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LETTER TO THE EDITOR

Letter to "Refractory cardiogenic shock due to atomoxetine overdose rescued by venoarterial extracorporeal membrane oxygenation: A case report"

To the Editor,

I commend Komoriya et al.[1] for their successful treatment described in the case report titled "Refractory cardiogenic shock due to atomoxetine overdose rescued by venoarterial extracorporeal membrane oxygenation: A case report," recently published in *Acute Medicine & Surgery*. Lipid emulsions are commonly used to manage local anesthetic systemic toxicity (LAST) and as an effective adjuvant therapy for mitigating severe cardiovascular depression caused by toxic doses of non-local anesthetic drugs with high lipid solubility (log P = log [octanol/water] partition coefficient: >2).[2] Moreover, lipid emulsion improves the condition of patients with seizure caused by norepinephrine reuptake inhibitor atomoxetine toxicity, which is unresponsive to intravenous benzodiazepine, suggesting lipid sink.[3] To help the readers better understand this case report, I would like to explain the possible mechanisms of lipid emulsion treatment for drug toxicity. The mechanism comprises indirect and direct effects.[2] The widely accepted lipid shuttle mechanism suggests that lipid emulsions absorb highly lipophilic drugs, such as bupivacaine (log P: 3.41), from tissues such as the brain and heart.[2] Once absorbed, they transport these drugs to the liver, muscles, and adipose tissue, where the drugs are detoxified and stored.[2] QT prolongation induced by bupivacaine, which produces Torsades de Pointes, is due to the inhibition of rapidly activating delayed rectifier potassium channels encoded by human ether-à-go-go-related gene (hERG).[2] Bupivacaine inhibits hERG potassium channels, which contributes to QT prolongation and cardiac arrest induced by LAST.[2] However, lipid emulsions reduce the bupivacaine-induced increase in the T-peak to T-end interval and restore the sinus rhythm.[2] Similar to local anesthetics, an overdose of atomoxetine in an 11-year-old patient produces life-threatening QT prolongation, which may be due to inhibition of hERG.[4] The direct effects of lipid emulsions include a positive inotropic effect, supplying fatty acids, and reducing mitochondrial dysfunction.[2] Considering previous reports,[2–4] scavenging lipid soluble atomoxetine (log P: 3.9) and the positive inotropic effect induced by lipid emulsions may have contributed to the early removal of the venoarterial extracorporeal membrane oxygenation (ECMO) in this patient. The authors stated that the potential side effects of lipid emulsions in the concomitant use of lipid emulsions and ECMO include layering, agglutination in the tube, and cracking of the stopcock.[1] A high dose of lipid emulsion (20 mL/kg, 4 g/kg) as an adjuvant drug to treat toxicity produces layering of the blood and lipid emulsion in ECMO circuit.[5] Thus, some experts advise limiting the use of lipid emulsions to no more than 10 mL/kg during ECMO.[5] Moreover, LAST is induced mainly by intravenous administration, whereas drug toxicity caused by non-local anesthetic drugs is induced mainly by oral administration. In terms of pharmacokinetics (oral administration: prolonged absorption from the gastrointestinal tract, first-pass effects, and decreased bioavailability), drug toxicity induced by non-local anesthetics via oral administration is different from LAST. Thus, further research is necessary to examine the optimal dose of lipid emulsions in patients undergoing ECMO for drug toxicity induced by non-local anesthetic drugs. Additionally, further study regarding treatment modality using simultaneous lipid emulsion and ECMO for atomoxetine toxicity is needed.

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The authors have nothing to report.

CONFLICT OF INTEREST STATEMENT

The author declares no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

Not applicable.

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