetics (Strichartz et al., 1993). This might be that lidocaine more easily permeate the nerve barrier and produce analgesia more quickly. Additionally, the sympathetic blocking caused by the lumbosacral injection of lidocaine's vasodilatation effect reduced the duration of analgesia (Gómez de Segura et al., 2000).

According to scores that modified from Steagall et al. (2017); Vnuk et al. (2006) and Park et al. (2009), our results in both groups showed that the absence of pain was excellent and there was no response locally. Following the administration of local anesthetics like lidocaine, motor block is anticipated because these medications not only cause analgesia but also block the motor fibers. This has to do with the motor neuron impact of acetylcholine, which can enhance the axonal conduction block brought on by local anesthetics. Because the mechanism of action of local anesthetics is not unique to the sensory tracts, unpleasant side effects such as motor paralysis can frequently be experienced (Skarda and Tranquilli, 2007).

However, based on our findings, there is no distinction between Liposomal Lidocaine and lidocaine in the severity of motor block or ataxia. The exceedingly efficient analgesia brought on by lumbosacral injections anesthesia has been attributed to blocking both the afferent and efferent nociceptive pathways (Wolf, 2012). The analgesia function was appearing strong reaction to pinprick stimuli in Liposomal Lidocaine groups single and double dose 25±0.447; 51±0.57 compared with lidocaine groups. Motor function after recovery turned into normal to stand and walk after 30±1.83; 65±6.06. In Liposomal Lidocaine groups while in lidocaine groups after 15±3.16; 30±1.29. Following the administration of spinal anesthetic, patients undergo a se-

quential recovery process characterized by the restoration of voluntary motor function, subsequent return of sensation, and ultimately.

These results are agreed with Day and Skarda, (1991). The action of acetylcholine on motor neurons can potentially worsen the axonal conduction block caused by local anesthetics. This is particularly evident in the case of lidocaine injection, when both analgesia and motor block are commonly observed. In the case of these animals, the administration of lidocaine in isolation induces a motor block that has a duration equivalent to that of analgesia. The lidocaine motor block could be strengthened with lumbosacral injections Liposomal Lidocaine. For Liposomal Lidocaine, motor block lasted substantially longer as evidenced by loss of weight support and loss of the flexor reflex. Notable was the lesser occurrence of front limb paresis, which was indicative of Liposomal Lidocaine having a less widespread and systemic action than lidocaine. While Liposomal Lidocaine increases analgesia, the reason could be the slow release of lidocaine from the liposome, which acts as a depot in the lumbosacral region tissue (release the drug slowly, along with the free drug), (SUO et al., 2020).

Following the administration of local anesthetics like lidocaine, motor block is anticipated because these medications not only cause analgesia but also block the motor fibers (Day and Skarda, 1991).

Our results agree with (Day and Skarda, 1991) in which Recumbence and ataxia that occurs could result from the blockage of both sensory and motor nerve fibers.

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Our results in both groups were better and showed early recovery. Furthermore, it was noted that there were significant differences between the Liposomal Lidocaine group and lidocaine, and this depended on the activity of the drug to block the nerve at the site of injection. Lidocaine exerts its effects on voltage-gated sodium channels by directly impeding membrane depolarization. Consequently, the progression and propagation of electrical currents within excitable tissue are impeded, resulting in accelerated, heightened, prolonged, and expanded anesthesia (Day and Skarda, 1991). According to Khante et al. (2019), In comparison to dogs without motor reflexes, postoperatively, the dogs with voluntary motor reflexes in their hind limbs had a noticeably shorter time to ambulation. Levine et al. (2002), made similar observations.

CONCLUSIONS AND RECOMMENDATION

Lumbosacral injection of liposomal lidocaine revealed a high safety without any complications and recorded a smooth fast induction period in comparison with lidocaine group in addition an excellent degree of analgesia in addition to smooth long recovery periods that could be used in obstetrical and surgical procedures. Therefore we recommended study another local anesthetic agents like tramadol via carrying method and/ or in comparison effect with Liposomal Lidocaine in different surgical operations (minor surgery).

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We appreciate the University of Baghdad's College of Veterinary Medicine for providing me with the resources necessary to complete this project.

CONFLICT OF INTEREST

There are no competing interests.

NOVELTY STATEMENT

The novelty of the study is focused on pharmacologically effect of liposome with lidocaine lead to anesthetic effect against in vivo and in vitro.

AUTHORS CONTRIBUTION

The authors each contributed equally.

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