SEMP

SOCIETY OF EMERGENCY MEDICINE PHARMACISTS

SEMP

ToxHack/s (Adme)

- Frank Paloucek BS, PharmD, FASCT, FASHP, eDABAT, Clinical Professor Emeritus UIC Retzky COP
- 8/12/26

Disclosures

No one involved in the development of this educational content has a relevant financial relationship to disclose

Case Introduction:

- 42 y/o M clinic referral in Friday AM for self reported ingestion of unknown amounts of hydroxyzine, fluoxetine, and ER 450mg $LiCO^3$ five hours prior. Denies ASA, APAP, illicits. B/C of past attempts, he get refills weekly.
- VSS, PE, initial POC labs all WNL except ASA 4.2mg % UDS (+ tca)
- Aggressive decon (lavage then AC) in ED, transferred to ICU (protocol for 1:1 care of active self-harm risk)
- Li Cps
  - (T0) HD#1 1.4 mEq/L
  - T+4 hrs 3.2mEq/L
  - T+8.5 2.7 mEq/L

  - Any questions? I'll answer up to three

SEMP

You have a great weekend!

But you have to return to work Monday

Paged (like I said an old case) to ICU

What is going on with your lithium patient?

Levels started increasing about 27hrs post admission, peaking at 5.0 mEq/L

- **Dialyzed**

Peaked again

- **Dialyzed again**

Best seen graphically

SEMP

What is going on?

