



Knowledge of the Research Assistants Regarding Local Anaesthetics and Toxicity

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Objective: Cardiovascular system depression, respiratory arrest, coma, convulsions, loss of consciousness, muscle twitching, blurred vision, vertigo, dizziness and numbness of the tongue can be seen in local anaesthetic toxicity. Treatment includes 20% lipid solutions, airway control, symptomatic treatment for arrhythmia and convulsions. The aim of this study is to present the knowledge of research assistants, who used local anaesthetics in daily practice, regarding these medications and toxicity treatment and to raise awareness.

Methods: The questionnaire comprising 20 questions was administered to 115 research assistants who worked at different specialities in our hospital.

Results: One hundred and two (88.6%) research assistants answered the questionnaire. Participants' mean age was 28.93 years. Most of them were from the Emergency Department (15.7%). A total of 40.6% of participants worked for 2–5 years at their departments. Local anaesthetics were used in daily practice for 44.4% of them, but 70.3% of them had not been educated about local anaesthetics. Research assistants from anaesthesiology and reanimation participated at a significantly higher rate than other departments (76.9%), in terms of training programs regarding local anaesthetics. While the most popular answers about early toxicity symptoms were anaphylaxis (12.7%) and arrhythmia (12.7%), late toxicity was hepatotoxicity (10.8%). However, 87.9% of participants had never encountered local anaesthetic toxicity. The great majority of participants had never heard of lipid therapy (67.4%), and those who were aware had heard it from their trainers (52.2%). Although lipid solution was available in our hospital, only 8.4% of participants knew this.

Conclusion: We believe that additional training programs regarding local anaesthetics and toxicity are needed.

Keywords: Local anaesthetic, toxicity, questionnaire

Introduction

Local anaesthetics constitute a motor and sensory block to prevent the transition of sodium through the neuronal cell membrane. This effect prevents sodium's rapid influx and, thus, the progress of the action potential in the depolarisation phase (1). Parameters such as agents binding to proteins, fat solubility, pH, vascularity of the injection site and the solubility constant (pKa) used in local anaesthesia are the main factors that influence both anaesthesia and systemic toxicity (1). By iatrogenically administering high doses of a local anaesthetic into circulation, local anaesthetic toxicity might develop. The target organ is usually the central nervous system (CNS) and cardiovascular system (CVS). Because the CNS is more sensitive to local anaesthetic effects than the CVS, CNS symptoms, such as dizziness and tinnitus, occur earlier than CVS symptoms (2). The first symptoms of CVS toxicity are associated with the CNS excitation phase and emerge with sympathetic nervous system activation. Afterwards, with the increase in plasma local anaesthetic concentration, arrhythmia and profound cardiovascular collapse are observed in the following period. Due to local anaesthetics, cardiac toxicity occurs when the blockage of permanent and prolonged sodium channels in diastole occurs, and serious arrhythmia susceptibility is seen to develop with an extensive QRS complex, a prolonged delivery time, a prolonged PR interval, an AV block and a re-entry mechanism. Local anaesthetics form cardiac toxicity by changing the mitochondrial metabolism and inotropic effect on cardiac cells. Therefore, the cardiac index, average arterial pressure, heart rate and left ventricular stroke work are reduced, and eventually, as a result of cardiac arrest, patients are lost (3). The local anaesthetic toxicity dose is affected by many factors, where the route of administration and rate of drug administration are critical. Gradual administration of the same dose makes the occurrence of toxicity difficult. However, an accidental overdose administration of local anaesthetics is substantially reduced, and the rate of these cases is reported to

be 0.2 to 0.01% (1, 4).

For toxicity treatment, the management of airway, the treatment of probable symptoms, such as convulsions, and the use of lipid solution in the treatment of cardiac toxicity have been recommended in recent years. For local anaesthetic toxicity, initially, the use of a 20% lipid emulsion at a dose of 1.5 mL kg⁻¹ is recommended. In case of the continuation of cardiac arrest, the same dose can be repeated at 5 min intervals. However, the total dose should not extend over 8 mL kg⁻¹ (5).

The aim of this study was to examine the information provided by our hospital research staff about widely used local anaesthetics and their toxicity and to raise awareness on local anaesthetics.

