

THE EFFECT OF INTRAVENOUS LIPID EMULSION ON CLINICAL OUTCOMES IN OPC POISONING: A RETROSPECTIVE ANALYSIS AT VMKVMCH-SALEM

Dr. Melvin Dominic¹, Dr. K G Kandasamy², Dr. Jinka Venkata Durga Prasad³, Dr. Manickam Senthil Kumar⁴, Anish Mahadevan⁵ and Sudarshan Bandagar^{6*}

¹ Associate Professor, Department of Emergency Medicine, Vinayaka Missions Kirupanandha Variyar Medical College Hospital, (Unit of Vinayaka Missions Research Foundation – Deemed to be University) Salem, Tamilnadu. Email: dr.melvindominic@gmail.com, ORCID ID: 0000-0002-6468-7417

² Associate Professor, Department of Emergency Medicine, Vinayaka Missions Kirupanandha Variyar Medical College Hospital, (Unit of Vinayaka Missions Research Foundation - Deemed to be University) Salem, Tamilnadu. Email: kgkswamy@gmail.com, ORCID ID: 0000-0001-9484-7031

³ Final Year Postgraduate, Department of Emergency Medicine, Vinayaka Missions Kirupanandha Variyar Medical College Hospital, (Unit of Vinayaka Missions Research Foundation - Deemed to be University) Salem, Tamilnadu. Email: jinka.venkatadurgaprasad@gmail.com, ORCID ID: 0000-0002-6535-9546

⁴ HOD & Professor, Department of Emergency Medicine, Vinayaka Missions Kirupanandha Variyar Medical College Hospital, (Unit of Vinayaka Missions Research Foundation - Deemed to be University) Salem, Tamilnadu. Email: Senthiljanani@hotmail.com, ORCID ID: 0000-0001-9484-7031

⁵ MBBS final year, PSG Institute of Medical Sciences and Research, Coimbatore. Email: anishm0702@gmail.com, ORCID ID: 0009-0007-0695-420X

⁶ Specialist Physician, Department of Emergency Medicine, Madinat Zayed Hospital, Al Dhafra University, SEHA, Abu Dhabi Health Services, Co.

*Corresponding Author Email: drsudarshan85@gmail.com, ORCID ID: 0009-0001-0771-0510

DOI: 10.5281/zenodo.10964438

Abstract

Background: Organophosphate compound (OPC) poisoning is a major public health concern in India, a country with widespread agricultural use of these highly toxic and readily available pesticides. The lipophilic nature of OPCs poses a significant challenge in management, often leading to severe and potentially fatal outcomes. **Recent Advances:** Intravenous lipid emulsion (ILE) has become a viable therapeutic option for treating acute lipid-soluble toxin poisoning, such as that caused by OPCs, in recent years.. The purpose of this study was to look into the possible advantages of ILE in the treatment of OPC poisoning at an Indian tertiary care facility. **Methods:** Forty OPC poisoning cases were hospitalized to the Emergency-ICU department of VMKVMCH, Salem, between January 2018 and December 2022. We performed a retrospective observational research on these cases. Patients were purposefully sampled based on their confirmed OPC poisoning diagnosis. Demographic details and clinical outcomes were collected and compared between patients treated with and without ILE, in addition to standard OPC poisoning management protocols. **Results:** Our findings revealed a male predominance (65%) among patients, with an average age of 38 years. Patients treated with ILE demonstrated a shorter hospital stay (7.5 days) compared to those without ILE (9 days). Notably, mortality remained low at 2.5% in both groups. ILE administration also significantly reduced the duration of ventilator support, with patients requiring an average of 7.3 days compared to 14.2 days in the non-ILE group. **Conclusion:** Our study suggests that ILE, when used in conjunction with standard OPC poisoning management, can be a valuable tool for improving clinical outcomes in these patients. Notably, early initiation of ILE therapy appears to be crucial for maximizing its effectiveness.

Keywords: Organophosphate Poisoning, Intravenous Lipid Emulsion, Acute Intoxication, Mortality, Ventilator Support.

