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Comparison of sensory and motor blocking action of lidocaine and lidocaine-tramadol following brachial plexus block in sheep

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ABSTRACT

The aim of the present study was to evaluate the effect of adding tramadol to lidocaine for brachial plexus block in sheep. Six healthy, adult ewes weighing 41.7 ± 3.82 kg were used. Using an electrical stimulator, brachial plexus block was performed with lidocaine (4 mg/kg) (LID), lidocaine (4 mg/kg)-tramadol (2 mg/kg) (LTL), and lidocaine (4 mg/kg)-tramadol (4 mg/kg) (LTH). All sheep received the three treatments with one-week interval. The final volume of administered solutions was adjusted to 0.3 mL/kg. Time to the onset and duration of anesthesia as well as changes in heart rate, respiratory rate, and rectal temperature were determined. Time to the onset of sensory blockade and motor blockade was not significantly different among groups. The duration of sensory blockade and motor blockade were significantly longer in LTH (128.3 ± 9.7 and 151.5 ± 21.5 min, respectively) compared with those of LID (88.6 ± 6.5 and 110.5 ± 21 min, respectively) and LTL (51.6 ± 11.8 and 89.6 ± 22.7 min, respectively). Although the onset of sensory blockade was longer than that of motor blockade in the three treatments, the difference was only significant in LTL. No significant differences were observed in heart rate, respiratory rate and rectal temperature among and within treatments. It was concluded that addition of tramadol (4 mg/kg) to lidocaine, without altering the onset, can provide more prolonged anesthesia than that of lidocaine in brachial plexus block in sheep.

Keywords

Brachial plexus block, Lidocaine, Nerve stimulator, Sheep, Tramadol

Abbreviations

BPB: Brachial plexus block
HR: Heart rate
f_R: Respiratory rate
RT: Rectal temperature
SB: Sensory blockade
MB: Motor blockade

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Introduction

Local and regional anesthesia are preferred over general anesthesia in ruminants. These techniques provide a cost-effective analgesia, require less monitoring and minimize considerable adverse effects suggesting a reliable alternative to general anesthesia in ruminants [1]. Brachial plexus block (BPB) is a regional anesthesia technique which has been described in cattle [1-3], goat [4] and sheep [5-9]. BPB produces analgesia in the thoracic limb to and below the elbow [1]. Ventral roots of the sixth, seventh and eighth cervical nerves (C6, C7 and C8) as well as the first and second thoracic nerves (T1 and T2) are desensitized in BPB in sheep [10].

Lidocaine is the mostly-used local anesthetic in veterinary medicine. Rapid onset, intermediate duration of action and moderate toxicity has made this drug as a choice for local and regional anesthesia in animals [11]. The mean duration of action of lidocaine in BPB in sheep has been reported as 100 min [8,9]. Prolonging the duration of anesthesia and/or analgesia is favorable because it reduces the need for re-administration of lidocaine and provides long-lasting postoperative analgesia. Various pharmacologic agents in combination of lidocaine have been investigated to provide more prolonged analgesia in BPB. Epinephrine, xylazine, morphine and tramadol have been investigated as adjuvants to lidocaine for BPB in sheep [8,9]. Among these additives, only xylazine increased the duration of both sensory and motor blockade of BPB; however, it was associated with sedation, bradycardia and increased urination [8].

Tramadol, an atypical opioid, is widely used to treat or relieve acute or chronic pain. In addition to systemic analgesic impacts, tramadol has been postulated to have some local anesthetic effects [12,13]. Availability, different mechanisms of action and lower incidence of serious adverse effects of tramadol have made this drug as an agent of interest for local and regional anesthesia. Using of tramadol alone or in combination with lidocaine has increased the duration of analgesia after epidural application in ruminants [14-17]. Tramadol (in a range of 100-200 mg) when added to different local anesthetics has increased the quality and duration of BPB in human studies [18-24]. In a recent study in sheep, addition of 1 mg/kg tramadol to lidocaine for BPB did not increase the duration of neither sensory nor motor blockade in comparison to those of lidocaine alone [9]. Since tramadol has been speculated that induces analgesia in a dose-dependent manner [14], employing of larger doses of tramadol might produce more prolonged analgesia following BPB in sheep. Thus, the objective of the present study was to evaluate the effect of tramadol (2 and 4 mg/kg) in combination with lidocaine on BPB in sheep. We hypothesized that using of these doses could increase the duration of anesthesia without serious adverse effects.