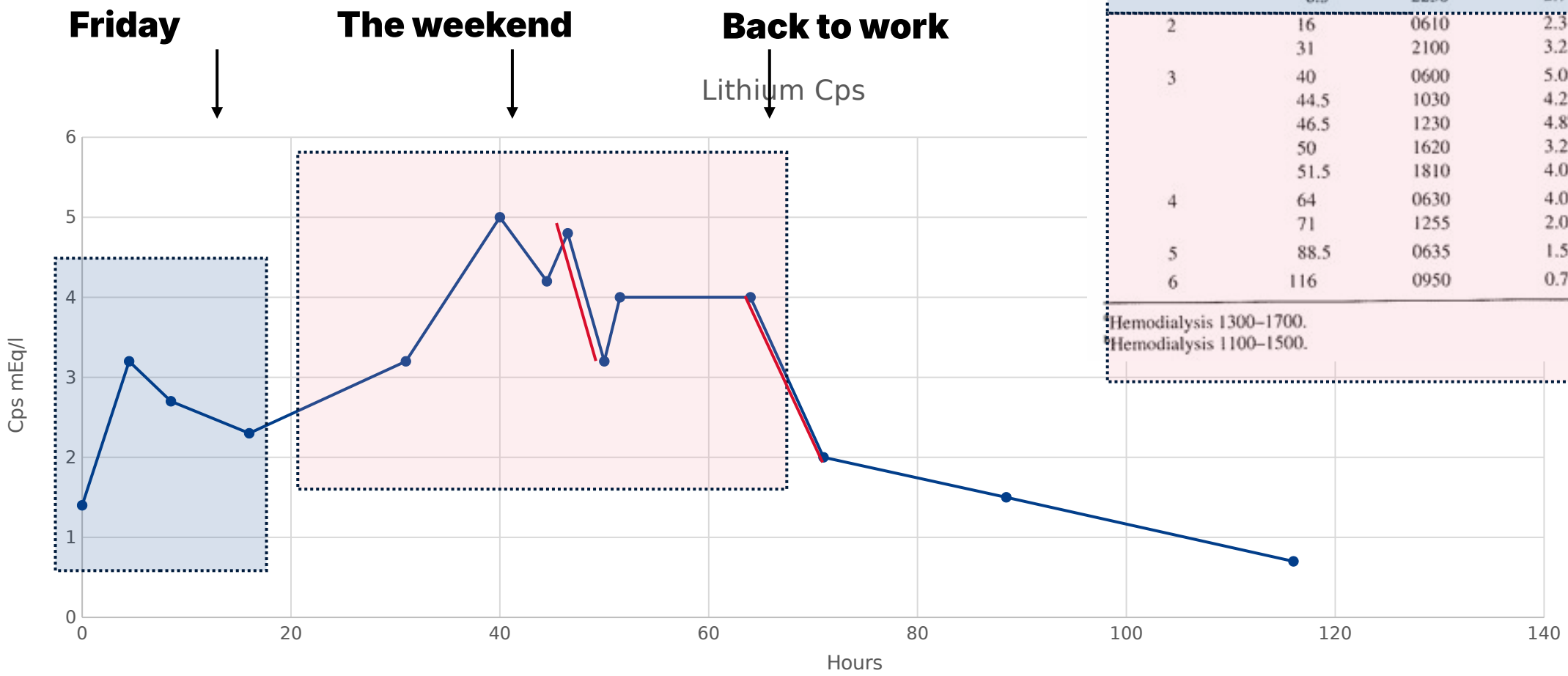


Table 1. Lithium Serum Concentrations

HOSPITAL DAY	TIME POSTADMISSION (h)	TIME OF DAY	CONCENTRATION (mEq/L)
1		1345	1.4
	4.5	1815	3.2
	8.5	2230	2.7
2	16	0610	2.3
	31	2100	3.2
3	40	0600	5.0
	44.5	1030	4.2
	46.5	1230	4.8[a]
	50	1620	3.2
	51.5	1810	4.0
4	64	0630	4.0[b]
	71	1255	2.0
5	88.5	0635	1.5
6	116	0950	0.7

[a] Hemodialysis 1300–1700.
[b] Hemodialysis 1100–1500.

SEMP

Polling Question #1

Based on the presentation and initial information, which *one* of the following events most likely explains what has happened to cause the initial rise?

1. **Discharged from the ICU to medicine floor**
2. **Lab error, whether processing, assay or reporting (always check units)**
3. **Lithium inadvertently ordered as maintenance medication**
4. **Surreptitious poisoning**
5. **Take 60sec to type answer in chat. Post with prompt**

Polling Question #2

Based on the presentation and initial information, which ***one* of the following investigations proved ***most*** useful in explaining the Cp vs time curve?**

1. **Activity and Dietary orders**
2. **Banning visitors**
3. **Repeating lithium CPs for unexpected results**
4. **Verifying charcoal dosing and administration**
5. **Take 60sec to type answer in chat. Post with prompt**

SEMP

Remember P1 year?

- Did you have mandatory pharmaceutics course/s?
  - Or Intro chemistry or physics or both ever?
- Ever been given FDA regulatory papers to read? Or sought them out to read?
- Do you know the FDA guidelines for determining if a drug qualifies as an immediate-release or an extended-released dosage form approved for human use?

SEMP

Lithium carbonate solubility

- Water at 40ºC — 1.08 gm / 100ml
- Ethanol at 30C — 0.140 gm / 100
- Simulated gastric fluid — at pH 1.2 complete
- Simulated intestinal fluid — 1.3 gm / 100ml

- What impact would diet have in assessing an overdose?

SEMP

FDA dissolution testing

1. Basket or Paddle method is to be used
2. Volumes of 500, 900 or 1000ml may be used
3. pH ranges of 1.2 (gastric) - 6.8 (intestinal)
4. Enzymes, e.g. pepsin or pancreatin, may be used pending review for justification
5. Water and hydro alcoholic media are discouraged
6. Immediate release 85% dissolution by 15min
7. Extended-release 85% dissolution by 45min

SEMP

Polling Question #2 (follow-up)

Based on the presentation and initial information, which ***one* of the following investigations proved ***most*** useful in explaining the Cp vs time curve?**

1. **Activity and Dietary orders**
2. **Banning visitors**
3. **Repeating lithium CPs for unexpected results**
4. **Verifying charcoal dosing and administration**

