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Phenytoin Dosing in the ED

Rapid Oral Phenytoin Loading

- Drug references say that an oral loading dose (15-20 mg/kg) of phenytoin should be administered in 3 divided doses given every 2 hours to decrease GI adverse effects and to ensure complete oral absorption. Who has time for 3 doses spanned over 4+ hours in a busy ED?
  - Trick of the trade: give the oral phenytoin load as a single dose
    - *Ann Emerg Med* 1987;16(4):407-12.
    - *Am J Hosp Pharm* 1980;37(2):232-5.
    - *J Neurol Sci* 1997;147(1):89-92.
  - If you're still uncomfortable giving a large single dose, there is also support for two-dose oral loading (which still cuts 2 hours off the ED stay compared to 3 doses).
    - *Ann Neurol* 1979;5(3):268-70.

Partial Loading

- A variation of the Winter-Tozer equation can be used to approximate a partial loading dose in patients with subtherapeutic phenytoin levels (Martin, et al. J Pharmacokinet Biopharm 1977;5(6):579-96.)
  - Take the resulted lab value (initial concentration)
  - Determine the desired concentration (usually 15 mg/L - midpoint of the 10-20 range)
  - $\Delta Cp = Dose * S / Vd$
    - ΔCp = (Final concentration - Initial concentration)
    - Dose = Loading dose of drug (mg)
    - S = Salt form (0.92 for phenytoin sodium or fosphenytoin)
    - Vd = Volume of distribution (L/kg)

Total vs Free Levels in the ED

- Free phenytoin levels used to be much more expensive than total levels. That doesn't seem to be the case any more.
- In most ED patients presenting with seizure and history of being on phenytoin, the level usually results as undetectable. So, in most cases a total level is adequate.
- A free level may be helpful in critically ill ED patients (eg, status epilepticus) or patients with potentially low albumin levels (eg, malnourished, liver disease).

Albumin

- Here is how to correct for hypoalbuminemia (Kane SP, et al. Ann Pharmacother 2013;47(5):628-36.)
  - Corrected phenytoin = (Measured phenytoin) / 0.29 * Albumin + 0.1
- If CrCl < 10 mL/min or hemodialysis:
  - Corrected phenytoin = (Measured phenytoin) / 0.1 * Albumin + 0.1

Adjustment for Obesity

- Not much data on adjusting phenytoin doses in obese patients (Abernethy DR, et al. Arch Neurol 1985;42(5):468-71.)
  - Dosing weight = (Ideal weight) + [1.33 * (Actual weight – Ideal weight)]