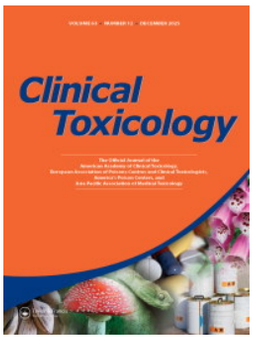

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CLINICAL RESEARCH

The effect of decontamination and elimination in large acute lithium overdoses

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ABSTRACT

Introduction: Acute lithium ingestion rarely results in neurotoxicity, except in larger ingestions, in which persistently high concentrations increase distribution into the brain. We investigated large acute ingestions of lithium and the effect of interventions.

Method: This was a retrospective review of 18 patients with acute lithium overdoses >25 g over 17 years. Data were collected on neurotoxicity, treatments and serum lithium concentrations. Outcomes included neurotoxicity, area under the curve, and time until serum lithium concentration decreased <1.0 mmol/L.

Results: The median reported lithium dose was 46 g (range 25.5–95 g). Two late presenting patients developed neurotoxicity. All patients had intravenous fluids, four received continuous kidney replacement therapy, and three whole bowel irrigation. In patients treated with intravenous fluids alone there was a significant association between dose and time until concentration decreases <1.0 mmol/L ($n=9$; $R^2 = 0.75$; $P=0.002$) and between dose and area under the curve ($n=10$; $R^2 = 0.68$; $P=0.003$). Three patients given whole bowel irrigation 4–9 h post-ingestion had lower area under the curve (54 mmol/L*h, 62 mmol/L*h, 155 mmol/L*h) compared to those given intravenous fluids alone ingesting similar doses (63 mmol/L*h, 199 mmol/L*h, 294 mmol/L*h). Continuous kidney replacement therapy increased lithium clearance.

Discussion: Large acute lithium overdoses result in persistent measurable lithium concentrations and higher area under the curve, which increases with dose ingested, potentially increasing risk of neurotoxicity. Whole bowel irrigation reduced area under the curve, even when administered >4 h post-ingestion.

Conclusion: Whole bowel irrigation appears to reduce lithium burden and potential neurotoxicity in patients with large acute lithium overdoses.

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Decontamination; haemodialysis; lithium poisoning; neurotoxicity; whole bowel irrigation

Introduction

Lithium has a narrow therapeutic index and most common and severe effects result from chronic toxicity, rather than acute overdose. The most important clinical effect due to lithium toxicity is neurotoxicity, with tremors, ataxia, myoclonus, confusion, agitation, and seizures [1]. This can result in significant mortality and morbidity, and is the main reason for critical care interventions, including kidney replacement therapy, being used in the treatment of patients with lithium toxicity [2,3]. Lithium toxicity can result in prolonged hospital stay, the requirement for critical interventions and the potential for long term sequelae.

Acute lithium overdose rarely results in neurotoxicity, because serum concentrations rise and fall too rapidly for significant distribution into the central nervous system to occur [2]. However, in massive acute ingestions, there is rate-limited gastrointestinal absorption (zero order) of lithium, with persistent high lithium serum concentrations facilitating ongoing distribution into the brain and other compartments, increasing the risk of neurotoxicity. For this reason decontamination with whole bowel irrigation to decrease absorption and continuous kidney replacement therapy to increase elimination, are often recommended for larger acute ingestions, typically >25 g [4].

Whole bowel irrigation is recommended based on expert opinion from case reports and observations, due to randomised controlled trials being very difficult to undertake and therefore a lack of any systematic reviews. This opinion is extrapolated from whole bowel

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irrigation being shown to be effective in preventing the absorption of sustained-release lithium in a controlled human study, as well as a small number of case reports in overdose [5,6].

We aimed to add to this body of evidence by investigating the pharmacokinetics of lithium for acute ingestions >25 g and the effect of whole bowel irrigation and continuous kidney replacement therapy.

Methods

Patients with acute lithium ingestions greater than 25 g were included from the Hunter Area Toxicology Service poisoning cohort. The toxicology service admits all patients from a population of over 500,000 people in a large regional city. The Hunter Area Toxicology Service has prospectively collected data on all poisoning since 1987. Patients present to the service directly via an ambulance bypass system for poisoned patients. No decontamination interventions are performed prehospitally. The use of a database to collect clinical data, including review of medical records, for research is approved by the Hunter New England Human Research Ethics Committee (HREC/05/03/09/3.11).