What was found

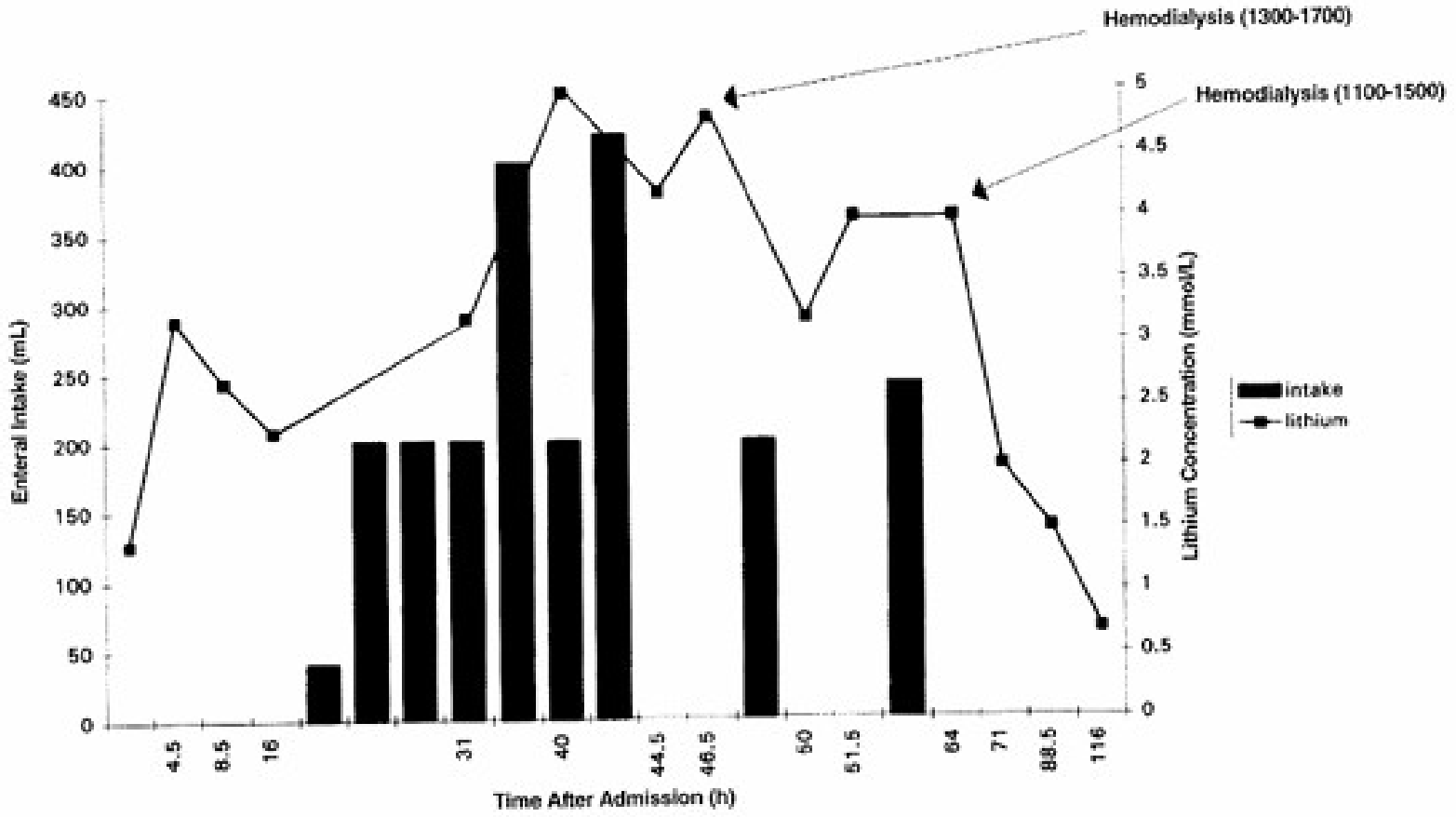


Figure 1. Enteral intake and lithium concentration versus time after admission.

Polling Question #1 (follow-up)

Based on the presentation and initial information, which ***one* of the following events ***most*** likely explains what has happened to cause the initial rise?**

1. **Discharged from the ICU to medicine floor**
2. **Lab error, whether processing, assay or reporting (always check units)**
3. **Lithium inadvertently ordered as maintenance medication**
4. **Surreptitious poisoning**

Summary of Key Learning Points

1. Toxicokinetics ≠ Pharmacokinetics
2. Reviewing known factors affecting dissolution may assist in anticipating irregular concentration time profiles, maybe even time of occurrence
    a) Coingested solvents
    b) Agents or conditions affecting motility and perfusion
    c) Body positioning and activity
    d) Enteral intake
    e) Changes occurring with disposition changes

Summary of Key Learning Points (cont)

3. Concentration profiles can be used to justify further intervention
    a) Continued or re-initiated gastric decontamination
    b) Elimination enhancement processes
3. New practice habits?
    a) Ingestion history to include liquid and food intake?
    b) Gut motility and perfusion
    c) Nutrition route
    d) Concentrations after d/c from ICU or start of enteral intake?
    e) Criteria for restarting decon or more RRT?