Methods

After obtaining approval from the Local Ethics Committee of Bursa Research and Training Hospital (2011-Kaek-25 2015 / 24-07) and the informed consent of participants, 115 research assistants who work in different branches of our hospital were included. A questionnaire consisting of 20 questions that evaluate participants' knowledge level about the pharmacokinetic–pharmacodynamic properties, toxicity symptoms and treatment with local anaesthetics was given to the participants.

Statistical analysis

For all statistical analysis, Statistical Package for the Social Sciences 21 for Windows (IBM SPSS Statistics, Armonk, NY, USA) was used. For numeric variables, descriptive statistics were given as the mean±standard deviation, while for categorical data, numbers and percentages were used.

Results

Of the participants, 102 (88.6%) completed the questionnaire. The average age of the participants was 28.73±3.17 years. The highest participation rate was from the Emergency Medicine Clinic with 15.7%. Of all participants, 40.6% had been research assistants for 2–5 years. Although 44.4% of the participants stated that they were using local anaesthetics every day, 70.3% of them had not received any training on this subject (Table 1). No significant difference was observed between participants who received training and those who had not in terms of their working years ($p>0.05$). Among the Anaesthesiology and Reanimation Clinic research assistants, 76.9% received training related to local anaesthetics. This rate was significantly higher than those in other clinics ($p<0.05$). The rate of participants who received training was 25% from the Emergency Medicine, 20% from the Obstetrics and Gynaecology, 16% from the General Surgery, 12.5% from the Orthopaedics and Traumatology and 10% from the Family Medicine clinics. It was found that the participants from the Urology, Otolaryngology, Paediatrics and the Internal Medicine clinics had not received any training on local

anaesthetics. The participants' answers given to the questions about the pharmacokinetic–pharmacodynamic properties of local anaesthetics are mentioned in Table 2.

The answers to the questions about local anaesthetic toxicity symptoms and treatments are given in Table 3. Among the participants, 87.9% had never seen local anaesthetic toxicity before. Although a 20% lipid solution was present in our hospital, only 8.4% of the participants knew about it, while 67.4% of the participants had never heard of 20% lipid use in local anaesthetic toxicity. The participants who had heard about 20% lipid use stated that they had learned about it from specialists (52.2%). Of all participants, one participant from the Otolaryngology Clinic, one from the Orthopaedic Clinic, one from the Anaesthesiology Clinic and three from the Emergency Clinic had experienced cases of toxicity.

Discussion

The results of our study investigating how well local anaesthetics are known, even though they are widely used in every branch, particularly in the Anaesthesiology and Reanimation Clinic, showed that despite the fact that most of the participants were senior research assistants, 70.3% of them had never received training on local anaesthetics.

In a survey conducted in Bezm-i Alem Valide Sultan Gureba Foundation Training Hospital, the rate of participants consisting of research assistants, specialists and general practitioners who had received training on local anaesthetics was 34.3% (6). We believe that as specialists had been included in that study, the rate was higher than that of our study. In the same study, when we compared the doctors working in the Anaesthesiology and Reanimation Clinic with the other participants from other clinics, we found that the rate for receiving training on local anaesthetics was higher, which was similar that in our study.

For the last 20 years, regional anaesthesia techniques have been an important part of anaesthesia administration, and local anaesthetics have begun to be widely used in adult and paediatric patients, both for anaesthesia and for postoperative analgesia purposes. In our clinic, local anaesthetics and toxicity are described in the training programme every year, and important points in daily practice are highlighted. However, our survey showed that in other branches, these issues were not included in their training programmes. Nevertheless, the fact that the knowledge level of the participants about local anaesthetics was at a basic level suggests that the participants had obtained this information from pharmacology courses during their university training rather than the clinics.

Regional anaesthesia is most commonly used in the Orthopaedics and Traumatology Clinic, and this frequent use increases the likelihood of encountering complications. In the literature, a large number of toxicity cases were found in Orthopaedics and Traumatology and Emergency Medicine

Table 1. Demographic data (mean±standard deviation, %)