A standardised data collection form is filled out for all patients admitted to the toxicology service and a record of all patients is recorded on a tablet-based electronic database for clinical care [7]. Data are entered into a relational database by a research assistant weekly and reviewed by a clinical toxicologist. Missing data are retrieved from medical records. Demographics, overdose details, clinical effects, investigations, complications, treatment, and outcomes are recorded in the database [8].

All patients ≥18 years old with an acute lithium overdose >25 g from January 2008 to March 2025 were included. Data were extracted from the database previously described including demographics (age, gender), neurotoxicity (delirium, seizures, cerebellar signs excluding tremor alone), treatments (intravenous fluid, whole bowel irrigation, and continuous kidney replacement therapy) and lithium concentrations.

Continuous variables are reported as medians and interquartile ranges (IQR) and compared using the non-parametric Mann-Whitney test. The area under the curve (AUC) was estimated on cases with more than three concentrations, using the trapezoid method, time to serum lithium concentration was estimated visually on plots of lithium concentration versus time and peak concentration was taken as the highest lithium concentration. All statistical and graphical analyses were done in GraphPad Prism version 10.4.1 (397) for Windows.

Results

Over 17 years we identified 255 patients with acute lithium overdoses, 18 of whom ingested >25 g, with a median age of 38 years (IQR: 25–44 years) and 11 were females. All but one patient ingested their own prescribed medication. The median reported dose ingested was 46 g (IQR: 35–57 g, range: 25.5–95 g; Figure 1A). Five ingested immediate release lithium, ten sustained release lithium, and three a combination of immediate release and sustained release (Figure 1B). Other medications or alcohol were ingested at the time of overdose in 13/18 patients. All patients were administered intravenous fluids. Three were administered whole bowel irrigation at 6 h for 58.5 g sustained release, at 9 h for 63.5 g immediate/sustained release and at 4h for 90 g sustained release (Figure 2A). Four underwent continuous kidney replacement therapy at 15 h, 24 h, 39.5 h and 36 h (Figure 2B).

Four patients had an estimated glomerular filtration rate (eGFR) <60 mL/min on presentation. Neurotoxicity developed in two of these patients, who both had an eGFR <30 mL/min on admission. The first was a 38-year-old female who presented 48 h post-ingestion of lithium sustained release 54 g, had a peak lithium concentrations of 3.04 mmol/L. On examination she had a wide-based ataxic gait and severe tremor resulting in her being unable to hold a drink without spilling it, which both improved without treatment. The second was a 54-year-old male who presented 24 h after taking lithium sustained release 90 g, with a peak lithium concentration of 7.8 mmol/L. On examination he had seizure-like activity, a reduced level on consciousness, tremor, delirium, and gait abnormalities. He underwent endotracheal intubation to facilitate continuous kidney replacement therapy with normalisation of kidney function and resolution of cognition and mobility. The two other patients with eGFR <60 mL/min, recovered without continuous kidney replacement therapy or neurotoxicity. There were no deaths.

The peak concentration and time course of lithium concentrations in patients only given intravenous fluids appeared to be associated with dose (Figure 1A) and there appeared to be no association with formulation (Figure 1B). The median AUC was 115 mmol/L*h (IQR: 73–193 mmol/L*h; Range 46–29 mmol/L*h). The three patients given whole bowel irrigation had a lower AUC (54 mmol/L*h, 62 mmol/L*h, 155 mmol/L*h) compared to those only given intravenous fluids ingesting similar doses (65 mmol/L*h, 198 mmol/L*h, 294 mmol/L*h; Figure 2A), and a shorter time until the lithium concentration decreases below 1.0 mmol/L (28 h, 35 h, 59 h) compared to those given intravenous fluids (72 h, 79 h, 95 h; Figure 2A). Continuous kidney