CLINICAL TOXICOLOGY
2019, VOL. 57, NO. 4, 271–281
https://doi.org/10.1080/15563650.2018.1513138

Taylor & Francis
Taylor & Francis Group

BASIC RESEARCH

Potential pharmacobezoar formation of large size extended-release tablets and their dissolution – an in vitro study

Lotte Christine Groth Hoegberg[a], Frank Refsgaard[b], Steen Hauge Pedersen[b], Mark Personne[c], Shahid Ullah[d], Georgios Panagiotidis[d], Tonny Studsgaard Petersen[e] and Anita Annas[c]

[a]Department of Anaesthesia and Intensive Care, The Danish Poisons Information Centre, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark; [b]Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark; [c]The Swedish Poisons Information Centre, Stockholm, Sweden; [d]Department of Laboratory Medicine, Division of Clinical Pharmacology and Karolinska University Laboratory, Karolinska University Hospital, Stockholm, Sweden; [e]Department of Clinical Pharmacology, The Danish Poisons Information Centre, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark

Table 1. Visual inspections of dissolution and pharmacobezoar formation of 30 tablets separated in each a nylon mesh bag, 30 tablets collected in one bag, and 2 tablets in one bag respectively of extended release tablets quetiapine/seroquel®XR 50 mg, paracetamol/pinex®retard 500 mg, verapamil/isoptin®retard 240 mg, and carbamazepine/tegretol®retard 200 mg, and immediate release tablets paracetamol/panodil®500 mg.

Generic name/ pharmaceutical	Observations (time, hours) 30 min	4 h	8 h	24 h	48 h	Additional comments
Quetiapine/Seroquel®XR 50 mg, 30 separated tablets	Intact tablets	Intact tablets	Intact tablets	Intact tablets	Complete disintegration	
Quetiapine/Seroquel®XR 50 mg, 30 collected tablets	Intact tablets	Pharmacobezoar formed	Pharmacobezoar	Pharmacobezoar	Complete disintegration	Strong sticky pharmacobezoar, solid for up to 24 h
Quetiapine/Seroquel®XR 50 mg, 2 collected tablets	Intact tablets	Intact tablets	Intact tablets	Intact tablets	Complete disintegration	
Paracetamol/Pinex®Retard 500 mg, 30 separated tablets	Intact tablets	Intact tablets	Intact tablets	Intact tablets	Eroded to smaller tablets	
Paracetamol/Pinex®Retard 500 mg, 30 collected tablets	Intact tablets	Pharmacobezoar formed	Pharmacobezoar	Pharmacobezoar	Pharmacobezoar partly disintegrated	Strong sticky pharmacobezoar
Paracetamol/Pinex®Retard 500 mg, 2 collected tablets	Complete tablet disintegration	–	–	–	–	
Verapamil/Isoptin®Retard 240 mg, 30 separated tablets	Swelled, intact tablets	Swelled, intact tablets	Swelled, intact tablets	Swelled, intact tablets	Swelled, intact tablets	
Verapamil/Isoptin®Retard 240 mg, 30 collected tablets	Swelled	Pharmacobezoar formed	Pharmacobezoar	Pharmacobezoar	Pharmacobezoar of sticking swelled tablets	Strong pharmacobezoar, but outer tablets tended to break off
Verapamil/Isoptin®Retard 240 mg, 2 collected tablets	Swelled, intact tablets	Swelled, intact tablets	Swelled, intact tablets	Swelled, intact tablets	Swelled, intact tablets	
Carbamazepine/ Tegretol®Retard 200 mg, 30 separated tablets	Complete tablet disintegration	–	–	–	–	Tablets disintegrated into microspheres
Carbamazepine/ Tegretol®Retard 200 mg, 30 collected tablets	Complete tablet disintegration	–	–	–	–	Tablets disintegrated into microspheres
Carbamazepine/ Tegretol®Retard 200 mg, collected tablets	Complete tablet disintegration	–	–	–	–	Tablets disintegrated into microspheres
Paracetamol/Panodil® 500 mg, 30 separated tablets	Complete tablet disintegration	–	–	–	–	
Paracetamol/Panodil® 500 mg, 30 collected tablets	Complete tablet disintegration	–	–	–	–	
Paracetamol/Panodil® 500 mg, 2 collected tablets	Complete tablet disintegration	–	–	–	–	