Age (years)	28.73±3.17
Gender	
• Male	50
• Female	50
Clinic	
• Emergency Medicine Clinic	15.8
• Gynaecology and Obstetrics	14.9
• Anaesthesiology and Reanimation	12.9
• Family Medicine Clinic	10.9
• Paediatrics	9.9
• Urology	8.9
• Orthopaedics	7.9
• Internal Medicine	7.9
• General Surgery	5.9
• Otolaryngology Clinic	5
Working period	
• 0 months	21.8
• 6 months–1 year	12.9
• 1–2 years	24.7
• 2–5 years	40.6
Which agents do you prefer?	
• Bupivacaine	14.6
• Lidocaine	61
• Prilocaine	61
• Other	3.9
Which route do you use?	
• Subcutaneous/intramuscular	73.5
• Topical	22.5
• Epidural	11.8
• Intravenous	10.8
• Intrathecal	6.9
• Intranasal	4.9
• Other	8.8
How frequently do you use?	
• Every day	44.4
• Less than 2 times a week	17.32
• Once a week	11.1
• Once a month	5.1
• 3–4 times a year	5.1
• Other	17.2
Do you perform test dose?	
• Yes	6
• No	94
Have you had any training on local anaesthetics?	
• Yes	19.8
• No	70.3
• I don't remember	9.9

Table 2. Questions and answers about the pharmacological properties of local anaesthetics (%)

	Correct	Incorrect
Presence of many protective layers around many myelinated and unmyelinated nerve fibres creates a major obstacle for the introduction of clinically used local anaesthetics	66.2	33.8
Local anaesthetics are divided into two groups as amide- and ester-structured	97.8	2.2
Sodium channels are the main target for the activity of local anaesthetics	88.4	11.6
Bupivacaine is ester-structured	55.3	44.7
Prilocaine is ester-structured	48.7	51.3
The addition of epinephrine enhances the effectiveness of the local anaesthetic	83.5	16.5
Maximum single dose for bupivacaine is 600 mg	70.8	29.2
Bupivacaine has the shortest half-life	84.5	15.5

clinics (7-11). In our study, although it seems that participants who encounter cases of toxicity are mostly Emergency Medicine Research assistants, when the percentages are compared, due to a lack of significant differences between the Anaesthesiology and Reanimation, Orthopaedics and Traumatology and Otolaryngology clinics, all practitioners should have knowledge of local anaesthetics and their toxicities.

As is known, 20% lipid treatment plays a very important role in local anaesthetic toxicity. In the local anaesthetic systemic toxicity treatment guideline published by the American Society of Regional Anaesthesia and Pain Medicine in 2012, 20% lipid therapy was presented (5). Although this guideline is easily accessible, apart from the Anaesthesiology and Reanimation Clinic, we believe that research assistants from other clinics are unaware of this guideline. In our study, 67.4% of the participants had never heard of 20% lipid therapy. In a study conducted with anaesthesiologists in Denmark, the rate of participants who knew about intralipid therapy was 65% (12). In our study, the fact that research assistants stated that they had been informed about this therapy from specialists suggests that this rate is higher among specialists. However, the participants' knowledge level on the symptomatic treatment approach was insufficient. Thus, this situation has strengthened the idea that knowledge gained about local anaesthetics had been obtained from basic pharmacology courses.

Our study demonstrated that research assistants working in our hospital did not have sufficient information about local anaesthetics even though they are frequently used and that this may result in fatal toxicity; furthermore, participants lack

Table 3. Questions and answers about local anaesthetic toxicity and treatment (%)

What are the early symptoms?	
• Anaphylaxis	12.7
• Arrhythmia	12.7
• Allergies	10.8
• Hypotension	2
• Metallic taste in the mouth	2
• Tinnitus	2
What are the symptoms of late stage?	
• Hepatotoxicity	10.8
• Loss of consciousness	2
• Cardiac arrest	2
• Infection	2
• Ischaemia	2
What is done in the treatment of toxicity?	
• 20% lipid	5.9
• Symptomatic	4
• Methylene blue	3
• Cardiopulmonary resuscitation	2.9
• Antihistamines	2.9
What measures do you take to prevent toxicity?	
• Monitoring	29.4
• Aspiration test	10.8
• Test dose with epinephrine	15.7
• I use the appropriate dose	65.7
• I perform intermittent injection	17.6
• I use USG	1
Have you ever seen local anaesthetic toxicity before?	
• Yes	6.1
• No	87.9
• I haven't noticed	3
• I don't remember	3
What do you know about 20% lipid use in local anaesthetic toxicity?	
• I haven't heard of it	67.4
• I have heard about it but I don't recall	12.6
• I have heard about it but I don't recall the dosage	17.9
• I have comprehensive knowledge of it	2.1
Where did you hear about 20% lipid use?	
• I read about it in scientific papers	13.1
• I learned about it from assistant seminar topics	30.4
• I learned about it from the congress seminars I attended	4.3
• I learned about it from the specialists	52.2
Do you have 20% lipid solution in your hospital?	
• Yes	8.4
• No	5.3
• I don't know	86.3