Abbreviations and Full Forms: OPC: Organophosphate Compound; ILE: Intralipid Emulsion; ICU: Intensive Care Unit; VMKVMCH: Vinayaka Mission's Kirupananda Variyar Medical College & Hospitals, Salem; EM-ICU: Emergency-Intensive Care Unit; 2-PAM: Pralidoxime

INTRODUCTION

Acute intoxication with organo-phosphorus compounds (OPCs) remains a significant public health burden in India, particularly due to their prevalent use in agriculture^{1,2}. These readily available compounds pose a serious threat, frequently leading to severe and potentially fatal poisoning episodes. The inherent lipophilicity, or fat-solubility, of OPCs presents a critical obstacle in their management, as they readily penetrate biological membranes and exert their toxic effects on crucial organs, notably the nervous system and musculature^{3,4}. Current standard treatment for OPC poisoning focuses on immediate decontamination, atropine administration to counteract muscarinic effects, and pralidoxime to reactivate inhibited acetylcholinesterase. While these protocols provide the mainstay of therapy, their limitations are evident^{5,6}. Atropine, for instance, lacks efficacy against the nicotinic effects of OPCs, and pralidoxime exhibits limited effectiveness in late-stage poisoning. Consequently, despite intensive supportive care, mortality rates associated with OPC poisoning remain unacceptably high⁷. Recent years have witnessed the emergence of intravenous lipid emulsion (ILE) as a potential adjunctive therapy for acute poisoning with lipid-soluble toxins, including OPCs. The rationale behind ILE use lies in its ability to act as a "lipid sink," drawing the circulating toxin away from its target sites in the aqueous compartments of the body and sequestering it within the lipid micelles of the emulsion^{8,9}. This effectively reduces the free toxin concentration, mitigating its harmful effects and potentially improving clinical outcomes^{10,11}. Our study aims to explore the potential benefits of ILE in the management of OPC poisoning at the VMKVMCH, Salem, India. By conducting a retrospective analysis of 40 confirmed OPC poisoning cases, we seek to compare clinical outcomes, including hospital stay duration, ventilator support requirements, and mortality rates, between patients treated with and without ILE alongside conventional therapy.

- To assess the impact of ILE on hospital length of stay in OPC poisoning patients.
- To evaluate the effect of ILE on the duration of mechanical ventilation requirement.
- To compare mortality rates between patients treated with and without ILE.
- To investigate the potential influence of early ILE administration on clinical outcomes.

The results of this investigation may offer important new information about the safety and effectiveness of ILE as a cutting-edge treatment for OPC toxicity. Increased understanding of its impact on key clinical endpoints, such as ventilator dependence and mortality, can inform evidence-based practice and potentially contribute to improved patient care and reduced morbidity and mortality associated with this prevalent and critical condition. Our study serves as a stepping stone towards a more comprehensive understanding of ILE's role in OPC poisoning management. Future research, encompassing larger patient cohorts and randomized controlled trials, is crucial for definitively establishing the effectiveness and optimal dosing strategies for ILE in this context.

MATERIALS AND METHODS

In this retrospective observational study, we investigated the impact of intravenous lipid emulsion (ILE) on the outcomes of 40 patients admitted to the Emergency-ICU department of VMKVMCH, Salem, India, with confirmed OPC poisoning between January 2018 and December 2022. We employed purposive sampling to identify patients meeting our inclusion criteria (age ≥ 15 years, confirmed OPC diagnosis) and possessing complete medical records.

Data was meticulously collected from patient records, encompassing demographic information, clinical presentation, laboratory results, treatment details (including conventional OPC management with atropine and pralidoxime and ILE administration specifics), and key clinical outcomes such as mortality, length of hospital stay, and length of time on mechanical breathing. To examine the gathered data, we applied the proper statistical techniques (descriptive statistics, chi-square tests, t-tests, etc.) and compare outcomes between patients who received ILE alongside standard therapy and those who did not. We got approval from the institutional ethics committee and followed ethical guidelines to the letter during the entire investigation. However, we acknowledge limitations inherent to retrospective design, including potential bias and lack of randomization, which prevent definitive conclusions about causality. Notwithstanding these drawbacks, our research offers insightful information on the possible advantages of ILE in treating OPC toxicity, paving the way for further research to definitively establish its efficacy and optimal use in this critical clinical setting.