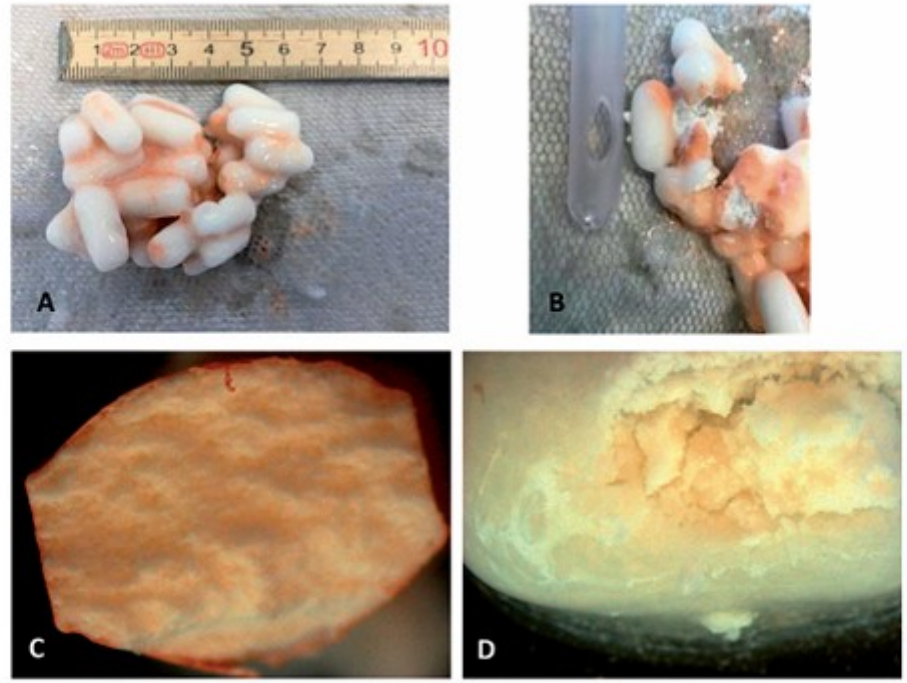
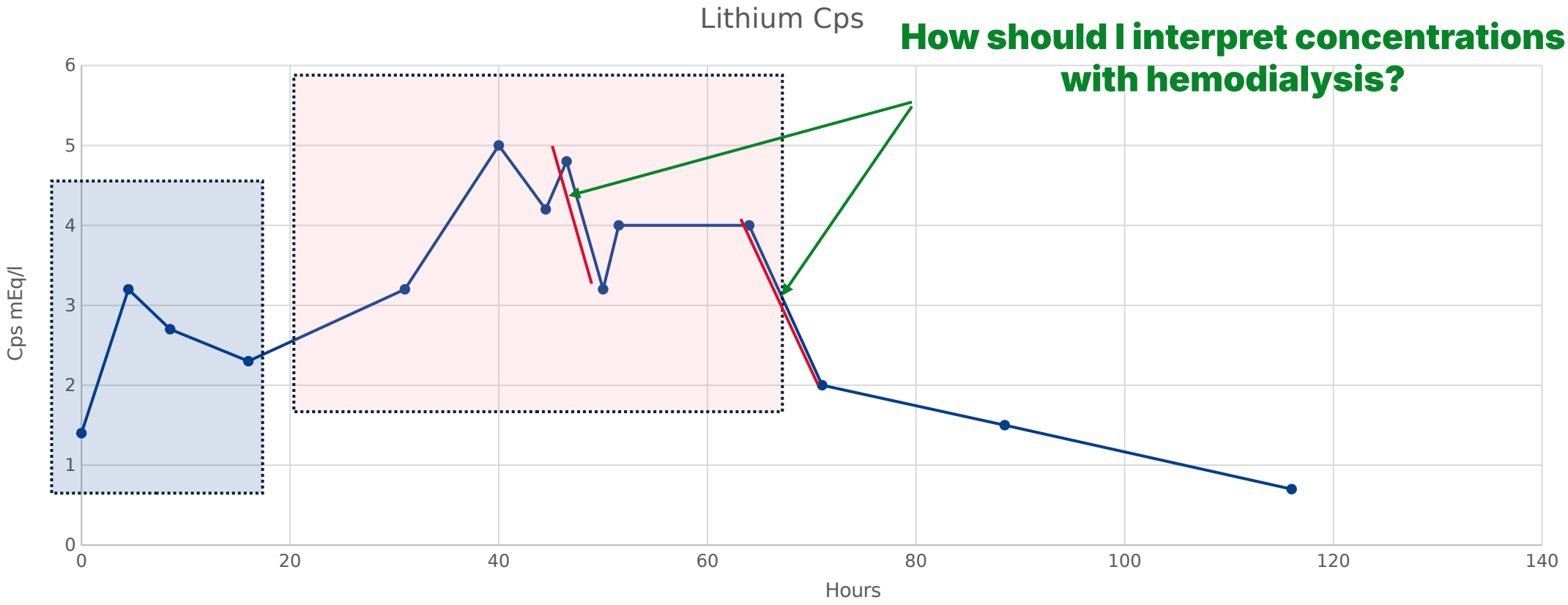


