



Contents lists available at ScienceDirect

Journal of Hand Surgery Global Online

journal homepage: www.JHSGO.org

Original Research

Safety of Lidocaine During Wide-Awake Local Anesthesia No Tourniquet for Distal Radius Plating



Shalimar Abdullah, BMedSci (Hons), MBBS, * Muhamad Fitri Tokiran, MBBS, Dr Ortho & Trauma, † Amir Adham Ahmad, MBBS, MS Ortho, ‡ Elaine Zi Fan Soh, MBBS, Dr Ortho & Trauma, * Suzana Makpol, BSc Hons (Clinical Biochemistry), PhD (Medical Biochemistry), § Jamari Sapuan, MD, MS Ortho *

* Hand and Microsurgery Unit, Department of Orthopaedics and Traumatology, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

† Department of Orthopaedics and Traumatology, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

‡ Prince Court Medical Center, Kuala Lumpur, Malaysia

§ Department of Biochemistry, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

ARTICLE INFO

Article history:

Received for publication December 4, 2022

Accepted in revised form December 12, 2022

2022

Available online January 9, 2023

Key words:

Distal radius plating
Lidocaine in adrenaline
Lidocaine toxicity
WALANT

Purpose: This study evaluated the clinical and biochemical safety profile of infiltration of lidocaine with adrenaline in wide-awake local anesthesia no tourniquet for distal radius plating.

Methods: Twenty-four participants were randomly assigned to the therapeutic group (n = 19) (1% lidocaine in 1:100,000 adrenaline) and control group (n = 5) (2% lidocaine alone). Clinical parameters, including skin necrosis, duration of recovery of sensation, and lidocaine toxicity, were monitored. The serum lidocaine level was measured at different time intervals using a high-performance liquid chromatography reagent.

Results: No lidocaine toxicity was recorded in any participant. The therapeutic group had a longer time for recovery of sensation. There was a significant difference in the serum lidocaine levels between both the groups at all time intervals up to 6 hours, with all participants exhibiting serum lidocaine levels below the mild toxicity level of 6.0 µg/mL.

Conclusions: Lidocaine used within a safe recommended dose in wide-awake local anesthesia no tourniquet for distal radius plating is clinically and biochemically safe.

Clinical relevance: Determining the clinical and biochemical safety profile of lidocaine with adrenaline in wide-awake local anesthesia no tourniquet can promote wider use of this technique.

Copyright © 2022, THE AUTHORS. Published by Elsevier Inc. on behalf of The American Society for Surgery of the Hand. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Distal end radius plating is a common orthopedic procedure. Conventionally, it has been performed under general anesthesia or regional anesthesia using a tourniquet to create a bloodless view for better visualization. However, patients may have an unpleasant or

painful experience during the procedure because of tourniquet application.^{1–3}

Wide-awake local anesthesia no tourniquet (WALANT) has pioneered over the last decade, with excellent results, with which extremity surgeries can be performed using a combination of 2 drugs that have been used in practice for hundreds of years, namely lidocaine, to block pain, and adrenaline, to reduce bleeding, resulting in improved intraoperative surgical field visualization. It has a number of significant advantages, including reduced operating time, reduced bleeding, and a bloodless field during surgery, which improves the ability to visualize functional bone and soft tissue repair and eliminates the use of tourniquets in the extremities as well as all complications that are associated with them. Furthermore, when patients are awake, it allows for better communication between the surgeon and the patients during the surgery.^{4–6}

Declaration of interests: No benefits in any form have been received or will be received related directly or indirectly to the subject of this article.

Given her role as Guest Editor of the Special Issue: WALANT, Dr Abdullah had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to Tamara D. Rozental, MD.

Corresponding author: Elaine Soh Zi Fan, MBBS, Dr Ortho & Trauma, Hand and Microsurgery Unit, Department of Orthopaedics and Traumatology, Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, Jalan Yaacob Latiff, 56000 Kuala Lumpur, Malaysia.

E-mail address: elainesoh86@gmail.com (E.Z.F. Soh).