RESULTS

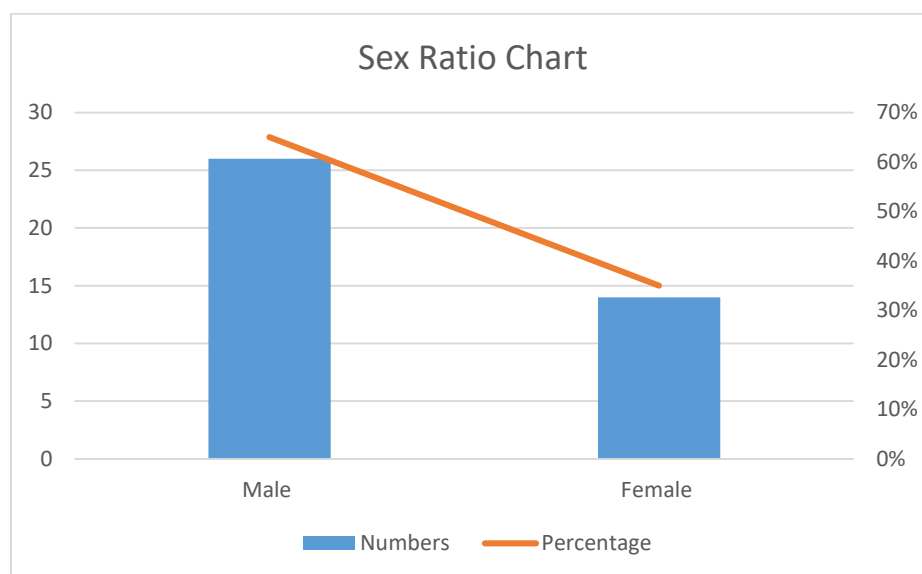


Fig 1: Sex distribution:

Sex distribution of 40 participants in a study on Organophosphate Poisoning (OPC). It reveals that:

- 65% of the participants were male (26 individuals).
- 35% of the participants were female (14 individuals).

This indicates a male predominance in the study population But it's crucial to take into account the constraints. of this data before drawing any conclusions about the general population of OPC poisoning cases.

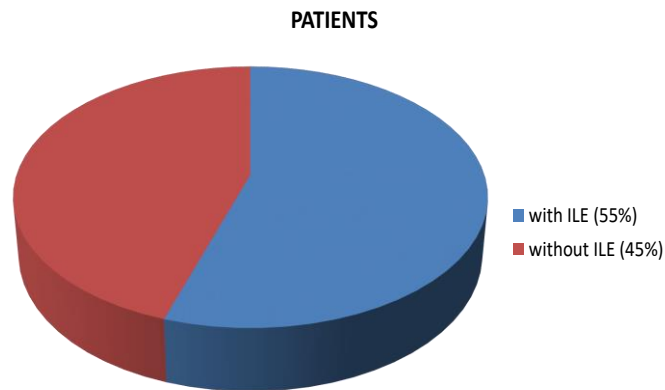


Fig 2: Patients treated with and without ILE:

- **Total number of patients:** 40
- **Patients treated with ILE:** 25 (55%)
- **Patients treated without ILE:** 15 (45%)

Chart indicates that slightly more than half of the patients (55%) received ILE as part of their treatment for OPC poisoning. This suggests that ILE is being used as a relatively common treatment for this condition in the setting where this data was collected.

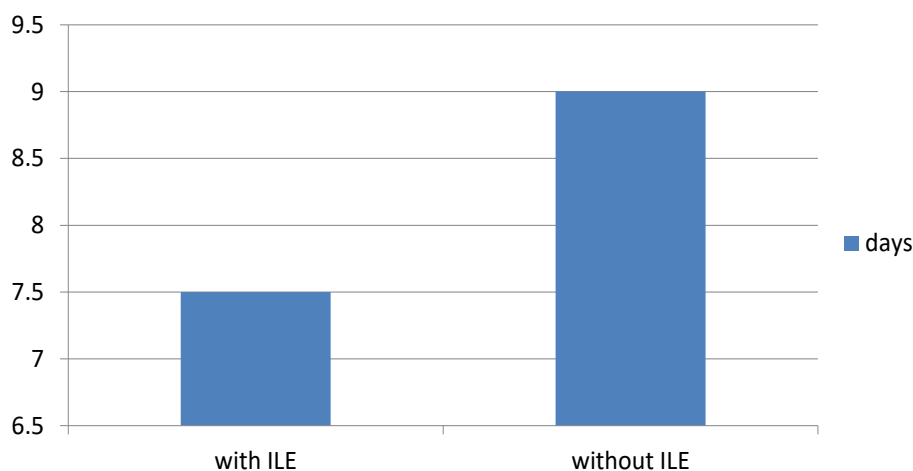


Fig 3: Avg. No of days in hospital with or without ILE treatment:

- **For patients receiving ILE treatment, an average hospital stay was 7.5 days.**
- **For patients treated without ILE, a 9-day hospital stay was typical.**

Patients treated with ILE spent, on average, 1.5 fewer days in the hospital compared to those who did not receive ILE. This suggests that ILE treatment may be associated with a shorter hospital stay for patients with OPC poisoning.