Results

There was no significant differences in body weights of animals: LID: 41.4 ± 4.5, LTL: 40.4 ± 4.5 and LTH: 43.5 ± 2.5. Overall, All the sheep tolerated the procedure well; however, movement and unrest at the time of needle advancement were occasionally seen. The proper site for administration of treatments was easily identified and all the aspirations were negative. BPB was failed in one sheep in LTL and one sheep in LTH. Successful BPB was achieved by the repetition of the procedure in the aforementioned sheep one week later. Injection of drugs took a time of 3-6 min in all groups. The pH of the administered solutions was measured as 6.34 ± 0.02 for LID, 6.33 ± 0.04 for LTL, and 6.33 ± 0.02 for LTH.

Time to the onset of sensory and motor blockade was not significantly different among groups ($p > 0.05$). Although the onset of sensory blockade in comparison to the onset of motor blockade was longer in the three treatments, the difference was only significant in LTL ($p < 0.05$; Figure 1). The duration of loss of sensation was significantly longer in LID than that of LTL ($p < 0.05$). The duration of sensory and motor blockade was significantly longer in LTH compared to those of LID and LTL (88.6 ± 6.5 and 110.5 ± 21 min for LID, 51.6 ± 11.8 and 89.6 ± 22.7 min for LTL and 128.3 ± 9.7 and 151.5 ± 21.5 min for LTH) ($p < 0.05$; Figure 2).

Statistical analysis of HR, f_R and RT did not show significant differences among and within treatments ($p > 0.05$; Table 1). No sedation and adverse reactions and no signs of local anesthetic`s toxicity were seen following BPB in any of the sheep. Some degree of hemorrhage was observed in the left lateral wall of the thorax in one out of two sheep which were slaughtered two weeks after the end of the last treatment.

Discussion

Adjuvants are used to increase the quality and duration of anesthesia induced by local anesthetics. A desirable adjuvant should provide better anesthetic characteristics; meanwhile, it should have less adverse effects. Based on the results of the present investigation, addition of 4 mg/kg tramadol to lidocaine for BPB, without altering the onset of action, prolongs the duration of sensory and motor blockade in sheep. Moreover, tramadol in combination with lidocaine did not result in noticeable side effects in sheep undergoing BPB.

Tramadol has been suggested that exerts its pe-

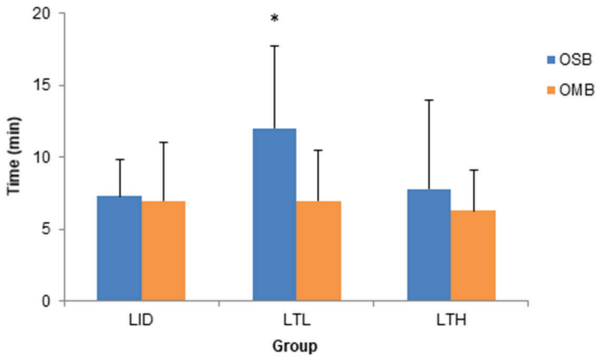

Figure 1
Mean and SD of time of onset of sensory and motor blockade (OSB and OMB, respectively) using lidocaine (4 mg/kg; LID), lidocaine (4 mg/kg) plus low dose of tramadol (2 mg/kg; LTL) and lidocaine (4 mg/kg) plus high dose of tramadol (4 mg/kg; LTH) for brachial plexus block in sheep (n = 6). Asterisks denote significantly different groups at $p < 0.05$.