<https://doi.org/10.1016/j.jhsg.2022.12.003>

2589-5141/Copyright © 2022, THE AUTHORS. Published by Elsevier Inc. on behalf of The American Society for Surgery of the Hand. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Lidocaine is a well-known local anesthetic drug used to numb tissues in specific locations. It can also be used to treat ventricular tachycardia and nerve block.⁷ Lidocaine's recommended dose and therapeutic level in the serum after administration are well known. For infiltration and regional nerve block procedures, the maximum dose of plain lidocaine is 280 mg (approximately 3–4 mg/kg) or 490 mg (7 mg/kg) with adrenaline in a ratio of 1:100,000 (based on a 70-kg patient).⁸ These figures are based on manufacturers' recommendations and animal studies, and they have been widely published and broadly accepted.⁹ However, the toxicity and complications of the combination of lidocaine and adrenaline have been a concern.^{10,11} There is no study that has assessed the biochemical aspect, specifically the serum lidocaine level after injection of lidocaine and adrenaline in WALANT.

This study aimed to evaluate the clinical and biochemical safety profile of lidocaine used in WALANT for distal radius plating. The primary outcome was to measure the serum lidocaine level after WALANT injection. We hypothesized that the serum lidocaine level after WALANT injection is below the toxicity level.

Materials and Methods

This was a randomized control trial involving a total of 24 participants with a distal radius fracture requiring open reduction and plating at a tertiary center in Malaysia. The inclusion criteria included an age group of 18–45 years, no comorbidities, and no known allergy to lidocaine. The participants were randomized into the following 2 groups: (1) therapeutic group, which received local injection of 1% lidocaine with adrenaline in a ratio of 1:100,000, and (2) control group, which received 2% lidocaine alone. Informed consent was obtained from all participants.

An 18-gauge-sized intravenous cannula was inserted in the cubital fossa prior to the procedure, specifically for blood collection. A local anesthetic solution was injected to the planned surgical site 30 minutes prior to skin incision. The timing of infiltration of local anesthesia was recorded as 0 minute. Blood samples were aspirated through the intravenous cannula in the cubital fossa at pre-determined time intervals: 5 minutes, 10 minutes, 30 minutes, 60 minutes, and 6 hours, with a total of 3.0-mL blood for each sample. The blood samples were sent to a biochemistry laboratory for measurement of serum lidocaine levels.

The participants were also closely monitored throughout the period after injection, during and after surgery, for signs and symptoms of lidocaine toxicity, including light headedness, paresthesia, tinnitus, blurring of vision, palpation, chest discomfort, nystagmus, ataxia, slurred speech, and confusion. The duration of numbness and the presence of skin or digital necrosis were assessed and recorded. A lipid emulsion (SMOFlipid, Fresenius Kabi, 20%) was made readily available throughout in case of an adverse event such as lidocaine toxicity.

In the biochemistry laboratory, a standardized stock of lidocaine solution (4 mg/mL) was made in 5% dextrose and stored at 4 °C. The working standard solution was prepared daily from the stock solution via serial dilution with high-performance liquid chromatography-grade water to prepare final concentrations of 40-, 4-, and 0.4-µg/mL lidocaine. An internal standard stock solution was prepared by dissolving 17 mg of procainamide hydrochloric acid in 100 mL of high-performance liquid chromatography-grade water. A calibration curve was prepared from serum samples containing lidocaine in the concentrations of 50, 125, 250, 500, 1,000, 2,000, 2,500, and 5,000 ng/mL.

A 1-step liquid-liquid extraction step was used to extract lidocaine from human serum. In the extraction procedure, 0.25 mL of serum was added to 50 µL of the internal standard solution, 200 µL of 1M sodium hydroxide, and 3 mL of diethyl ether and then

Table 1

General Characteristic of the Participants in the Study

Variables	Therapeutic Group	Control Group	P Value
Number, n (%)	19 (79.17)	5 (20.83)	
Age (y), mean ± SD	36.05 ± 7.08	29.40 ± 12.28	.301*
Age (y), median (IQR)	38.00 (9.00)	24.00 (24.00)	
Body weight (kg), mean ± SD	71.00 ± 10.23	62.40 ± 5.32	.086*
Body weight (kg), median (IQR)	69.00 (10.00)	61.00 (9.50)	

IQR, interquartile range.

