LOCAL ANAESTHETIC SYSTEMIC TOXICITY AWARENESS AMONG CLINICAL PRACTITIONERS

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ABSTRACT

Objective: To assess comprehension of local anaesthetic systemic toxicity among clinical practitioners.
Study Design: Cross-sectional study.
Place and Duration of Study: Tertiary Care Institute, from Dec 2019 to Mar 2020.
Methodology: Methodology constituted of a web-based questionnaire. A pilot study carried out at 15-20 participants for questionnaire validation and reviewed by independent experts for face validity, a final questionnaire comprised of 10 multiple-choice questions in addition to demographic profile.
Results: A total of 950 participants participated in the study and data was extracted from their responses. Out of 738 (77.8%) participants declared that they are unaware of local anaesthetic systemic toxicity complication, 26 (2.7%) encountered local anaesthetic systemic toxicity and 185 (19.5%) never experienced. Ninety (9.5%) were aware of the availability and utilization of 'Lipid Emulsion' therapy to treat 'Local Anaesthetic Systemic Toxicity' (LAST).
Conclusion: Although clinicians have significant awareness level regarding local anaesthetic toxicity but unfortunately compliance with management of this life-threatening complication is deficient.

Keywords: Aspiration, Local anaesthetics, Lipid emulsion.

How to Cite This Article: *Abbas S, Akram A, Abbas B, Fayyaz M, Mehmood B, Hayat U. Local Anaesthetic Systemic Toxicity Awareness among Clinical Practitioners. Pak Armed Forces Med J 2021; 71(5): 1642-1646. doi: https://doi.org/10.51253/pafmj.v71i5.4035*

INTRODUCTION

Local anaesthetics are one of the most commonly employed drugs in clinical practice particularly in surgery and allied domains. Surgeons used local anaesthetic almost >100 years ago when cocaine given as injectable for extraction of wisdom tooth. Addictive properties and mortality associated with cocaine led to the search and development of safer options such as lignocaine. Local anaesthetics administered with various techniques (topical, infiltration, regional) to act on specific nerve pathways for motor and pain sensation block[1].

Broadly classified as esters (cocaine, benzocaine, procaine etc.) and amides (lignocaine, bupivacaine, ropivacaine etc.) or based on duration of action (short, intermediate or long-acting). Furthermore available as a combination with a vasoconstrictor such as epinephrine to enhance duration of action and hemostasis[2].

On account of the rapid anaesthetic effect, amides gained more popularity when compared with esters due to the propensity for allergic reactions. Local anaesthetics primarily act by inhibition sodium influx at voltage-gated sodium channels, therefore, causing interruption of action potential consequently lead to inhibition of signal conduction, therefore, producing neuronal blockade[3].

Local anaesthetics considered safe generally, when proper technique with meticulous dose calculation adopted. However, with an inappropriate approach, they can cause local and systemic adverse effects. Common local manifestations include infection, hematoma, paresthesias and allergic reactions[4,5].

Local anaesthetic systemic toxicity (LAST) is although rare with an incidence of 1 in 1000 patients but potential fatality attributing greater mortality and morbidity of surgical patients make this complication a point of concern. Type, site, technique and dose injected are factors affecting the risk of developing local anaesthetic systemic toxicity. Overdosing can lead to hypotension, bradycardia, apnea, hypoxia, seizures. Biotransformation and elimination carried out by liver and kidneys respectively, therefore, can impair hepatic and renal profile[6,7]. Onset of local anaesthetic systemic toxicity symptoms is between 1-5 minutes (typically after 60 seconds). Earliest presentation is circumoral numbness, metallic taste, disorientation and dizziness followed by seizures, respiratory depression, loss of consciousness, arrhythmias, circulatory collapse eventually cardiac arrest and death[8,9]. Meticulous monitoring by

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Received: 26 Mar 2020; revision received: 13 Jul 2020; accepted: 14 Jul 2020

the surgical team is crucial to management. Immediate management includes, cease local anaesthetic administration, airway maintenance along with 100% oxygen and intravenous access to institute pharmacotherapy for seizures and cardiovascular support. Protocol for advanced cardiac support instituted on the advent of cardiac arrest. Lipid emulsion should be administered immediately as per AABGI (Association of Anesthetists of Great Britain and Ireland) safety guidelines as it can produce dramatic results in patient resuscitation in addition to Cardiopulmonary resuscitation as lipid emulsion therapy may take up to an hour for notable effects[10].

