Knowledge and practices of local anesthetic systemic toxicity among doctors in Sri Lanka

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Abstract

Background & Objective: Local anesthetic systemic toxicity (LAST) could be potentially life threatening. This study describes the current knowledge and practices of the use of local anesthetics (LA) among the doctors of Sri Lanka and their ability to identify and manage an event of LAST in their clinical practice.

Methodology: A descriptive cross-sectional study was conducted among doctors in Sri Lanka using an online self-administered questionnaire, based on Association of Anesthetists of Great Britain and Ireland (AAGBI) Guidelines (2010). Descriptive statistics were analyzed by cross-tabulations and presented as numbers and percentages using IBM-SPSS 25.

Results: The response rate was 60% out of 600 doctors. A majority of the respondents were males (58%); while 45% of all of the respondents were anesthetists. Ultrasonography was used by 47.4% during LA administration. The majority (74%) of the respondents calculated the dose of LA on the basis of total body weight. Around 50% of respondents identified bupivacaine as the most cardiotoxic. 77% of them utilized some form of monitoring and were knowledgeable on identification, prevention and initial management of the LAST. Approximately 45% identified Intralipid® 20% emulsion (ILE) as the definitive treatment of LAST; out of which, 66.8% knew the correct dose, 77.2% and 26.5% knew the availability and site of storage, respectively.

Conclusion: The basic knowledge on LAST was satisfactory among the respondents. Significant difference in knowledge on maximum safe dose of LA, the use of Intralipid® in established LAST, its dosage and the availability, was identified between anesthetists and non-anesthetists, as well as between the postgraduate trainees and the rest of the doctors. Overall, significant lapses were noted for the use of total body weight for dose calculation, use of ultrasound during LA administration and dosage, availability and storage of the definitive therapy – Intralipid®.

Key words: Local anesthetic systemic toxicity; LAST; Cardiac toxicity; Intralipid®

Abbreviations: LAST - Local anesthetic systemic toxicity; PG – Postgraduate trainees; LA - Local anesthetic agents; ERAS - Enhanced recovery after surgery; ILE - Intralipid® 20% emulsion


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1. Introduction

Local anesthetic systemic toxicity (LAST) is quite a rare phenomenon, perhaps due to being under diagnosed and underreported, yet when it does occur, it can result in serious morbidity and mortality. Existing literature emphasizes the importance of being aware about the potential risks of the LAST to formulate standard practices to recognize and promptly manage it to reduce the adverse results.

We reviewed the literature on factors contributing to LAST and management protocols and studied the knowledge and practices among the doctors in our study population regarding identification, prevention and management of the LAST.

2. Methodology

The study was conducted as a descriptive cross-sectional study among middle and intermediate-grade doctors in Sri Lanka. Considering a population of 20,000 practicing doctors was eligible for our study, and the level of awareness about the LAST in an earlier regional study among doctors was 30% (outcome factor of 30% selected), at 7.5% confidence limit and 95% confidence interval with a design effect (2.0) for cluster sampling, a sample size of 285 was calculated. Following attrition for non-responders, the minimum sample size required was calculated to be 342. A self-administered questionnaire was prepared following review of literature and the Association of Anesthetists of Great Britain and Ireland (AAGBI) guideline on LAST (2010). Face and content validity and appropriateness to the culture were assessed and certified by an expert panel. A single-stage cluster sampling method was utilized. Hospitals were chosen randomly. Following establishing remote verified individual communications (via email or social media (WhatsApp/Viber/Facebook) the questionnaire was distributed. The data analysis was done with IBM SPSS (version 25) by applying relevant statistical tests. A p < 0.05 was considered as statistically significant.

Ethical approval was obtained from the Ethics Review Committee (ERC) of the Sri Lanka Medical Association. (ERC/20/023).

3. Results

Out of 600 participants, 360 responded (response rate 60%); 58.3% were males (210), and the median age was 32 y (Q1=29.7, Q3=34.4, IQR=4.7).

Half of the participants had an experience of 2-5 y as doctors. About 30% were postgraduate trainees from different specialties. Distribution of responders according to subspecialty is shown in Table 1.

### Table 1: Distribution of responders according to subspecialty

<table>
<thead>
<tr>
<th>Subspecialty</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesia/ ICU</td>
<td>160</td>
<td>44.4</td>
</tr>
<tr>
<td>Emergency Medicine</td>
<td>20</td>
<td>5.6</td>
</tr>
<tr>
<td>General surgery</td>
<td>36</td>
<td>10.0</td>
</tr>
<tr>
<td>Medicine</td>
<td>39</td>
<td>10.8</td>
</tr>
<tr>
<td>Gynecology and Obstetrics</td>
<td>20</td>
<td>5.6</td>
</tr>
<tr>
<td>Paediatrics</td>
<td>12</td>
<td>3.3</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>Oral and maxillofacial surgery</td>
<td>7</td>
<td>1.9</td>
</tr>
<tr>
<td>Orthopedics</td>
<td>6</td>
<td>1.7</td>
</tr>
<tr>
<td>Radiology</td>
<td>7</td>
<td>1.9</td>
</tr>
<tr>
<td>Others (\d)</td>
<td>48</td>
<td>13.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>360</td>
<td>100</td>
</tr>
</tbody>
</table>

\(\d\) ENT, plastic surgery, urology, vascular surgery etc.