* Comparison of mean ± SD between the therapeutic and control groups was performed using the Student *t* test.

vortexed for 30 seconds, followed by centrifugation at 3000 g for 3 minutes. The organic solvent layer was pipetted to new tubes and evaporated to dryness for 20 minutes in the ScanVac vacuum concentrator (LaboGene). The dried samples residues were reconstituted with 150 µL of high-performance liquid chromatography-grade water. Chromatographic separation was performed using the Waters Acquity H-Class Ultra Performance Liquid Chromatographic system (Waters), which was equipped with Acquity Quaternary Solvent Manager, Acquity Sample Manager, and Acquity Photo Diode Array Detector. The chromatographic separation of lidocaine and procainamide hydrochloric acid (internal standard) was achieved using the Kinetex Evo C18 column (100 × 2.1 mm, particle size, 1.7 µm; Phenomenex) at an ambient temperature (approximately 24 °C). A mixture of acetonitrile and phosphate solution (25mM potassium dihydrogen phosphate, 3mM sulfuric acid, and 3.6mM triethylamine) in a ratio of 12:88 (vol/vol) was used as the mobile phase. Prior to use, the mobile phase was degassed by filtering it under vacuum pressure through a 0.45-µm-pore-size nylon filter. The mobile phase was pumped through the ultra performance liquid chromatographic system at 0.4 mL/min. Ultraviolet detection was accomplished at 277 nm for procainamide. At 4 minutes after injection, the ultraviolet detector was programmed to switch to a wavelength of 210 nm for lidocaine. The injection volume was 10 µL, and both the compounds were separated within 5 minutes. Data were collected and processed using the Empower 3 chromatography software (Waters). The results of the serum level of lidocaine were recorded. All data were analyzed using the statistical application SPSS Statistics, version 26 (IBM Corp). The observed power of the statistical analysis was 0.863, which is more than the acceptable value of 0.80.

Written informed consent was obtained from all participants before the study. Ethical approval for this study was obtained from the Universiti Kebangsaan Malaysia Ethical Committee.

Results

A total of 24 participants were recruited, with 19 in the therapeutic group and 5 in the control group.

At all the time intervals following local anesthetic agent infiltration, the data on age, body weight, and serum lidocaine level were normally distributed. All the variables had skewness and kurtosis values between –3.00 and +3.00, which was considered acceptable. However, substantial *P* values of the Shapiro-Wilks statistics revealed that the data on age and restoration of sensation in the therapeutic group were not normally distributed. As a result, parametric testing was used to assess the data on age and body weight, whereas nonparametric testing was used to assess data on serum lidocaine level at all the time intervals following the procedure and recovery of sensation.

The overall characteristics of the subjects participating in the study are shown in Table 1. The therapeutic and control groups' mean (±SD) age was 36.05 (±7.08) and 29.40 (±12.28) years, respectively, and the median (interquartile range [IQR]) age was

Table 2
Serum Lidocaine Level After Infiltration of Local Anesthesia at Different Intervals for Each Participant