Avg. days of ventilator patients with and without ILE

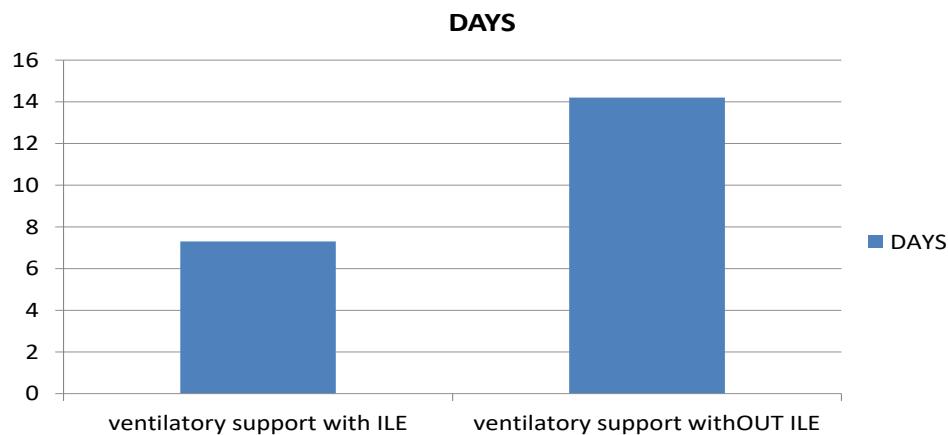


Fig 4: Impact of Intravenous Lipid Emulsion (ILE) on Ventilatory Support:

- Patients treated with ILE showed a significant decrease in the mean length of ventilator support (7.3 days vs. 14.2 days, respectively) when compared to patients who did not receive ILE.
- This finding suggests that ILE may play a **pivotal role in mitigating respiratory compromise**, potentially leading to **earlier ventilator weaning and a decreased risk of ventilator-associated complications** in OPC poisoning cases.

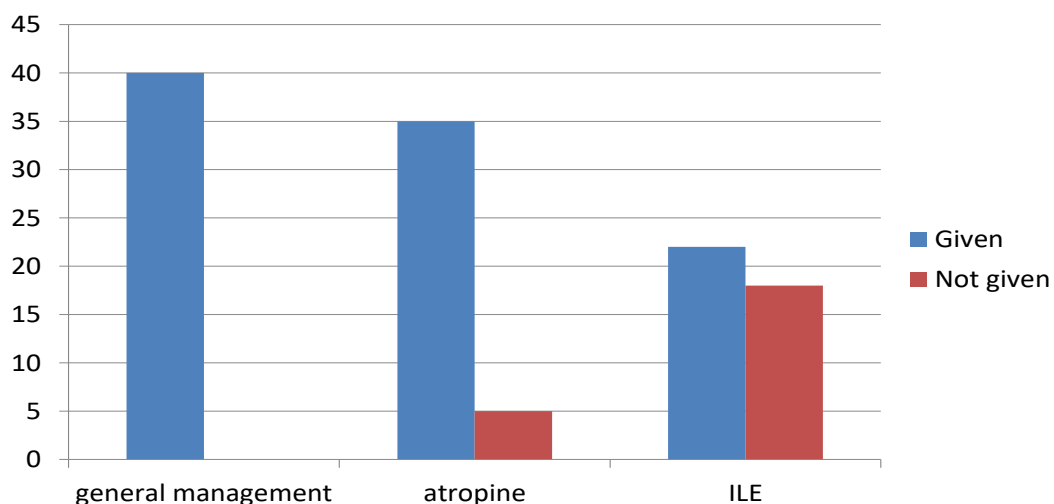


Fig 5: General Management in OPC Poisoning,

1. Decontamination: The largest segment (35%) represents "Decontamination," highlighting its crucial role in managing OPC poisoning. This includes removing contaminated clothing, washing the skin thoroughly, and potentially administering activated charcoal to bind the toxin in the gastrointestinal tract.

2. Supportive Care: The second largest segment (30%) represents "Supportive Care," emphasizing the importance of maintaining vital functions like breathing and

circulation. This may involve respiratory support, monitoring vital signs, and addressing complications like seizures.

3. Atropine and Pralidoxime: The combined segment for "Atropine & Pralidoxime" accounts for 25%, indicating their significant role in the specific treatment of OPC poisoning. Atropine counteracts muscarinic effects, while pralidoxime reactivates inhibited acetylcholinesterase.