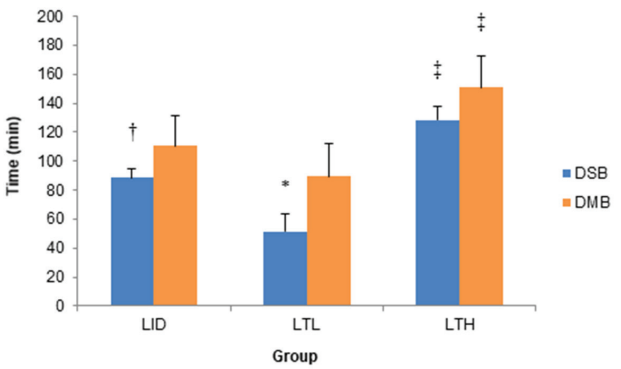

Figure 2
Mean and SD of duration of sensory and motor blockade (DSB and DMB, respectively) using (4 mg/kg; LID), lidocaine (4 mg/kg) plus low dose of tramadol (2 mg/kg; LTL) and lidocaine (4 mg/kg) plus high dose of tramadol (4 mg/kg; LTH) for brachial plexus block in sheep (n = 6).
† Significantly different from DSB in LTL.
‡ Significantly different from DSB and DMB in LID and LTL.
*Significantly different from DMB in LTL.

ripheral anesthetic properties through various mechanisms. Blockade of opioids and α-2 agonist receptors [25], blockade of sodium and potassium channels in the cell membranes [26-29], and blockade of peripheral nerve conduction [13,29] have been proposed for possible local anesthetic`s characteristics of tramadol. Longer duration of analgesia as a result of systemic effects of tramadol following local application of tramadol and levobupivacaine has also been reported in human patients undergoing shoulder arthroplasty. However, the same effects have not been observed after systemic administration of tramadol [30].

Conflicting results have been obtained with respect to the onset of action after addition of tramadol to local anesthetics in human`s axillary blocks. While sveral reports indicate faster onset of anesthesia [18,19,22,23], other reports have documented a delay in the initiation of action [20,24]. Several authors failed to detect any changes in the onset of anesthesia [21,23,31]. A study in sheep demonstrated that 1 mg/kg tramadol did not alter the onset of sensory and motor blockade when used in combination with lidocaine for BPB [9].

Duration of anesthesia was significantly longer in sheep which received larger dose of tramadol (i.e. 4 mg/kg). In human studies, addition of tramadol in a range of 100-200 mg to different local anesthetics has increased the duration of action of BPB [18-24]. Ghadirian et al. [9] did not observe increase in the duration of sensory and motor blockade after addition of 1 mg/kg tramadol to lidocaine for BPB in sheep. Considering the sheep`s weights in the latter study (i.e. 27.0 ± 2.2 mg), the authors have used tramadol with the total dose of 27.0 ± 2.2 mg which is much less than that of human`s investigations. In the current study, the total doses of tramadol were 80.8 ± 9.0 and 173.2 ± 10.0 mg in LTL and LTH, respectively. While several factors such as type, concentration, volume and method of application can affect the duration of anesthesia in local and regional nerve blocks [9], it seems that the total dose of tramadol plays an important role in the duration of action in BPB. Therefore, although tramadol with the dose rate of 4 mg/kg increased the duration of anesthesia, the weights of the sheep is also a substantial factor to achieve a successful more prolonged block. Further studies are needed to determine the exact effective total dose of tramadol for increasing the duration of anesthesia of BPB in sheep.

In the current study, the combination of 2 mg/kg tramadol and lidocaine not only did not increase the duration of anesthesia, but also decreased both the sensory and motor blockade of BPB. However, just the duration of sensory blockade was significantly lower than that of lidocaine alone. Although it was not significant, the duration of sensory and motor blockade in the study of Ghadirian et al. [9] were also lower in lidocaine-tramadol group than those of lidocaine alone following BPB in sheep. Further studies are necessary to confirm these findings and to clarify the exact reason(s) and/or mechanism(s).