Participants	Lidocaine Dose (mg)	Lidocaine Dose per Body Weight (mg/kg)	Serum Lidocaine Level ($\mu\text{g/mL}$)				
			5 Min	10 Min	30 Min	60 Min	6 h
T1	400	5.56	3.69	0.90	0.63	0.47	0.12
T2	500	5.56	3.58	0.91	0.65	0.50*	0.16
T3	400	5.33	2.11	1.52	0.82*	0.43	0.12
T4	550	6.11	2.50	0.85	0.71	0.47	0.10
T5	400	5.88	5.06	1.51	0.75	0.37	0.09
T6	400	5.48	4.96	0.63	0.48	0.32	0.17*
T7	400	5.63	4.42	0.55	0.57	0.37	0.14
T8	400	6.15	4.92	1.20	0.54	0.42	0.16
T9	400	6.15	4.62	0.64	0.58	0.42	0.14
T10	560	6.22	3.24	0.69	0.64	0.43	0.12
T11	350	6.36	3.50	0.73	0.60	0.42	0.11
T12	400	6.15	4.37	1.24	0.53	0.36	0.14
T13	400	5.80	4.27	1.19	0.57	0.40	0.14
T14	400	5.97	5.08*	1.26	0.75	0.38	0.17*
T15	400	6.67	3.32	1.59	0.68	0.39	0.09
T16	500	6.41	5.04	1.89*	0.80	0.38	0.16
T17	400	6.78	3.59	1.32	0.72	0.43	0.11
T18	400	5.41	4.67	1.36	0.57	0.39	0.15
T19	400	6.35	4.72	1.31	0.54	0.41	0.16
C1	200	2.86	2.44	0.66	0.68	0.44	0.08
C2	200	3.08	2.96	0.86	0.54	0.37	0.12
C3	200	3.33	3.49	1.14	0.45	0.36	0.10
C4	200	3.28	2.98	1.03	0.40	0.39	0.09
C5	200	3.57	3.13	0.96	0.47	0.42	0.13

* Maximum serum lidocaine level in each time interval among the participants.

38.00 (9.00) and 24.00 (24.00) years, respectively. The difference in the mean (\pm SD) and median (IQR) age between the 2 groups, however, was not statistically significant ($P > .05$). The therapeutic group had a greater mean (\pm SD) body weight (71.00 [\pm 10.23] kg) and median (IQR) body weight (69.00 [10.00] kg) than the control group (62.40 [\pm 5.32] and 61.00 [9.50] kg), respectively; however, the differences were not significant ($P > .005$).

Table 2 illustrates the serum lidocaine levels of each participant at various time intervals following the infiltration of local anesthesia. The maximum dose of lidocaine mixed with adrenaline (WALANT) and lidocaine alone was 7.0 and 4.5 mg/kg, respectively, according to established guidelines. The maximum concentration of serum lidocaine levels was recorded in the therapeutic group among different participants at each time interval following the WALANT technique.

A 1-way repeated-measure analysis of variance was performed to compare the serum lidocaine levels at 5 minutes, 10 minutes, 30 minutes, 60 minutes, and 6 hours after the WALANT procedure. The mean (\pm SD) serum lidocaine levels are presented in Table 3. The participants in the therapeutic group demonstrated higher mean (\pm SD) serum lidocaine levels than those in the control group at all the time intervals. The P value for Wilks Lambda is less than 0.001; therefore, it can be concluded that there was a statistically significant effect of time. This suggests that there was a change in the mean (\pm SD) serum lidocaine levels across the 5 different time periods. The multivariate eta squared of 0.993 demonstrates a large effect size between both the groups.

There was a significant difference in the serum lidocaine levels between the therapeutic and control groups at all the time intervals, ie, at 5 minutes, 10 minutes, 30 minutes, 60 minutes, and 6 hours, after local anesthesia infiltration ($P < .001$), as shown in the Figure. The serum lidocaine levels for both the therapeutic and control groups were found to be below the mild toxicity level of 6.0 $\mu\text{g/mL}$ and central nervous system toxicity and cardiotoxic levels of ≥ 8.0 $\mu\text{g/mL}$ (Figure).

A 2-way repeated-measure analysis of variance was performed to assess the effect of body weight and administered lidocaine dose

on serum lidocaine levels among the participants. The independent variables were body weight and administered lidocaine dose. The dependent variable consisted of serum lidocaine level measured at 5 minutes. The main effects of the administered lidocaine dose were statistically significant ($P = .01$); however, the effects on the participants' body weight was not significant ($P = .15$). These results suggest that patients respond differently based on the administered lidocaine dose. Besides, it was found that all the participants in the therapeutic and control groups did not experience skin necrosis at the procedure site and other clinical features of lidocaine toxicity.

The participants in the therapeutic group had a longer mean (\pm SD) and median (IQR) time to regain sensation than those in the control group ($P < .001$) (Table 4). Hence, the combination of lidocaine and adrenaline in WALANT had a longer numbness effect than lidocaine alone.