3.1. Practices of use of three local anesthetic agents (LA)

The frequency and route of usage of the three LA; lignocaine, bupivacaine and prilocaine were studied. Plain Lignocaine and Prilocaine were the most commonly used (Table 2).

3.1.1. Route: Subcutaneous infiltration was the commonest route (39.7%) followed by regional nerve blocks (39.7%) and epidurals (13%).

3.1.2. Usage of ultrasound: About 53% (191) never used ultrasound during LA administration (Figure 1). Out of these, 20% (38) were anesthetists. Only 20% (73) responded as using ultrasound ‘always’ or ‘frequently’. Majority of this category were anesthetists [63 (86%)].

3.1.3. Monitoring: The preferred mode of monitoring was found to be the pulse oximetry during LA (n = 234 (65%), 120 (33.3%) utilized pulse oximetry, ECG and Non-invasive blood pressure, and 51 (14.2%) used at least pulse-oximetry. Whereas 86 (23.9%) did not use any monitoring.

3.1.4. Test dose: A test dose of LA was administered by 90 (25%) (95% CI 20.4-29.6) of the respondents.

For dose calculations 154 (42.7%) considered the age factor, 168 (46.6%) took the comorbidities into account and 97 (26.9%) ideal or lean body weight. There were no statistically significant differences identified between...
Knowledge on safe doses was significantly different between PG trainees (PG) and non PG trainees (NG), and anesthetists (A) and non- anesthetists (NA) (p < 0.05) (Table 3 & 4).

Roughly, 47.8% (172) recognized bupivacaine as the most cardiotoxic. There was a statistically significant difference between A and NA (p < 0.001) and E vs. NE (p = 0.0003). 336 (93.3%) had heard about LAST and 81 (22.5%) had witnessed an episode. Approximately 95% (95% CI 92.7-97.3) or more had knowledge on cardiovascular (n = 352), and neurological features (n = 345) of the LAST. Hypertension, and tachycardia were the clinical features quoted by 81 (22.5%) and 165 (45.8%) of the participants. Comparatively higher knowledge was elicited among A vs. NA group (p = 0.05) and PG vs. NPG group (p = 0.01).

### Table 3: Association of the knowledge of safe doses among PG trainees (PG) and non–PG trainees (NPG)

<table>
<thead>
<tr>
<th>Agent</th>
<th>PG (Correct %)</th>
<th>NPG (Correct %)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain lignocaine</td>
<td>75.0</td>
<td>51.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Lignocaine with Adrenaline</td>
<td>70.2</td>
<td>46.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Plain Bupivacaine</td>
<td>67.3</td>
<td>42.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Prilocaine</td>
<td>17.3</td>
<td>6.6</td>
<td>0.002</td>
</tr>
</tbody>
</table>

The knowledge on steps in preventing LAST revealed that, 271 (75.3%) chose monitoring during LA, 282 (78.33%) aspiration and 234 (65%) ultrasound use. Around 153 (42.5%) accepted that the addition of adrenaline to the LA is useful. More anesthetists recognized the latter (p = 0.00007) compared to the non-anesthetists group. Similar statistical significance (p = 0.0005) was identified between PG and NPG categories.

Approximately 300 (83%) (95% CI 79.0-86.9) respondents identified intravenous fluid and oxygen as part of the management of an established LAST while 205 (57%) opted for prolonged cardiopulmonary resuscitation. Only 53 (14.7%) considered cardiopulmonary bypass as part of the therapy; 55 (15%) respondents considered use of intravenous propofol.

Intravenous ILE as the definitive therapy for the LAST was recognized by 162 (45%) (95% CI 39.7-50.2) of the respondents. A vs. NA and PG vs. NPG groups yielded a p-value of 0.0001, and E vs. NE it was 0.015 which were significant statistically. 107 (66%) (95% CI 61.01- 70.9) of this group identified the correct dose of the ILE where knowledge among A was statistically significantly more than NA (p = 0.001). Approximately 54 (33.3%) respondents from this subcategory stated that ILE was not available in their institution. The respondents who were knowledgeable on the availability (PG vs. NPG, p = 0.012) (108, 66.6%), 43 (26.5%) knew where it was stored. A statistically significant difference (p = 0.012) was observed between PG vs. NPG subcategories.