The onset of sensory blockade was longer than that of motor blockade in the three groups; however, the difference was only significant in LTL. The same results have been reported following BPB in sheep [8,9], dogs [32,33], and goats [4]. The more rapid onset of sensory blockade has been explained by somatotopical arrangement of nerve fibers in brachial plexus where motor and sensory fibers are located in the periphery (mantle bundles) and center (core) of the nerve trunk, respectively [34].

HR, f_R and RT did not show significant chang-

Table 1
Mean ± SD of heart rate (HR), respiratory rate (fR) and rectal temperature (RT) in sheep (n = 6) received lidocaine (4 mg/kg; LID), lidocaine (4 mg/kg) plus low dose of tramadol (2 mg/kg; LTL), and lidocaine (4 mg/kg) plus high dose of tramadol (4 mg/kg; LTH) for brachial plexus block

		Base	5 (min)	10 (min)	15 (min)	20 (min)	30 (min)	45 (min)	60 (min)	75 (min)	90 (min)	105 (min)	20 (min)	50 (min)	80 (min)
HR	LID	73 ± 16	97 ± 11	102 ± 23	96 ± 19	86 ± 22	78 ± 20	80 ± 24	86 ± 16	75 ± 13	80 ± 12	77 ± 15	74 ± 21	75 ± 17	70 ± 14
	LTL	80 ± 15	95 ± 16	87 ± 18	91 ± 18	84 ± 15	80 ± 15	80 ± 17	75 ± 19	73 ± 18	77 ± 15	77 ± 15	76 ± 13	71 ± 17	70 ± 15
	LTH	91 ± 16	92 ± 10	89 ± 14	91 ± 16	90 ± 8	88 ± 19	81 ± 18	96 ± 28	89 ± 25	85 ± 22	84 ± 22	81 ± 26	80 ± 27	77 ± 23
fR	LID	40 ± 10	42 ± 7	47 ± 3	43 ± 9	43 ± 11	42 ± 13	44 ± 13	50 ± 25	51 ± 16	42 ± 9	45 ± 11	47 ± 6	45 ± 12	36 ± 9
	LTL	46 ± 14	54 ± 18	50 ± 23	42 ± 14	39 ± 18	39 ± 16	38 ± 15	49± 22	51± 21	47 ± 25	49 ± 23	49 ± 20	49 ± 19	47 ± 17
	LTH	40 ± 6	58 ± 19	50 ± 18	52 ± 16	50 ± 18	52 ± 15	55 ± 15	56 ± 22	54 ± 24	56 ± 21	60 ± 26	57 ± 20	50 ± 11	50 ± 12
RT	LID	39.2 ± 0.5	39.5 ± 0.4	39.4 ± 0.4	39.3 ± 0.3	39.3 ± 0.3	39.3 ± 0.3	39.3 ± 0.3	39.3 ± 0.3	39.2 ± 0.4	39.2 ± 0.4	39.2 ± 0.4	39.2 ± 0.4	39.3 ± 0.5	39.1 ± 0.5
	LTL	39.1 ± 0.4	39.4 ± 0.3	39.4 ± 0.4	39.3 ± 0.5	39.3 ± 0.4	39.3 ± 0.6	39.4 ± 0.4	39.3 ± 0.3	39.3 ± 0.3	39.3 ± 0.3	39.3 ± 0.3	39.3 ± 0.2	39.2 ± 0.1	39.0 ± 0.2
	LTH	39.1 ± 0.2	39.2 ± 0.3	39.4 ± 0.3	39.2 ± 0.4	39.3 ± 0.3	39.3 ± 0.4	39.2 ± 0.3	39.3 ± 0.4	39.4 ± 0.4	39.2 ± 0.4	39.1 ± 0.4	39.0 ± 0.3	39.0 ± 0.3	38.9 ± 0.2

es within the groups when compared with the base values. No significant differences in HR and fR have also been reported following application of 1 mg/kg tramadol and lidocaine for BPB in sheep [9]. Addition of tramadol (100 mg) to mepivacaine for BPB in human patients did not alter HR, blood pressure and fR [21]. One of the main advantages of tramadol is its minimal effects on cardiovascular variables [35], and according to the results of the present study, tramadol is a safe adjuvant for addition to local anesthetics even when the dose rate of as high as 4 mg/kg were used for BPB in sheep.

