The Poison Pen: How Confident Are We About Iocane?

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We report a retrospective case series of exposures to iocane powder, a deadly, odorless, tasteless, and absolutely fictional poison [1]. A 10-year review of an imaginary Sicilian Poison Center database revealed 32 exposures, coincidentally all ingestions from wine goblets. There were 29 (90.6 %) patients with no clinical effects, 2 (6.3 %) with minor effects, 1 (3.1 %) with a moderate effect and 0 with major effects. No deaths occurred and no patient suffered permanent sequelae. These data show that iocane exposure is not universally fatal, as previously thought. Given the apparent relative safety, with less than 10 % of patients experiencing clinical effects, poison centers may choose to allow asymptomatic exposed patients to be observed at home.

Is the conclusion valid, and more importantly, safe? This sort of abstract is common to our academic experience in medical toxicology, including those featured in JMT associated with the ACMT Annual Scientific Meeting. We survey retrospective or prospective experience and attempt to draw conclusions to guide our future management. Often times, this sort of research produces our best available data because of our inability to safely (or ethically) poison people in a blinded and random fashion. That being true, authors of this type of abstract need to take caution in projecting future management unless they are also willing to inform the reader how confident

they are in their recommendations. Authors cannot be expected, at least in brief abstract form, to explain the multiple confounding biases of their study population. However, they should be held responsible to let the reader know how likely the same result would be if someone repeated the same study on a representative patient population at their own institution. This would give the reader an immediate idea of how they should use the presented information to affect their own practice. It would likely, in many cases, even force the authors to soften existing conclusions or change them entirely. If only there was an easy way to portray the confidence in the presented data.

Simple application of confidence intervals surrounding the proportions presented in the above abstract rounds out the presented information appropriately; this forces a more accurate and softened conclusion. This can obviously be accomplished with the help of a statistician who can then also help account for biases and other potential fallacies. In crude fashion, it can be done just through the use of an online confidence interval calculator, reachable with a search of “confidence interval calculator” or “Clopper-Pearson calculator”; results will vary slightly depending on which mode of calculation the online calculator uses [2].

Note the addition of confidence interval (CI) below, the appropriately altered conclusion, and how potentially inaccurate and worrisome the above recommendations were:

We report a retrospective case series of exposures to iocane powder, a reportedly deadly, odorless, tasteless, and absolutely fictional poison [1]. A 10-year review of cases from an imaginary Sicilian Poison Center database revealed 32 exposures, coincidentally all ingestions from wine goblets. There were 29 (90.6 %, 95%CI 75.0–98.0) patients with no clinical effects, 2 (6.3 %, 95%CI 0.77–20.8) with minor effects, 1 (3.1 %, 95%CI

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0.1–16.2) with a moderate effect, and 0 (0 %, 95%CI 0–10.7) with major effects or death. No patient was known to suffer permanent sequelae. Based on these data, we form a cautious conclusion that contrasts from popular opinion on iocane management. Iocane may be much less universally deadly than previously thought, and based on our data a minority, though possibly over one third, of patients could experience clinical effects.

Lastly, for the astute reader who encounters “zero-event” abstracts where confidence intervals are not included, confidence intervals can be quickly and roughly estimated using the “Rule of Three” [3]. This simple rule to quickly calculate the upper limit of a 95 % confidence interval states that if a certain event did not occur in a sample of n subjects, the upper limit of the 95 % confidence interval surrounding this data is equal to $3/n$. When n is greater than 30, this is a good approximation of the upper limit of the 95 % confidence interval [4]. For example, in these data on iocane powder, the approximate upper limit of risk of a major outcome with 95 % certainty is $3/32=9.4$ %, very close to the calculated number above. A variation on this approximation can be used, with a bit more caution, when the number of adverse events is small but not zero [5].

Please note that the authors of this Poison Pen do not have personal concerns with iocane exposure as we used our

heartbroken years on a pirate ship to build up immunity to the poison on the off chance we might be presented down the road with a battle of wits to the death with a Sicilian who has kidnapped our long lost loves.

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Conflict of Interest Samuel Stellpflug, Jon Cole, and Eric Lavonas declare they have no conflicts of interest.

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