Figure 1. Visual inspection of the pharmacobezoar formation of quetiapine/Seroquel® XR 50 mg 30 tablets collected in one bag after incubation in simulated gastric fluid for 4 h (A), and compared to a 30F orogastric lavage tube (B). Light microscopy of one tablet show the polymer film coating material in the dry section (C) swelled in contact with simulated gastric fluid forming a diffusion controlled gel-layer surrounding the tablet, photo at 4 h (D).

References

1. Dupuis RE, Cooper AA, Rosamond LJ, Campbell-Bright S. Multiple delayed peak lithium concentrations following acute intoxication with an extended-release product. Ann Pharmacother. 1996 Apr;30(4):356-60. doi: 10.1177/106002809603000406. PMID: 8729888.
2. https://www.fda.gov/drugs/drug-approvals-and-databases/dissolution-methods-database
3. Hoegberg LCG, Refsgaard F, Pedersen SH, et al. Potential pharmacobezoar formation of large size extended-release tablets and their dissolution - an in vitro study. Clin Toxicol (Phila). 2019 Apr;57(4):271-281. doi: 10.1080/15563650.2018.1513138. Epub 2018 Oct 11. PMID: 30306811.
4. Any introductory chemistry and physics textbook you want.

By the way…if you liked this I have more



Thoughts or Questions?

- "Thank you. I am now ready for a Q&A and discussion session.“
- If I don’t get to see or hear your question, please feel free to contact me directly
  - Paloucek@uic.edu


That's all Folks!

Initial Data & Developments (1-2 slides; Approx. 2-3 minutes)

- Present initial key laboratory values (use tables, highlight critical abnormal findings).
- Show initial ECG (if central to the case, highlight key findings succinctly).
- Briefly mention crucial initial interventions or diagnostic steps.
- Interactive Element (brief, if used): "What is the most critical finding here?"

The Crossroads: Key Decision Point / Diagnostic Challenge (1 slide + Focused Deep Dive; Approx. 3-4 minutes total for this section)

- Clearly define the main challenge or critical decision point your case illustrates. This is the core of your presentation.
- Polling Question (optional, ensure it's quick): Pose a specific question to the audience related to this decision (e.g., "Given these findings, which of the following is the most appropriate next step?").
- Focused "Mini Deep Dive" (integrated within this section, 1-2 slides maximum):
  - Very briefly discuss essential pharmacology, pathophysiology, or toxicology directly pertinent to the decision point.
  - If citing literature, refer to 1-2 key pieces that directly inform this specific decision. Focus on the "why.

Case Progression & Management (1-2 slides; Approx. 2-3 minutes)

- Succinctly describe the critical actions taken and the patient's immediate response.
- Show essential follow-up labs, vitals, or other data that reflect the impact of interventions.
- Briefly highlight any further critical complexities or decisions that arose

Resolution & The Clinical Pearl (1-2 slides; Approx. 1-2 minutes)

- Describe the patient's outcome as it relates to your clinical pearl.
- Explicitly and Clearly State Your Clinical Pearl(s): This is the key takeaway message for the audience.
- Briefly explain the importance and applicability of this pearl for EM pharmacy practice.

Assessment Question #1

Add question with multiple choice answers, and rationale for correct answer

Assessment Question #2

Add question with multiple choice answers, and rationale for correct answer

Do you know what a pharmacobezoar is? Or a concretion? Pharmacolith?

Table 1. Lithium Serum Concentrations

HOSPITAL DAY	TIME POSTADMISSION (h)	TIME OF DAY	CONCENTRATION (mEq/L)
1		1345	1.4
	4.5	1815	3.2
	8.5	2230	2.7
2	16	0610	2.3
	31	2100	3.2
3	40	0600	5.0
	44.5	1030	4.2
	46.5	1230	4.8[a]
	50	1620	3.2
	51.5	1810	4.0
4	64	0630	4.0[b]
	71	1255	2.0
5	88.5	0635	1.5
6	116	0950	0.7

[a]Hemodialysis 1300–1700.
[b]Hemodialysis 1100–1500.