Various methods including blind, nerve stimulator and ultrasound-guided techniques have been described for performing BPB [36]. Since the success rate of a regional anesthesia depends on the ability to accurately locate the target nerves and to place the solution as close as possible to nerves, two latter methods offer to increase the rate of successful anesthesia. Performing BPB using nerve stimulator has raised the success rate from 20% to 75% and 95% in dogs and goats, respectively [4,33]. No differences in success rate and complications following nerve stimulator- and ultrasound-guided BPB were observed in humans [37]. In the current study, an overall success rate of 88% was recorded, which is comparable with the results of the other studies reporting the success rate of 86% and 89% after BPB in sheep using a nerve stimulator [8,9]. It is trustworthy to note that, in the present study, BPB was failed in two sheep which were in the higher range of weight (i.e. 44 and 45.5 kg).

The final volume of local anesthetic solution can play an important role on overall outcome of BPB (38, 39). A total volume of 10-40 mL has been proposed for BPB in cows and sheep [2,3,5]. Moens (1995) [4] used 0.3-0.4 mL/kg for performing BPB in goats. Applying of 0.25 mL/kg of anesthetic solution for BPB in sheep may not be enough [8,9]. In the current study, mainly because of using the large volume of tramadol, the final volume of administered solutions was adjusted to 0.3 mL/kg. However the overall rate of successful block did not increase compared with those of the aforementioned investigations (88% vs 86% and 89%).

Intravascular injection, hemorrhage, pneumothorax, lung injury, nerve injury and infection are the possible complications associated with BPB [38,40]. Administration of high doses of local anesthetics may be resulted in systemic toxicity [11]. Pruritus after application of tramadol (100-200 mg) and mepivacaine combination has been reported in humans undergoing BPB [23]. In the current study, no adverse effect related to tramadol and/or lidocaine was observed. However one out of two slaughtered sheep showed some degree of hemorrhage in the left lateral wall of the thorax most probably due to displacing the needle to find the appropriate twitches in the limb.

Conclusion

Nerve stimulator-guided block is an acceptable method for performing BPB in sheep. Addition of tramadol (4 mg/kg) to lidocaine (4 mg/kg) in BPB, without changing the onset, increased the duration of sensory and motor blockade in comparison to lidocaine alone (4 mg/kg) in sheep. The occurrence of complications associated with BPB in sheep is rare; however, negative aspiration for blood and air is strongly recommended.

Materials and methods

Six healthy, adult ewes with weight of 41.7 ± 3.82 (mean ± SD) kg and age of 1-2 (range) years old were used. The sheep were transferred to Veterinary Hospital, at least 2 weeks prior to the beginning of the investigation, to be acclimatized to the circumstances. The animals were considered to be healthy based on a thorough physical examination and normal complete blood count and total protein. The sheep were fed alfalfa, straw and grain, and water ad libitum and were not fasted before the experiments. All the procedures were performed in the evening (2:00-5:00 PM). The institutional Animal Care and Research Committee approved all the protocols of the present study [95/3/24/4550].

Sheep were assigned to receive one of the three treatments on a blinded random fashion: lidocaine (4 mg/kg; Caspian Tamin, Pharmaceutical Co, Iran) (LID), lidocaine plus low dose of tramadol (2 mg/kg; Darou Pakhsh, Iran) (LTL) and lidocaine plus high dose of tramadol (4 mg/kg) (LTH). Using normal saline, the total volume of administered drugs was fixed at 0.3 mL/kg. A digital pH meter (Suntex, Taiwan) was employed to determine the pH of solutions. Each sheep was used on three occasions with at least one-week interval. The study was designed in a way that in each group three right and three left thoracic limbs were administered.