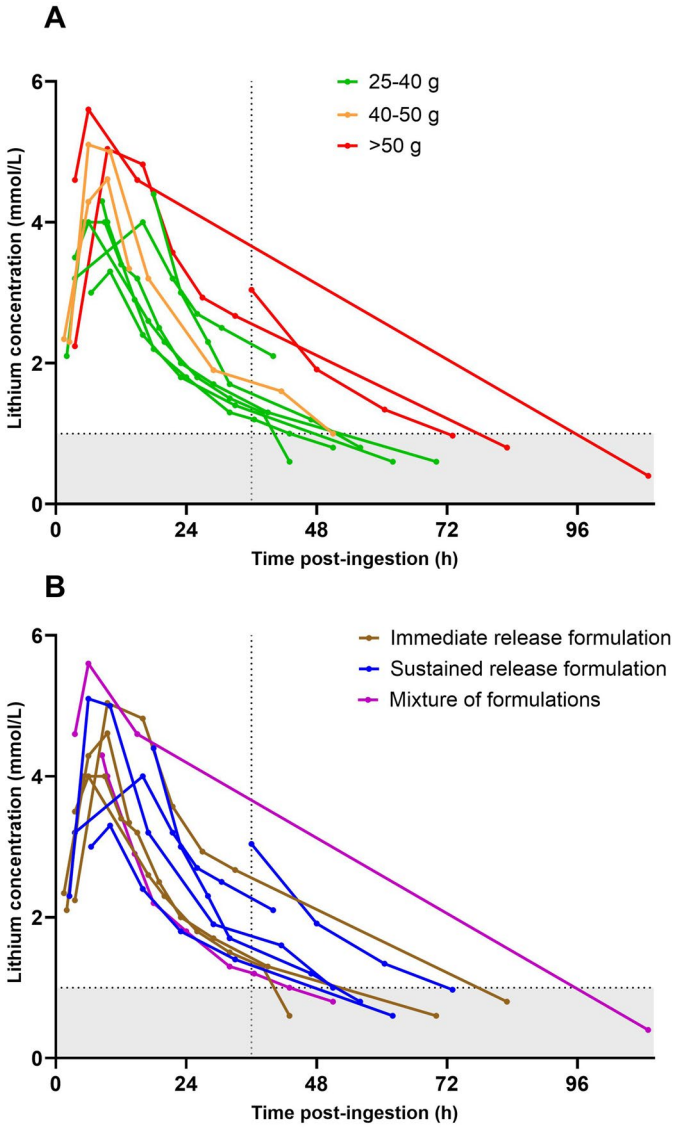

Figure 1. Plots of serum lithium concentrations versus time, for all patients only treated with intravenous fluids categorised by dose in Panel (A); with patients taking 25–40 g (green), 40–50 g (orange) or over 50 g (red; and separated by formulation in Panel (B) in patients with immediate release formulations (brown), sustained release formulations (blue) and a mixture of formulations (purple).

replacement therapy appeared to increase the clearance of lithium (Figure 2B).

In patients only treated with intravenous fluid with sufficient lithium concentrations there was a significant association between dose and time until concentration decreases below 1.0 mmol/L ($n = 11$; $R^2 = 0.45$; $P = 0.023$; Figure 3A), and between dose and AUC ($n = 11$; $R^2 = 0.57$; $P = 0.011$; Figure 3B), but not between dose and peak concentration.

Discussion

Our data suggests that large acute ingestions of lithium >25 g can result in sustained elevated serum lithium concentrations above 1.0 mmol/L. Previous recommendations have suggested that clinicians should aim to reduce serum lithium concentrations to <1.0 mmol/L within 36 h to prevent the development of neurotoxicity [9,10]. In our cohort, neurotoxicity occurred in 2/18 patients (11%) in the context of acutely impaired kidney function (eGFR <30 mL/min), reported ingestion >50 g and delayed presentation.

Over two-thirds of patients ingested sustained-release lithium, but there did not appear to be an association with prolonged lithium concentrations in these patients compared to immediate release. In contrast, there was a clear association between dose and time course, AUC and time to lithium concentration <1 mmol/L. Previous studies have demonstrated prolonged