Research-based on the hypothesis that despite widespread local anaesthetics utilization and clinicians are essentially equipped with basic knowledge of the subject, but the grip on life-threatening complication Local Anaesthetic Systemic Toxicity manifestations and management is deficient.

METHODOLOGY

This cross-sectional study was carried out at Tertiary Care Institute from December 2019 to March 2020, approval was taken from the ethics research committee of the Institute (ERC Number–207/ERC).

Methodology constituted of a web-based questionnaire devised by relevant studies on the subject. A pilot study carried out at 15-20 participants for questionnaire validation and reviewed by independent experts for face validity. The questionnaire comprised of 10 structured multiple-choice questions (close-ended) with a variable number of stems [Neither Likert nor Dichotomous Scale adopted] in addition to information on the demographic and professional profile. There is no statistical method that can be employed to validate the questionnaire in this case. After reliability and authenticity establishment via cross-validation with the pilot study and experts overview web-based survey launched among participants to achieve a significant number of responses within a stipulated time. All questions aimed to detect knowledge about Local Anaesthetic Systemic Toxicity. Feedback received from (100%) participants. Minimum sample size calculated to be 166 (open epi calculator), hypothesized % frequency of outcome factor in the population 87.7% ± 5, with 5% margin of error and 95% confidence level where the prevalence of local anaesthetic toxicity awareness was considered to be 87.7% as reported by as per by Lopez *et al*[11].

A non-probability consecutive sampling technique was employed and the questionnaire was distributed among (n=950) participants.

Inclusion Criteria: Practitioners in the field of anaesthesia and surgery (general surgery, ophthalmology, gynaecology & obstetrics), dermatology and dentistry were incorporated in the study.

Exclusion Criteria: Clinicians in medicine (including allied specialities), medical students and house officers were excluded.

Questions were included to analyze demographic profile such as age, gender, profession, work experience. Frequency of local anaesthetic utilization per month and type of local anaesthetic most commonly used. Awareness regarding local anaesthetic toxicity and whether participants ever encountered local anaesthetic toxicity. We determined precautions taken by clinicians to prevent adverse effects and compliance with early and late signs of local anaesthetic systemic toxicity. We inquired about the treatment approach if any of such adverse event occurred and adherence with guidelines of lipid emulsion therapy along with its availability in the immediate vicinity.

Data was entered and analysed using SPSS-23. The descriptive statistics of continuous variables were presented as mean and standard deviation, while for categorical data frequencies and percentages were used. Categorical grouped data was analyzed by either chi-square or Fischer-exact test as applicable. *p*-value of ≤0.05 was considered to be statistically significant.

RESULTS

Total 950 participants enrolled with a mean age 32.4 ± 4.3 and age range 25-44 years were enrolled. Out of 410 (43.2%) participants had experienced less than 5 years, 290 (30.5%) had between 5-10 years, 250 (26.3%) had experience of 10-15 years. We assessed the frequency of local anaesthetic use on monthly basis, 410 (43.2%) stated that they used local anaesthetic for less than 5 times a month, 290 (30.5%) used 5-10 times per month, 250 (26.3%) indicated 10-15 times per month and 470 (49.5%) used local anaesthetic in their procedures >15 times a month. Frequently used local anaesthetics by participants were lignocaine plain 368 (36.7%), Lignocaine with Adrenaline 510 (53.7%), Bupivacaine 72 (7.6%). In 738 (77.8%) participants declared that they are not aware of this complication, 26 (2.7%) encountered local anaesthetic systemic toxicity and 185 (19.5%) never had any such experience (Table-I). Only 88 (9.3%) were aware of the availability and utilization

Table-I: Summary of results co related with experience.

Parameters		Experience			*p*-value
		<5 years	5-10 years	10-15 years	
How Frequently LA used	<5 times a month	-	180 (62.1%)	60 (24%)	<0.001*
	5-10 times a month	50 (12.2%)	-	70 (28%)	
	10-15 times a month	-	-	120 (48%)	
	>15 times a month	360 (87.8%)	110 (37.9%)	-	
Most Frequent LA Used	Lignocaine Plain	28 (6.8%)	140 (48.3%)	200 (80%)	<0.001*
	Lignocaine with Adrenaline	87 (8%)	150 (51.7%)	-	
	Bupivacaine	22 (5.4%)	-	50 (20%)	
Have you ever Encountered LAST	Not Aware of the Complication	401 (97.8%)	264 (91%)	74 (29.6%)	<0.001*
	Not Encountered	4 (1%)	19 (6.6%)	162 (64.8%)	
	Encountered	5 (1.2%)	7 (2.4%)	14 (5.6%)	
What will be Management of LAST	CPR	33 (8%)	255 (87.9%)	9 (3.6%)	<0.001*
	Symptomatic	353 (86.1%)	-	40 (16%)	
	Adrenaline Therapy	1 (0.2%)	20 (6.9%)	151 (60.4%)	
	Lipid Emulsion Therapy	23 (5.6%)	15 (5.2%)	50 (20%)	