All 19 participants in the therapeutic group underwent open reduction and plating of the distal radius under WALANT successfully. There were no complications reported, and none required conversion to general anesthesia.

Discussion

Lidocaine is approximately 95% metabolized (dealkylated) in the liver mainly by CYP3A4 to the pharmacologically active metabolite monoethylglycinexylidide and subsequently to the inactive glycine xylidide.¹² Lidocaine has a biphasic elimination half-life of 90–120 minutes in most people. In individuals with hepatic impairment (average, 343 minutes) or congestive heart failure, this may take longer (average, 136 minutes).¹³ Lidocaine is passed through urine (90% as metabolites and 10% as unchanged drug).¹⁴

Lidocaine toxicity can manifest in a variety of ways, from mild to life-threatening local anesthetic systemic toxicity. They usually occur between 1 and 5 minutes after administration; however, clinical toxicity might take up to 30 minutes or longer.¹⁵ The diagnosis of lidocaine toxicity is usually performed clinically because serum levels are not readily available. Hence, by measuring

Table 3
Mean Serum Lidocaine Level After Infiltration of Local Anesthesia at Different Intervals Between Groups of Participants

Interval	Group	n	Mean ($\mu\text{g/mL}$)	SD ($\mu\text{g/mL}$)	Wilk Lambda (<i>P</i> Value)	Eta Squared
5 min	Therapeutic	19	4.09	0.89	<.001*	0.993
	Control	5	2.99	0.38		
10 min	Therapeutic	19	1.12	0.38		
	Control	5	0.93	0.18		
30 min	Therapeutic	19	0.64	0.10		
	Control	5	0.51	0.11		
60 min	Therapeutic	19	0.41	0.04		
	Control	5	0.40	0.03		
6 h	Therapeutic	19	0.13	0.03		
	Control	5	0.10	0.02		

* Indicates significant statistical result.

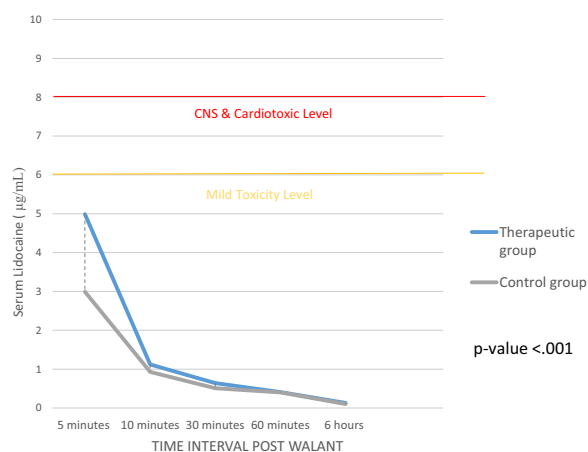


Figure. Mean serum lidocaine level between the therapeutic and control groups after infiltration of local anesthesia at different intervals. CNS, central nervous system.

the serum level of lidocaine at various intervals after administration, we can determine whether the dose given to participants and the serum level in peripheral blood are within safe limits. The therapeutic level of lidocaine in serum plasma is between 0.50 and 5.50 $\mu\text{g/mL}$.¹⁶ Mild signs and symptoms of lidocaine toxicity, such as light headedness, paresthesia, tinnitus, blurring of vision, nystagmus, ataxia, slurred speech, and confusion, can occur at a concentration of 6.00 $\mu\text{g/mL}$. Patients usually experience central nervous system toxicity and cardiotoxicity at concentrations of 8.00–12.00 $\mu\text{g/mL}$ and higher.^{17,18} Following lidocaine infiltration, serum plasma levels peak between 20 and 30 minutes and toxic manifestations can arise after 30 minutes or even later, which requires careful monitoring. The half-life of lidocaine is 90–120 minutes. Between 7 and 10 hours, the plasma serum lidocaine level drops to roughly 3% in the body, which is considered subtherapeutic, and lidocaine is predicted to be completely eliminated from the plasma at 23 hours.¹⁹