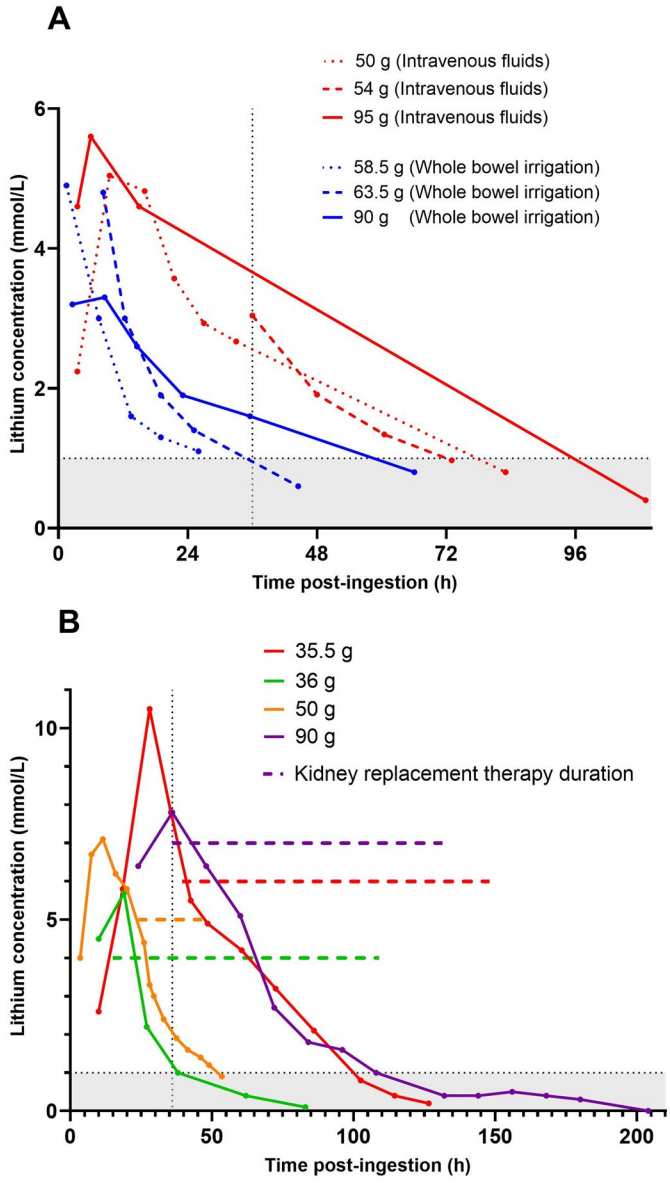

Figure 2. Plots of serum lithium concentrations versus time for three patients who ingested >50 g and given whole bowel irrigation (blue) compared to three patients who ingested >50 g treated with intravenous fluids only (red), with dotted, dashed and thick lines indicating different patients for each colour (A); and the four patients treated with continuous kidney replacement therapy, with doses of 35.5 g (red), 36 g (green), 50 g (orange) and 90 g (purple); duration of continuous kidney replacement therapy indicated by dashed lines for each patient (B).

absorption of lithium [11,12], whether this is from a gastrointestinal drug reservoir or zero order absorption remains unclear (Table 1).

Comparing AUC and time until the serum lithium concentration was <1 mmol/L enabled a comparison between patients treated with only intravenous fluids and those receiving whole bowel irrigation or continuous kidney replacement therapy. The impact of decontamination was clinically significant, with the AUC being much lower in patients receiving whole bowel irrigation, and the time to lithium concentration being <1 mmol/L much shorter, compared to patients with similar estimated doses ingested without decontamination. Whole bowel irrigation has been previously shown to be effective when given 1 h post ingestion of sustained release lithium [5], and it is most likely to be effective early to prevent absorption of lithium and should be instituted based on the dose ingested rather than waiting for lithium concentrations. Interestingly, in our cases whole bowel irrigation was initiated between 4 h and 9 h post ingestion and it still appeared to be effective later than 4 h, In contrast to whole bowel irrigation, we believe that continuous kidney replacement therapy should be reserved for patients presenting late in which the majority of the dose has been absorbed and there are already high concentrations (Figure 2B).