**Significant p-value; p-value was calculated by applying Fischer-exact test*

of 'Lipid Emulsion' therapy to treat 'Local Anesthetic Systemic Toxicity' (LAST) 860 (90.5%). Three hundred (31.6%), 60 (6.3%), 230 (24.2%) and 360 (37.9%) believed that aspiration, test dose, monitoring and meticulous dose calculation respectively can prevent 'Local Anesthetic Systemic Toxicity' (LAST). Regarding Early Signs of local anaesthetic toxicity responses of participants were, circumoral numbness or tongue numbness 240

Table-II: Local anaesthetic toxicity clinical presentation.

Parameters		Frequency (n=950) (%)
Early Signs	Circumoral Numbness or Tongue Numbness	240 (25.3%)
	Hypotension	520 (54.7%)
	Allergy	120 (12.6%)
	Anaphylaxis	70 (7.4%)
Complications	Cardiac Arrest	414 (43.6%)
	Seizures	346 (36.4%)
	Hepatoxicity	190 (20%)

(25.3%), hypotension 520 (54.7%), allergy 120 (12.6%) and anaphylaxis 70 (7.4%). Whereas upon inquiry of complications cardiac Arrest 414 (43.6%), seizures 346 (36.4%) and hepatoxicity 190 (20%) were submitted responses (Table-II). Response on management extracted to be cardiopulmonary resuscitation (CPR) 297 (31.3%), symptomatic 393 (41.4%), adrenaline therapy 172 (18.1%) and lipid emulsion therapy 88 (9.3%) (Figure).

DISCUSSION

Data analysis of the study demonstrated that adequate comprehension of local anaesthetics dosage and adverse effects was prevalent among participants as awareness turnover was (92.68%). However, an extreme paucity of knowledge was observed with management of LAST and Lipid emulsion therapy 90 (9.5%).

Lopez *et al*, evaluated operation room staff knowledge and comprehension regarding local anaesthetics toxicity based on 81 questionnaires. Most frequently used local anaesthetics were lidocaine (91.4%), as in our case lidocaine (90%). Local anaesthetic frequency used was monthly 5 times but less than weekly 5 times (35.8%). Toxic dose for lidocaine was known by 21% and for bupivacaine by 46.9%. Awareness level of local anaesthetic toxicity signs 87.7% consistent with our results of 92.7%. Lipid emulsion use for toxicity treatment awareness was 59.3% but 14.8% treatment strategy as in our case only 10% had compliance with management[11].

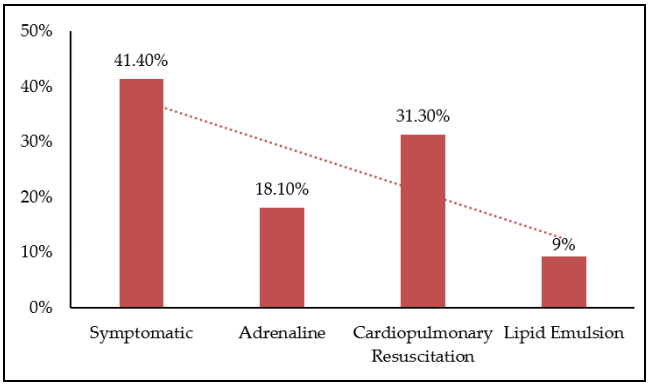

Figure: Management of local anesthetic systemic toxicity.

Karasu *et al*, in there study assessed knowledge of research assistants primarily from anesthesiology of local anaesthetics and their toxicity. They found out that (87%) of individuals never encountered local anaesthetic systemic toxicity as in our results (75.6%) participants never came across this complication, (67%) were not aware of management with lipid emulsion therapy. Although lipid emulsion was available at

their hospital still only (8%) of participants, whereas (10%) respondents in our research knew about it[12].

