

# From Palliation to Recuperation: Phenytoin & Pharmacist to the Rescue

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## KEY LEARNING POINTS

1. Hypoalbuminaemia increases phenytoin toxicity risk

2. Phenytoin toxicity symptoms may present as seizure-related medical complications

3. Being cognizant of potential medication-causes of patient illness is crucial

4. Effective communication within multi-disciplinary teams leads to improved patient outcomes

## Overview

Phenytoin is a widely used, broadly effective anticonvulsant.<sup>1</sup> It is associated with significant adverse effects, in part due to its non-linear pharmacokinetics, resulting in its narrow therapeutic index.<sup>1,2,3,4,5</sup> It is essential to consider the impact of blood albumin levels on phenytoin pharmacodynamics.<sup>1</sup> This case review demonstrates how failure to consider this interplay nearly led to inappropriate patient palliation.

## Patient Journey

**Presenting complaint:** 63 y/o male RACF resident BIBA 2° status epilepticus (SE), fevers and GCS = 3, on the background of a medically managed seizure disorder, traumatic SDH and chronic alcohol misuse.

**Progress:** Ongoing poor GCS (fluctuating between 4-8) despite successful termination of SE, as confirmed by serial electroencephalograms. Four different anticonvulsants were prescribed including phenytoin, supposedly within therapeutic range. Treating medical team thought persistently low GCS 2° to hypoxic brain injury following prolonged SE, alcoholic encephalopathy, or a combination of both. Palliation was being considered at this point.

## Biochemistry

Total phenytoin level = 16mg/L (ref. range: 10 – 20)  
 Albumin level = <15g/L (ref. range: 35 – 50)

$$C_{\text{normal}} = \frac{C_{\text{observed}}}{0.02 \text{ ALB} + 0.1}$$

Corrected total phenytoin level = 40mg/L

**X2 OVERDOSE**

Current literature supports that phenytoin at toxic levels, may induce serious adverse effects such as increased sedation, depressed conscious state and coma<sup>2,3,4,5</sup>

## Phenytoin and Albumin in the Literature

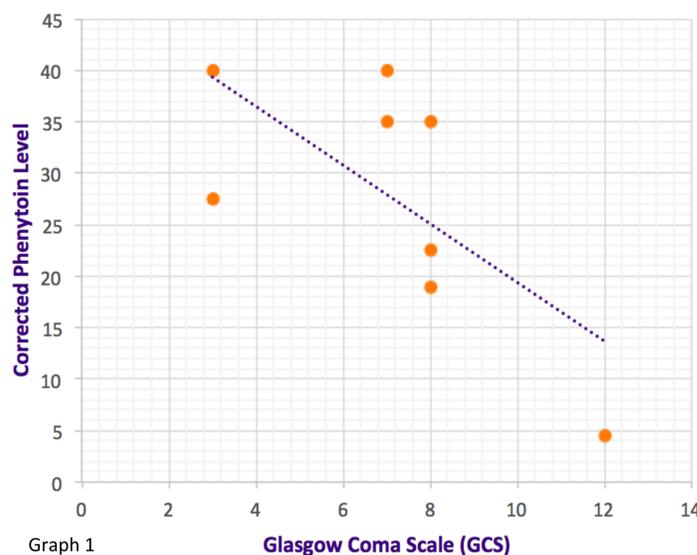
Total phenytoin concentration corrected for serum albumin is demonstrated numerous times in the literature to provide a safer basis for phenytoin toxicity monitoring.<sup>6,7,8</sup> Hypoalbuminaemia increases the unbound (free) phenytoin concentration, which increases the pharmacological activity of the administered dose. As such, despite blood-work displaying normal total phenytoin concentrations, active phenytoin levels may indeed be under-represented. It is crucial for treating teams, when determining safe phenytoin dosing, to consider that hypoalbuminaemia is a well-established, common cause of phenytoin toxicity.<sup>6</sup>

## Pharmacist to the Rescue

During multidisciplinary team meetings, the pharmacist raised the possibility of phenytoin toxicity contributing to the patient's low GCS, despite total serum phenytoin concentrations appearing to be within normal reference ranges. They communicated that due to the patient's hypoalbuminaemia, the corrected phenytoin level was indeed toxic.

The pharmacist recommended that palliation be suspended until the phenytoin blood levels decreased, and the resulting clinical effect on conscious state observed.

## A Remarkable Recuperation



Remarkably, as the phenytoin level decreased, the patient's consciousness improved linearly (Graph 1).

The patient was safely discharged home in approximately their pre-morbid state.

Ultimately, the pharmacist-initiated intervention prevented the inappropriate palliation of a patient who in fact had a reversible, drug-induced cause of a persistent decreased conscious state.

## References

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