sufficient knowledge on toxicity treatment. It is suggested that although local anaesthetics are frequently used and their basic impact mechanisms are well known, research assistants lack clinical practice and this subject has been ignored during training programmes given after their basic medical education.

The limitations of our study are that it was a unicentre study, and we could not provide an adequate number of participants from all clinics. In addition, apart from the research assistants, if more specialists and general practitioners had participated in this study, we could have determined how the knowledge level about local anaesthetics is distributed among those groups.

Conclusion

In practice, all clinics should have sufficient knowledge and equipment on toxicity, its treatment and pharmacological properties of local anaesthetics that are frequently used in every clinic and which may lead to fatal toxicities. Apart from Anaesthesiology and Reanimation Clinic, all clinics should include local anaesthetics, local anaesthetic toxicity and the guidelines written on this subject in their annual training program and their daily practice training.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Bursa Yüksek İhtisas Training and Research Hospital (2011-KAEK-25 2015/24-07).

Informed Consent: Written informed consent was obtained from participants who participated in this study.

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References

- Ökten F, Hasdoğan M, Tarhan A. Bupivakain kardiyotoksitesini ne derece önemlidir? *Anestezi Dergisi* 2010; 18: 189-93.
- Dickerson DM, Apfelbaum JL. Local anesthetic systemic toxicity. *Aesthet Surg J* 2014; 34: 1111-9. [CrossRef]
- Fettiplace MR, Weinberg G. Past, present, and future of lipid resuscitation therapy. *JPEN J Parenter Enteral Nutr* 2015; 39: 72S-83S. [CrossRef]
- Vasques F, Behr AU, Weinberg G, Ori C, Gregorio GD. A review of local anesthetic systemic toxicity cases since publication of the American Society of Regional Anesthesia Recommenda-

- tions to whom it may concern. *Reg Anesth Pain Med* 2015; 40: 698-705. [\[CrossRef\]](#)
5. Neal JM, Mulroy MF, Weinberg GL; American Society of Regional Anesthesia and Pain Medicine. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. *Reg Anesth Pain Med* 2012; 37: 16-8. [\[CrossRef\]](#)
 6. Başaranoğlu G, Teker MG, Saidoğlu M, Muhammedoğlu L, Haluk NÖ. Lokal anestezi kullanan hekimlerin toksisite ve intralipid tedavisi hakkında bilgileri. *Turk J Anaesthesiol Reanim* 2010; 38: 262-7.
 7. Turhan SÇ, Özçelik M, Koza EA, Adaklı B, Ökten F. Aksiller brakial pleksus blokajı sonrası gelişen levobupivakain toksisitesi. *Turkiye Klinikleri J Anest Reanim* 2014; 12: 110-3.
 8. Süzer MA, Özhan MÖ, Eşkin MB, Atik B. Lipit infüzyonu kullanılarak başarıyla tedavi edilen bir lokal anestezi toksisitesi. *Turk J Anaesthesiol Reanim* 2011; 39: 159-63.
 9. İnceöz H, Tural ZB, Babayigit M, Kepek A, Horasanlı E. İnfraklaviküler blok sonrası geç dönemde gelişen lokal anestezi toksisitesi. *Turk J Anaesthesiol Reanim* 2015; 43: 199-201.
 10. Özer AB, Erhan ÖL. Sünnet olacak infantta lokal anestezi toksisitesi. *Ağrı* 2014; 26: 43-6.
 11. Tierney KJ, Murano T, Natal B. Lidocaine-induced cardiac arrest in the emergency department: effectiveness of lipid therapy. *J Emerg Med* 2016; 50: 47-50. [\[CrossRef\]](#)
 12. Gadegaard PJ, Skjonnemand M, Jensen JD, Gottschau B. Limited knowledge of lipid rescue therapy in local anaesthetic systemic toxicity. *Dan Med Bul* 2011; 58: 1-3.