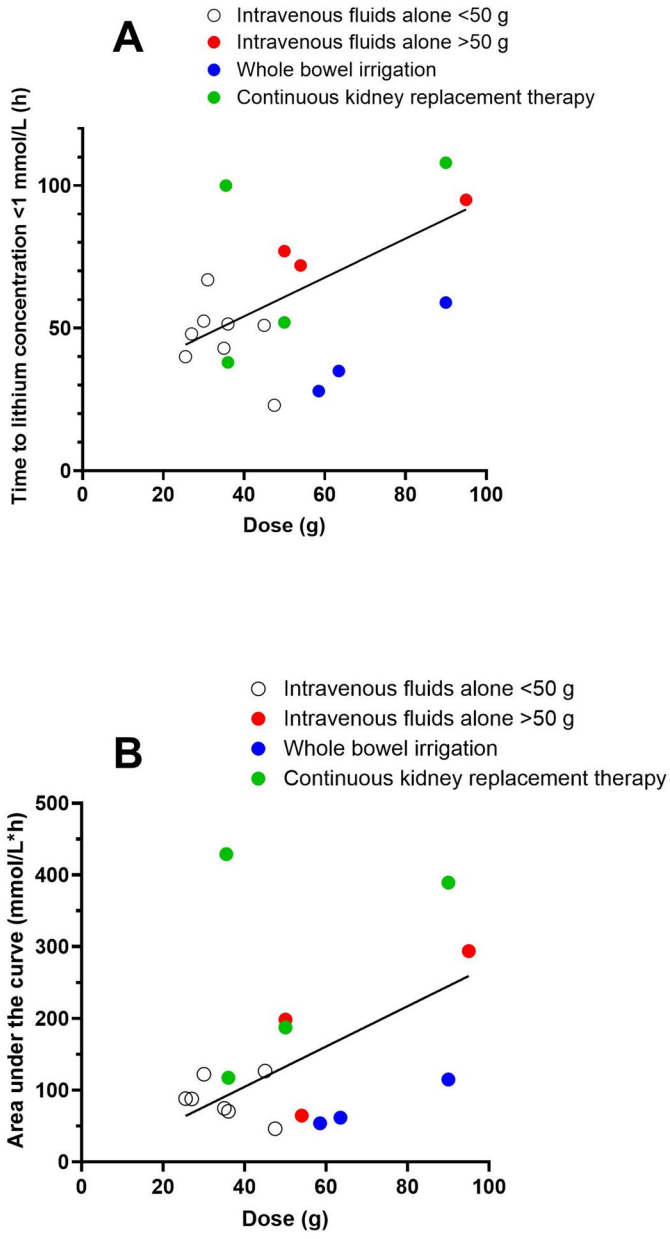

Figure 3. Panel A: Plot of time to lithium concentration <1 mmol/L versus dose ingested for eight patients ingesting <50 g and treated with intravenous fluids (open circle), three patients ingesting >50 g and treated with intravenous fluids (filled red circles), three patients given whole bowel irrigation (filled blue circles) and four administered continuous kidney replacement therapy (filled green circles); Panel B; a plot of area under the curve versus dose ingested for eight patients ingesting <50 g and treated with intravenous fluids (open circle), three patients treated with intravenous fluids taking >50 g (filled red circle), three patients given whole bowel irrigation (filled blue circles) and four administered continuous kidney replacement therapy (filled green circles). The solid lines represent a trend line.

Table 1. The lithium dose and concentration data for the 18 included cases of acute lithium ingestion >25 g separated into treatment, intravenous fluids only, whole bowel irrigation, and continuous kidney replacement therapy.

	Intravenous fluids only	Intravenous fluids only (>50 g)	Whole bowel irrigation	Continuous kidney replacement therapy
Number of cases	8	3	3	4
Report dose, g, median (IQR[a])	33 (29–38)	50, 54, 95	58.5, 63.5, 90	35.5, 36, 50, 90
Initial lithium concentration, mmol/L, median (IQR[a])	3.1 (2.3–4.1)	2.2, 3.0, 4.6	3.2, 4.8, 4.9	2.6, 4.0, 4.5, 6.4
Peak lithium concentration, mmol/L, median (IQR[a])	4.2 (4.0–4.6)	3.0, 5.0, 5.6	3.3, 4.8, 4.9	5.7, 7.1, 7.8, 10.5
Time to peak concentration, h, median (IQR[a])	9 (6.4–15)	6, 9.5, 12	1.5, 8.3, 8.6	11.5, 19, 28, 36
Area under the curve, mmol/L[a] h, median (IQR[a])	88 (74–114)	65, 198, 294	54, 62,115	117, 188, 389, 429
Time to lithium concentration <1 mmol/L, h, median (IQR[a])	50 (44–51)	72, 79, 95	28, 35, 59	38, 52, 100, 108

[a]If <5 data points no IQR is provided, and each data point is provided.