There is literature that has recommended the safe dosage of lidocaine in WALANT surgery.²⁰ However, there is no study that investigated the level of serum lidocaine after the infiltration of lidocaine that can provide a more objective measurement of the safety level. There was a similar study on lidocaine and epinephrine levels in tumescent technique liposuction surgery but none that we could refer to for upper-extremity surgery.²¹

In our study, all the participants received lidocaine according to the safe recommended dose for their body weight. There were no clinical signs and symptoms of lidocaine toxicity. Considering the objective measurement of lidocaine levels in the serum samples at certain intervals, it was observed that all the values were below 5.50 $\mu\text{g/mL}$, which is within the safe limit and below

Table 4

Return of Sensation Between Therapeutic and Control Groups Following Infiltration of 1% Lidocaine in 1:100,000 Adrenaline (WALANT) and 2% Lidocaine Alone

Variables	Therapeutic	Control	<i>P</i> value*
Return of sensation (h)			
Mean \pm SD	5.11 \pm 0.66	3.00 \pm 0.00	<.001†
Median (IQR)	5.00 (1.00)	3.00‡	

IQR, interquartile range.

* Comparison of mean hours for return of sensation between the therapeutic and control groups was done using the Mann-Whitney U test.

† Indicates significant statistical result.

‡ Return of sensation is constant among all the participants. Therefore, IQR was omitted.

the mild toxicity level. Furthermore, the data showed that the serum lidocaine level was affected by both body weight and the dose of lidocaine injected. Participants with a higher body weight had a lower serum lidocaine level when a fixed dose of lidocaine was injected.

Our results also showed that there was a significant effect of serum lidocaine level in response to time. The mean level of serum lidocaine showed a significant reduction of more than 50.0% (72.6% in the therapeutic group and 68.9% in the control group) from 5 minutes (mean, 4.09 $\mu\text{g/mL}$ in the therapeutic group and 2.99 $\mu\text{g/mL}$ in the control group) to 10 minutes (mean, 1.12 $\mu\text{g/mL}$ in the therapeutic group and 0.93 $\mu\text{g/mL}$ in the control group) after lidocaine administration, indicating that the risk of lidocaine toxicity was significantly reduced after 10 minutes and continued to substantially reduce until only trace amounts were present at 6 hours after administration (mean, 0.13 $\mu\text{g/mL}$ in the therapeutic group and 0.10 $\mu\text{g/mL}$ in the control group). Our data also show that at all the predetermined time intervals, the serum lidocaine levels for both the groups were below the mild toxicity level of 6.00 $\mu\text{g/mL}$. This provides evidence that the current practice and recommended dosage of lidocaine and adrenaline in WALANT are clinically and biochemically safe.

The limitations of our study were that a small number of patients were recruited and that this was a single-center study. The uneven distribution of the number of patients in each arm could be a potential bias. The procedures were also performed by different surgeons, which could have introduced a bias in the results. However, despite the limitations, we believe that the current study is a stepping stone to further larger-scale clinical trials to prove the safety profile of lidocaine and adrenaline in WALANT surgery.

Acknowledgments

We would like to acknowledge Nur Fathiah Abdul Sani, Siti Nor Asyikin Zakaria, and Ahmad Fais Abdul Rashid for their help in technical aspect of blood sample analysis.