### 4. Discussion

Local anesthetic agents are frequently used in most subspecialties of medicine. The growing interest in regional nerve blocks, enhanced recovery after surgery (ERAS) protocols and multimodal analgesic regimens, have led to an increase in the usage
cardiovascular symptoms,\textsuperscript{10} which include both tachyarrhythmias and bradyarrhythmias, which could progress to cardiac arrest.\textsuperscript{8} However, 40\% of the patients can present atypically, where symptoms are either delayed or cardiovascular symptoms occur without neurological manifestations.\textsuperscript{11}

Our study demonstrates that one-quarter (24\%) of the operators did not use any monitoring during LA administration. Monitoring electrocardiography (ECG), pulse oximetry and blood pressure are important in detecting LAST early\textsuperscript{3} and should be continued for recurrent and late-onset toxicity, especially with continuous infusions.\textsuperscript{1, 12}

A higher percentage (25\%) of participants used a test dose. Conversely, a cross-sectional study among emergency physicians in Turkey,\textsuperscript{13} demonstrated its use by only 5\% of the operators. The ophthalmologists in Turkey not using a test dose were 97.1\%.\textsuperscript{14, 15}

Dose calculations based on body weight vary according to ideal body weight,\textsuperscript{16} or lean body weight.\textsuperscript{16} Total body weight can overestimate the total dose in obese and pregnant patients, and ideal or lean body weight is more appropriate.\textsuperscript{12} A quarter of our respondents used ideal or lean body weight. The patients with organ dysfunction are at a higher risk of LAST thus doses should be titrated.\textsuperscript{11} Comorbidities were taken into consideration by just under 50\% of the respondents.

A significant lapse of knowledge was noted with regard to maximum safe dose. Only half of the respondents identified bupivacaine as the most cardiotoxic. Seven respondents considered intravenous use of bupivacaine to be catastrophic and must be avoided at all times.

Airway management, oxygenation, ventilation and control of seizures are essential components of supportive management in established LAST.\textsuperscript{3, 8} ILE and management protocols should be readily available where LA is utilized.\textsuperscript{1, 8}

Addition of adrenaline to LA was the least opted choice. The physiological response to adrenaline (increments of heart rate by 0 beats/min and blood pressure by 10-15 mmHg) could be an important marker of intravascular injection, as aspiration test could be falsely negative in
about 2%. An overall comparative lack of knowledge on the prodromal features of LAST was evident. Given that the typical pattern of toxicity may not be seen in 40% of the cases, the detection of prodromal features could be decisive.

Ultrasound use minimizes LAST by real-time visualization and use of lower volumes with evidence of 65% reduction compared to nerve stimulation alone. Even though, the majority of the participants in our study considered ultrasound use as beneficial, its practical use was much less. Almost 90% participants using ultrasound ‘Always’ or ‘Frequently’, were anesthetists, who performed regional nerve blocks.

The basic management of an established LAST was known by a significantly higher number of respondents with preference for fluids, oxygen, seizure management and prolonged cardiopulmonary resuscitation.

The definitive therapy, ILE was relatively less known by the respondents while few chose propofol. ILE should not be substituted by propofol due to relatively low lipid content, potential cardiovascular compromise and the need of larger volumes. A study by Edwards et al. demonstrated an overall deficit in knowledge on LAST (including ILE therapy) in a UK Hospital maternity unit. However, teaching programs led to a significant improvement in the knowledge. A Danish study conducted among anesthetists, revealed that around 50% knew about the lipid therapy but were not aware how to acquire ILE. In a cross-sectional study in Turkey, 42% of the emergency physicians identified ILE dosage correctly. LAST being an acute emergency, quick access to ILE is undoubtedly required.

A significant statistical differences in knowledge were found between postgraduate trainees vs. non-postgraduate trainees, anesthetists vs. non-anesthetists and experienced (>10 y) vs. less experienced, regarding maximum safe dosage, cardiotoxicity of bupivacaine, prodromal cardiovascular features and addition of adrenaline and performance of a test dose. ILE as the drug of choice, dosage, availability and the site of storage were known with by anesthetists and postgraduate trainees as compared to non-anesthetists and non-postgraduate trainees.

5. Limitations

The response rate was relatively low for the study. The correct answers were provided to the respondents, however, the prevailing COVID-19 pandemic hindered the completion of audit cycle, which could have been much useful.

6. Conclusion

The basic knowledge on LAST was satisfactory among the respondents. Significant lapses were identified with regard to use of total body weight for dose calculations, use of ultrasound during LA administration and dosage and importantly availability and site of storage of the definitive therapy, Intralipid®.

7. Recommendations

The authors suggest the following:

- Continuing medical education programs on LAST to be conducted particularly for non-anesthetic doctors, doctors who are not engaged in postgraduate studies and who have completed a certain number of years in service (e.g. 5 y)
- Inclusion of LAST to the curriculum of the non-anesthetic postgraduate trainees.
- LAST management protocols to be displayed at locations of LA use. (e.g., operating rooms, OPD emergency rooms, radiology and dental suites, and any other place of high volume LA use.)
- Intralipid® to be made available in places where LA is used / daily checklists / stocks to be displayed.
- Prompt reporting and auditing of adverse events related to LA.

8. Authors’ contribution

BM conceived the concept for the study. BM, SN, NS did the literature review; developed the proposal for ethical approval; collected data. BM, SN, NS and WJ designed the study. All authors involved in data analysis, compiling, and reviewing the final manuscript.

9. Acknowledgment

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10. Conflict of interests

No conflicts of interest were declared by the authors. Study was self-financed by the authors No external funding was received.
11. References