These data have limitations, primarily being a small dataset, with only two patients with neurotoxicity. The data relied on patient reported dose, time of the first and last lithium concentrations and whether the patients were compliant with their prescribed lithium regimen. There are a number of studies that demonstrate that patient reported dose is a good estimate of the dose ingested [13]. There is also a bias using a cut off of 25 g to the worst cases (highest serum concentrations, mixed ingestions) and results in large AUCs and higher rates of neurotoxicity.

In our series all but one patient took their own lithium, demonstrating that a pure acute lithium overdose is exceedingly rare. However, it is often unclear at the time of presentation whether patients are compliant, and therefore determining their baseline serum lithium concentration was difficult.

Conclusion

Acute large lithium overdose results in a longer duration of measurable serum lithium concentrations (above 1 mmol/L) and higher AUC, which increases with estimated dose ingested. This potentially increases the risk of neurotoxicity. Whole bowel irrigation was associated with a reduced AUC and time to lithium concentration <1 mmol/L, and continuous kidney replacement therapy appeared to increase lithium clearance.

Disclosure statement

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References

[1] Mesquita J, Cepa S, Silva L, et al. Lithium neurotoxicity at normal serum levels. J Neuropsychiatry Clin Neurosci. 2010;22(4):451. doi: 10.1176/jnp.2010.22.4.451.e29.
[2] Baird-Gunning J, Lea-Henry T, Hoegberg LCG, et al. Lithium poisoning. J Intensive Care Med. 2017;32(4):249–263. doi: 10.1177/0885066616651582.
[3] Wen J, Sawmiller D, Wheeldon B, et al. A review forlithium: pharmacokinetics, drug design, and toxicity. CNS Neurol Disord Drug Targets. 2019;18(10):769–778. doi: 10.2174/1871527318666191114095249.
[4] Acute lithium poisoning. In: Therapeutic guidelines. Melbourne: Therapeutic Guidelines Limited; 2020 [cited 2025 July 4]. https://www.tg.org.au.
[5] Smith SW, Ling LJ, Halstenson CE. Whole-bowel irrigation as a treatment for acute lithium overdose. Ann Emerg Med. 1991;20(5):536–539. doi: 10.1016/s0196-0644(05)81610-5.
[6] Thanacoody R, Caravati EM, Troutman B, et al. Position paper update: whole bowel irrigation for gastrointestinal decontamination of overdose patients. Clin Toxicol. 2015;53(1):5–12. doi: 10.3109/15563650.2014.989326.
[7] Downes MA, Page CB, Berling I, et al. Use of a tablet-based application for clinical handover and data collection. Clin Toxicol. 2020;58(7):692–697. doi: 10.1080/15563650.2019.1674322.
[8] Berling I, Isbister GK. Chlorpromazine overdose: a case series. Clin Toxicol. 2024;62(6):372–377. doi: 10.1080/15563650.2024.2367672.
[9] Decker BS, Goldfarb DS, Dargan PI, et al. Extracorporeal treatment for lithium poisoning: systematic review and recommendations from the EXTRIP workgroup. Clin J Am Soc Nephrol. 2015;10(5):875–887. doi: 10.2215/CJN.10021014.
[10] Buckley NA, Cheng S, Isoardi K, et al. Haemodialysis for lithium poisoning: translating EXTRIP recommendations into practical guidelines. Br J Clin Pharmacol. 2020;86(5):999–1006. doi: 10.1111/bcp.14212.
[11] Friedberg RC, Spyker DA, Herold DA. Massive overdoses with sustained-release lithium carbonate preparations: pharmacokinetic model based on two case studies. Clin Chem. 1991;37(7):1205–1209. doi: 10.1093/clinchem/37.7.1205.
[12] Achong MR, Fernandez PG, McLeod PJ. Fatal self-poisoning with lithium carbonate. Can Med Assoc J. 1975;112(7):868–870.
[13] van Gorp F, Whyte IM, Isbister GK. Clinical and ECG effects of escitalopram overdose. Ann Emerg Med. 2009;54(3):404–408. doi: 10.1016/j.annemergmed.2009.04.016.