References

1. Gunasagaran J, Sean ES, Shivdas S, Amir S, Ahmad TS. Perceived comfort during minor hand surgeries with wide awake local anaesthesia no tourniquet (WALANT) versus local anaesthesia (LA)/tourniquet. *J Orthop Surg*. 2017;25(3):2309499017739499.
2. Ralte P, Selvan D, Morapudi S, Kumar G, Waseem M. Haemostasis in open carpal tunnel release: tourniquet vs local anaesthetic and adrenaline. *Open Orthop J*. 2010;4(1):234–236.
3. Braithwaite BD, Robinson GJ, Burge PD. Haemostasis during carpal tunnel release under local anaesthesia: a controlled comparison of a tourniquet and adrenaline infiltration. *J Hand Surg Br*. 1993;18(2):184–186.
4. Ahmad AA, Yi LM, Ahmad AR. Plating of distal radius fracture using the wide-awake anesthesia technique. *J Hand Surg Am*. 2018;43(11):1045.e1–1045.e5.
5. Huang YC, Hsu CJ, Renn JH, et al. WALANT for distal radius fracture: open reduction with plating fixation via wide-awake local anesthesia with no tourniquet. *J Orthop Surg Res*. 2018;13(1):1–11.
6. Abd Hamid MH, Abdullah S, Ahmad AA, et al. A randomized controlled trial comparing wide-awake local anesthesia with no tourniquet (WALANT) to general anesthesia in plating of distal radius fractures with pain and anxiety level perception. *Cureus*. 2021;13(1).
7. El-Boghdady K, Pawa A, Chin KJ. Local anesthetic systemic toxicity: current perspectives. *Local Reg Anesth*. 2018;11:35–44.
8. Weinberg L, Peake B, Tan C, Nikfarjam M. Pharmacokinetics and pharmacodynamics of lignocaine: a review. *World J Anesthesiol*. 2015;4(2):17–29.
9. Bill TJ, Clayman MA, Morgan RF, Gampper TJ. Lidocaine metabolism pathophysiology, drug interactions, and surgical implications. *Aesthet Surg J*. 2004;24(4):307–311.
10. Fitzcharles-Bowe C, Denkler K, Lalonde D. Finger injection with high-dose (1:1,000) epinephrine: does it cause finger necrosis and should it be treated? *Hand*. 2007;2(1):5–11.
11. Lalonde D, Bell M, Benoit P, Sparkes G, Denkler K, Chang P. A multicenter prospective study of 3,110 consecutive cases of elective epinephrine use in the fingers and hand: the Dalhousie Project clinical phase. *J Hand Surg Am*. 2005;30(5):1061–1067.
12. Lewin NA, Nelson LH. Chapter 61: Antidysrhythmics. In: Flomenbaum N, Goldfrank LR, Hoffman RL, Howland MD, Lewin NA, Nelson LH, eds. *Goldfrank's Toxicologic Emergencies*. 8th ed. McGraw-Hill; 2006:963–964.
13. Thomson PD, Melmon KL, Richardson JA, et al. Lidocaine pharmacokinetics in advanced heart failure, liver disease, and renal failure in humans. *Ann Intern Med*. 1973;78(4):499–508.
14. Collinsworth KA, Kalman SM, Harrison DC. The clinical pharmacology of lidocaine as an antiarrhythmic drug. *Circulation*. 1974;50(6):1217–1230.
15. Neal JM, Neal EJ, Weinberg GL. American Society of regional anesthesia and pain medicine local anesthetic systemic toxicity checklist: 2020 version. *Reg Anesth Pain Med*. 2021;46(1):81–82.
16. Chu R, Umukoro N, Greer T, et al. Intravenous lidocaine infusion for the management of early postoperative pain: a comprehensive review of controlled trials. *Psychopharmacol Bull*. 2020;50(4 suppl 1):216–259.
17. Foldes FF, Molloy R, McNall PG, Koukal LR. Comparison of toxicity of intravenously given local anesthetic agents in man. *JAMA*. 1960;172(14):1493–1498.
18. Brosh-Nissimov T, Ingbir M, Weintal I, Fried M, Porat R. Central nervous system toxicity following topical skin application of lidocaine. *Eur J Clin Pharmacol*. 2004;60(9):683–684.
19. Estes III NA, Manolis AS, Greenblatt DJ, Garan H, Ruskin JN. Therapeutic serum lidocaine and metabolite concentrations in patients undergoing electrophysiologic study after discontinuation of intravenous lidocaine infusion. *Am Heart J*. 1989;117(5):1060–1064.
20. Lalonde DH, Wong A. Dosage of local anesthesia in wide awake hand surgery. *J Hand Surg Am*. 2013;38(10):2025–2028.
21. Burk III RW, Guzman-Stein G, Vasconez LO. Lidocaine and epinephrine levels in tumescent technique liposuction. *Plast Reconstr Surg*. 1996;97(7):1379–1384.