Sagir *et al*, conducted a cross-sectional questionnaire-based survey in their hospital multi-speciality postgraduate residents to assess awareness of local anaesthetic systemic toxicity. They included 200 participants in their study, however only (2%) knew about lipid emulsion therapy in local anaesthetic systemic toxicity. (93%) of participants were unaware of toxic doses of anaesthetics such as bupivacaine. (27%) and 25% of responders correctly mentioned the toxic doses of lidocaine and lidocaine with adrenaline, respectively. (70%) performed a negative aspiration of blood before administration, (27%) occasionally and rest of (3%) never aspirated. Level of local anaesthetic toxicity awareness was (70%) and (81%) knew signs and symptoms of cardiotoxicity. We found their results parallel to our evaluation[13].

Oksuz *et al*, studied about dentist's knowledge of lipid treatment of local anaesthetic systemic toxicity. As per their results (86%) never encountered local anaesthetic systemic toxicity and (67%) had no clue about lipid emulsion therapy. Only (1.5%) knew how to administer lipid emulsion in case of local anaesthetic toxicity whereas (67.3%) were not aware, (21.3%) just heard of therapy and (9.8%) read an article but did not have knowledge of guidelines. Results interpreted that (86.66%) respondents never experienced LAST. (13.33%) participants had seen LAST but managed with other treatment modalities instead of lipid emulsion[14].

Aykut *et al*, evaluated knowledge of ophthalmologists on local anaesthetic toxicity and intravenous lipid treatment via questionnaire-based study. They included a total of 104 participants. Out of them (62.5%) participants never encountered local anaesthetic systemic toxicity and only (0.9%) of them used lipid emulsion to treat the complication. (72%) of them believed that proper monitoring can prevent local anaesthetic systemic toxicity. (76%) of the participants used local anaesthetic every day, only (56.7%) had been trained on this subject. Bupivacaine was the most preferred local anaesthetic contrary to our results where bupivacaine use was (10%) only. (97.1%) did not use a test dose before administration. (76%) reported allergy whereas (68.3%) reported hypotension among adverse findings. (57.4%) and (56.4%) were feedbacks for cardiac arrest and hepatotoxicity respectively. The most of response for prevention (72.4%) said monitoring and (58.2%) stated the use of appropriate doses. (72.4%) opted for symptomatic treatment whereas (58.8%) selected cardiopulmonary resuscitation and antihistamine treatment. Of the ophthalmologists in the study, 62.5% had never encountered LAST[15]. Duraisamy *et al*, conducted a telecom survey across 34 anaesthetists. (58%) accurately identified the maximum safe dose whereas (41%) for a combination of local anaesthetics. Only (44%) of the respondents knew the dose of 20% lipid emulsion[16].

Kaira *et al*, conducted a survey across dental participants concerning local anaesthetics. (71.4%) were general dental practitioners whereas (28.5%) were dental specialists. (69%) of the participants were unaware of the maximum safe dose. (49%) respondents never performed a negative blood aspiration however (38%) performed aspiration before administration. (84%) dentists had deficient knowledge of dose calculation and (31%) came across complications[17].

Walsh *et al*, analyzed the comprehension of dermatologists regarding local anaesthetics. (90%) of respondents had good command on signs and symptoms of LAST recognizing paresthesia of the tongue, lips, or mouth; metallic taste; light-headedness; tinnitus; slurred speech; muscle twitching; convulsions; cardiovascular instability; and respiratory arrest. Only (21.7%) had cognition with intravenous lipid emulsion[18].

Gadegaard *et al*, conducted an interview-based survey across 38 hospitals via telecom which included 34 participants. (65%) were aware of intralipid emulsion therapy as a treatment option in local anaesthetics toxicity. (41%) confirmed availability with their department/hospital. (24%) stated that their department had local guidelines on lipid rescue therapy[19].

Local anaesthetic systemic toxicity is a life-threatening and lethal intricacy, regardless of common employment of local anaesthetics and adequate awareness level clinicians are unaware of management of this preventable reason of mortality and morbidity. It is tremendously recommended to raise awareness and comprehension concerning local anaesthetic systemic toxicity fundamental harmful signs, the pathophysiology of the condition and prompt management. Clinicians ought to be encouraged to report the LAST occurrence at lipid rescue organization.

CONCLUSION

Although clinicians have significant discernment, level regarding local anaesthetic toxicity but predestinated compliance with management of this life-threatening complication is meagre.

Conflict of Interest: None.

Authors' Contribution

SA: Conception, manuscript drafting, AA: Supervision, BA: Conception, data collection and analysis, BM: Conception, data collection and analysis, UH: Conception, data collection and analysis.

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