After recording heart rate (HR), respiratory rate (f_R) and rectal temperature (RT) as well as confirming of the normal sensory and motor functions of the thoracic limb, an area of about 15 cm of the skin overlying the scapulohumeral joint was aseptically prepared. Then, sheep were positioned in lateral recumbency with the target limb uppermost. Two mL lidocaine 1% was injected subcutaneously at the site of needle puncture. BPB was performed using an insulated needle (SonoPlex stim cannula, 22 G × 80 mm, Pajunk,Germany) connected to an electrical stimulator (Neurodyn710, Novin Medical Engineering CO, Iran). The method employed for BPB was based on previous studies in sheep [8, 9]. In summary, the negative electrode was connected to the insulated needle and the positive electrode was attached to the skin with about 10-cm distance from the shoulder joint. The needle was inserted at the cranial and medial to the acromion and advanced caudally to the costochondral junction of the first rib. After about 4-5 cm insertion, the stimulator was turned on and was set at the current of 1 mA, 0.2 Hz and 0.1ms. Once the eligible twitches (flexion or extension of the elbow and not pronation of the extremities and twitches of the shoulder) were elicited, the current was gradually decreased to 0.1 mA, 0.2 Hz and 0.1ms (the threshold current) in 0.2 mA increment until the same motor responses with the least current were detected. By negative aspiration for blood or air, the solution was injected slowly and repositioned in a fan-like fashion until all the twitches were disappeared. By accomplishing the procedure, the animals were placed in standing position.

Time to onset and duration of sensory and motor blockade were recorded. Complete sensory blockade was evaluated

at antebrachial and interdigital areas (below the elbow) and was considered to be present when responses to superficial and deep pin-prick test using a 25-gauge hypodermic needle as well as pinching of skin using a hemostat (8-inch Rochester Dean Haemostatic Forceps; Martin, Tuttlingen, Germany) closed to the first ratchet were absent. Sensory blockade was assessed every 30 sec until complete sensory blockade was confirmed. Onset of motor blockade was also recorded when the animals were no longer able to bear their own weights on the affected limb. Duration of sensory and motor blockade was defined as the time elapsed from the complete lack of response until a normal response was exerted. Duration of anesthesia was evaluated every 15 min by the methods stated before.

HR, fR and RT were recorded at base and at 5, 10, 15, 20, 30 min and then every 15 min until 180 min after drugs administration. HR was monitored via thoracic auscultation and fR was counted via chest movement in a 1-min period. RT was measured per rectum using a digital thermometer (AEG, Germany). All injections were applied by the same investigator (H.I.R) and all evaluations were performed by another one (M.K) who was not aware of the treatments.

Statistical analysis

Statistical analysis was performed by IBM SPSS Statistics for Windows Version 22 (IBM Corporation, NY, USA). The normal distribution of data was confirmed using Kolmogrov-Smirnov test. All data were expressed as mean ± standard deviation (SD). Analysis of variance (ANOVA) with repeated measures followed by Bonferroni`s test was employed for comparison of the weight, the onset and duration of sensory and motor blockade among treatments as well as HR, fR and RT among and within groups. Comparison of the time to the onset and duration of sensory and motor blockade in each treatment was done using paired-sample *t* test. $p < 0.05$ was considered as the significance level.

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Author Contributions

H.I.R: designing and conducting the study, drafting the manuscript; H.N: collecting and analyzing the data, reviewing the manuscript; A.A.N: carrying out the experiments, reviewing and revising the manuscript; M.K: carrying out the experiments, collecting and analyzing data

Conflict of Interest

The authors do not have any potential conflicts of interest to declare.

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