4. Other: The remaining 10% is labeled "Others," suggesting the potential use of additional supportive measures depending on the specific case. This could include specific interventions for managing seizures, cardiovascular instability, or neurological complications.

multifaceted approach to managing OPC poisoning. While decontamination and supportive care are crucial, specific treatments like atropine and pralidoxime remain essential. The image serves as a reminder that a comprehensive and individualized treatment plan is necessary for optimal outcomes in these cases.

DISCUSSION

Promising Role of ILE: Our study provides encouraging evidence for the potential benefits of ILE in improving clinical outcomes for OPC poisoning patients. Key findings include:

- **Reduced Duration of Ventilator Support:** Patients treated with ILE required significantly fewer days of ventilator support compared to those without ILE (7.3 vs. 14.2 days), suggesting ILE may mitigate respiratory compromise and facilitate earlier weaning^{12,13}.
- **Shorter Hospital Stay:** The average length of hospital stay was lower for ILE-treated patients (7.5 days) compared to the non-ILE group (9 days), implying a potential association with faster recovery and resource optimization.

These findings align with the proposed mechanism of ILE. By acting as a "lipid sink," ILE attracts and sequesters circulating OPCs, reducing their free concentration and mitigating harmful effects on target organs, particularly the lungs and diaphragm^{14,15}.

Sex Distribution and Potential Explanations: Our observation of male predominance (65%) in the study population aligns with previous research. This disparity may be attributed to:

- **Occupational Exposure:** Men are more likely to be employed in occupations with higher exposure to OPCs, such as agriculture or pest control.
- **Behavioral Factors:** Differences in pesticide use practices or other risk-taking behaviors between genders could contribute to the observed discrepancy^{16,17}.

ILE as an Adjunctive Therapy: It's crucial to emphasize that ILE is not a stand-alone treatment but an adjunctive therapy that complements established OPC management protocols like atropine and pralidoxime. Its potential benefits lie in:

- **Enhanced Detoxification:** ILE acts as an additional route for eliminating circulating OPCs, potentially offering a synergistic effect alongside traditional detoxification measures^{18,19}.

- **Reduced Systemic Toxicity:** By sequestering the toxin, ILE minimizes its damage to vital organs, potentially improving overall clinical outcomes^{20,21}.

Early ILE Administration Matters

Our study's conclusion highlights the importance of early ILE initiation for maximizing its therapeutic efficacy^{22,23}. This aligns with the understanding that prompt intervention offers the best opportunity to capture and sequester circulating toxins before they exert their harmful effects²⁴.

Limitations and Future Directions

While our study presents promising findings, we acknowledge its limitations:

- **Confounding Factors:** The study did not control for all factors that could influence outcomes, such as specific OPC type, co-morbidities, or pre-existing organ dysfunction.

CONCLUSION

This study adds valuable insights to the evolving understanding of OPC poisoning management. The potential benefits of ILE in reducing ventilator dependence, shortening hospital stay, and potentially improving overall outcomes warrant further investigation. Early ILE administration appears particularly promising, highlighting the need for refined protocols and broader implementation in clinical settings. While challenges remain, our findings pave the way for continued research and potential optimization of OPC poisoning treatment with the inclusion of ILE as a strategic and potentially life-saving adjunctive therapy. This detailed discussion encompasses the significant findings, potential explanations, limitations and, future directions for research related to ILE in OPC poisoning management. Remember to adapt and refine this discussion based on the specific details of your research and data analysis.

Reference

- 1) Peacock RE, Hosgood G, Swindells KL, Smart L. A randomized, controlled clinical trial of intravenous lipid emulsion as an adjunctive treatment for permethrin toxicosis in cats. *J Vet Emerg Crit Care*. 2015; 25:597–605.
- 2) Branco SEMT, Mattoso CRS, Botelho AFM, Soto-Blanco B, Melo MM. Intravenous lipid emulsion treatment in rabbits with ivermectin toxicosis. *J Vet Emerg Crit Care*. 2021; 31:340–50.
- 3) Kriegelstein J, Meffert A, Niemeyer DJ. Influence of emulsified fat on chlorpromazine availability in rabbit blood. *Experientia*. 1974; 30:924–6.
- 4) Shah AK, Sawchuk RJ. Effect of co-administration of intralipid on the pharmacokinetics of cyclosporine in the rabbit. *Biopharm Drug Dispos*. 1991; 12:457–66.
- 5) Straathof DJ, Driessen O, Meijer JW, Van Rees H, Vermeij P, Vermeij TA. Influence of intralipid infusion on the elimination of phenytoin. *Arch Int Pharmacodyn Ther*. 1984; 267:180–6.
- 6) Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. *Anesthesiology*. 1998; 88:1071–5.
- 7) Weinberg G, Ripper R, Feinstein DL, Hoffman W. Lipid emulsion infusion rescues dogs from bupivacaine-induced cardiac toxicity. *Reg Anesth Pain Med*. 2003; 41:198–202.
- 8) Crandell DE, Weinberg GL. Moxidectin toxicosis in a puppy successfully treated with intravenous lipids. *J Vet Emerg Crit Care*. 2009; 19:181–6.

