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Reference: Shively RM et al. Acute salicylate poisoning: risk factors for severe outcome. Clin Toxicol (Phila) 55(3), 175-180. 2017.

Question/Objective: "We aimed to establish early predictors of severe in-hospital incomes in Emergency Department patients presenting with acute salicylate poisoning."

Introduction:

- Salicylate is one of the most commonly used drugs
- In 2014, over 24,000 exposures noted, with morbidity/mortality rates as high as 30%
- Mortality rates for those admitted to the hospital with undiagnosed salicylate poisoning is THREE TIMES greater than if diagnosed in the ER
- 1960s—Done nomogram devised to predict severe outcome—validation studies failed—no longer used
- Clinical factors associated with severe outcome = age, CNS features, metabolic acidosis, delayed diagnosis
- Given previous studies, they hypothesized that serum salicylate concentration, age, elements of the BMP, and coma would predict severe outcomes

Methods:

- Secondary analysis of salicylate overdoses from a retrospective cohort study of suspected acute drug overdoses initiated on consecutive adult ER patients from 2009-2013
- Two urban, tertiary-care hospitals; only confirmed salicylate overdoses were screened for inclusion
- Exclusion criteria—alternative diagnosis, chronic presentation, nondrug overdose, dermal or inhalational exposures only, age less than 18 yo, anaphylaxis, patients with incomplete data, DNR orders
- Because this study aimed to determine early clinical predictors for demise, a repeat salicylate level was not noted or pursued; only the initial level was utilized
- Severe outcome = acidemia (pH <7.3 or bicarb <16), hemodialysis, death

Results:

- Over the course of the study, 1997 suspected acute drug overdoses, 50 were included, 48 were left over after 2 were excluded for age less than 18 yo
- 43.8% male, median age 32, mean initial salicylate concentration 28.1 mg/dL
- 10 had severe outcomes—2 died, 2 hemodialysis, 7 met acidemia criteria
- What was associated with severe outcome? [univariate analysis]
    - Age ($p = 0.04$)
    - RR ($p = 0.04$)
    - Lactate ($p = 0.002$)
    - Coma ($p = 0.05$)
    - Co-ingestion ($p = 0.04$)
- What was the independent risk factor associated with severe outcome? [multivariate logistic regression]
    - Age (95% CI 1.02-1.26)
    - RR (95% CI 1.02-1.63)

- **Initial salicylate concentration NOT PROGNOSTIC**

Discussion:

- This study allows us to initiate more aggressive treatment for those at the highest risk of morbidity and mortality
    - Sodium bicarbonate
    - Hemodialysis
    - ICU admission
- Co-ingestions, CNS features also associated with severe outcome but not so when adjusted for initial salicylate concentration
- The strongest predictor of severe outcome was initial RR elevation; results from 2 pathophysiologic processes:
    - Direct stimulation of the medullary respiratory center
    - Uncoupling of oxidative phosphorylation → CO_2 production → indirect stimulation of respiration via chemoreceptors
- Increasing age portends poor prognosis for many reasons:
    - Poor physiologic reserve
    - Presence of comorbidities
    - Alteration of drug kinetics
    - End-organ sensitivities to drugs
- This was the first study to find that lactate was a significant predictor for severe outcome in salicylate toxicity specifically; however, statistical significance disappeared when adjusted for initial salicylate concentration
    - Levels >2.25mmol/L
- Although initial salicylate concentration did not predict morbidity/mortality in this specific study, the smaller sample size and lower initial serum concentrations may have played a role; trending a rise or decrease in salicylate level in the first few hours of resuscitation remains critical in prediction of mortality and morbidity
- **BOTTOM LINE: Even if the initial serum concentration of salicylate is low, if AGE is high and/or if RR is high, if lactate is high, TRIAGE to HIGHER LEVEL OF CARE**

Limitations:

- Smaller sample size
- Urban center → can you extrapolate to non-urban, non-teaching environments?
- Lower serum concentrations than other salicylate toxicity studies → may rise over time?
- Co-ingestions not always identified
- RR based on hospital protocol, no confirmation by standard protocol → may vary?
- Not applicable to chronic salicylate toxicity nor pediatric ingestions