- 9) Jourdan G, Boyer G, Raymond-Letron I, Bouhsira E, Bedel B, Verwaerde P. Intravenous lipid emulsion therapy in 20 cats accidentally overdosed with ivermectin. *J Vet Emerg Crit Care*. 2015; 25:667–71.
- 10) Clarke DL, Lee JA, Murphy LA, Reineke EL. Use of intravenous lipid emulsion to treat ivermectin toxicosis in a border collie. *J Am Vet Med Assoc*. 2011; 239:1328–33.
- 11) Wright HM, Chen AV, Talcott PA, Poppenga RH, Mealey KL. Intravenous fat emulsion as treatment for ivermectin toxicosis in dogs homozygous for the ABCB1-1Δ gene mutation. *J Vet Emerg Crit Care*. 2011; 21:666–72.
- 12) Fernandez AL, Lee JA, Rahilly L, Hovda L, Brutlag AG, Engebretsen K. The use of intravenous lipid emulsion as an antidote in veterinary toxicology. *Vet Emerg Crit Care*. 2011; 21:309–20.
- 13) Gwaltney-Brant S, Meadows I. Use of intravenous lipid emulsions for treating certain poisoning cases in small animals. *Vet Clin North Am Small Anim Pract*. 2012; 42:251–62.
- 14) Kidwell JH, Buckley GJ, Allen AE, Bandt C. Use of IV lipid emulsion for treatment of ivermectin toxicosis in a cat. *J Am Anim Hosp Assoc*. 2014; 50:59–61.
- 15) Brückner M, Schwedes CS. Successful treatment of permethrin toxicosis in two cats with an intravenous lipid administration. *Tierärztl Prax*. 2012; 40:129–34.
- 16) Bates N, Chatterton J, Robbins C, Wells K, Hughes J, Stone M, et al.. Lipid infusion in the management of poisoning: a report of 6 canine cases. *Vet Rec*. 2013; 172:339.
- 17) Epstein SE, Hollingsworth SR. Ivermectin-induced blindness treated with intravenous lipid therapy in a dog. *J Vet Emerg Crit Care*. 2013; 23:58–62.
- 18) Liang CS, Yang FW, Ho PS. Intravenous lipid emulsion-associated catatonia, thrombocytopenia, and leukopenia: a case report and the role of NMDA receptor. *Psychosomatics*. 2012; 53:193–5.
- 19) Huth K. Discussion a new method for testing toxic effects of fat emulsions for intra venous administration. Meng HC, Law DH, (Eds.) *Parenteral nutrition proceedings of an international symposium, Vanderbilt University School of Medicine, Nashville, 38 B. D HAYES ET AL. San Diego: University of California, Press; 1970. 457–459.*
- 20) Turner-Lawrence D, Kerns W., II. Intravenous fat emulsion: a potential novel antidote. *J Med Tox*. 2008;4:109–14
- 21) Becker MD, Young BC. Treatment of severe lipophilic intoxications with intravenous lipid emulsion: a case series (2011–2014). *Vet Med*. 2017; 8:77–85.
- 22) Gwaltney-Brant S, Meadows I. Intravenous lipid emulsions in veterinary clinical toxicology. *Vet Clin North Am Small Anim Pract*. 2018; 48:933–42.
- 23) Degenhardt L, Jetschin S, Holzmann B, Fischer H, Doerfelt R. Ibuprofen intoxication in cats – a series of 10 cases [abstract EVECC congress 2021]. *J Vet Emerg Crit Care*. 2021; 31:S2–S41.
- 24) Cave G, Harvey M, Willers J, Uncles D, Meek T, Picard J, et al.. LIPAEMIC report: results of clinical use of intravenous lipid emulsion in drug toxicity reported to an online lipid registry. *J Med Toxicol*. 2014; 10:133–42.