The Role of Chemical Analysis in Causality Assessment of Herbal and Dietary Supplement (HDS) Induced Liver Injury

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Introduction

- Drug Induced Liver Injury (DILI) is difficult to diagnose especially in the setting of HDS which may have inaccurate labels and undisclosed ingredients.
- The U.S. DILI Network (DILIN) determines likelihood of DILI & attribution of injury to an agent through structured consensus causality assessment with expert opinion; however, chemical analysis of the HDS implicated in liver injury have not been available until recently.

Aim

- To determine the impact of chemical analysis data on causality assessment scores.

Materials & Methods

- 56 DILIN cases in which HDS were consumed by patients and available for chemical analysis were reassessed for causality using chemical analysis data.
- HDS were analyzed by high performance liquid chromatography – mass spectrometry. Products were evaluated for the presence of selected botanical and non-botanical hepatotoxins, as listed in Table 1.
- Overall case likelihood of DILI and agent (HDS) specific causality scores were assigned as a probability: definite (>95%); very likely (75-94%); probable (50-74%); possible (25-49%); and unlikely (<25%) DILI.
- Reviewers were blinded to original causality scores.
- Overall case causality scores (likelihood of DILI) derived with chemical analysis were compared to original scores.

Results

Botanical	Non-Botanical
Ashwagandha	Alfatoxins
Green Tea Extract	Pyrrolizidine
Garcinia Cambogia	Anthraquinones
Polygonum Multiflorum	EGCG/Caffeine
Chinese Skullcap	Anabolics
Kratom	Pharmaceuticals

Table 1: Specific hepatotoxins evaluated for by chemical analysis

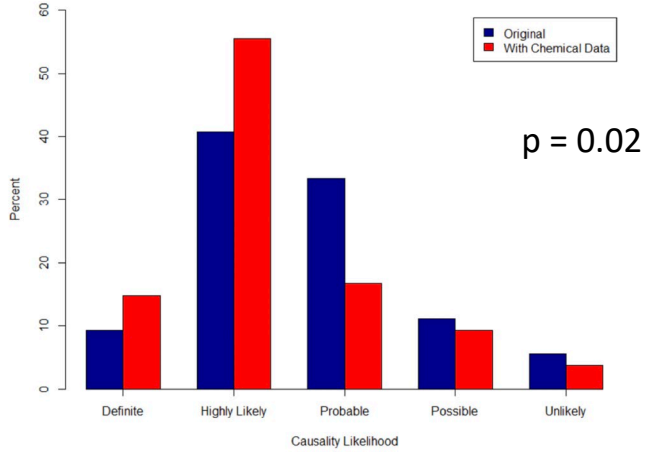

Figure 1: Bar graph representation of percent change in overall case causality scores (likelihood of DILI) with use of chemical analysis data

- Using chemical analysis data:
  - 37% of cases were scored with a higher likelihood of DILI compared to the original causality scores
  - 52% of cases had no change in causality score
  - 11% of cases were scored as lower likelihood of DILI.
- The percent likelihood of DILI was higher (p=0.02) in cases assessed with use of chemical analysis than those without (fig 1).
- Two cases were excluded as new information became available since original scoring.

Conclusions

- There is value in using HDS chemical analysis data in the causality assessment process for DILI.
- In over a third of cases, chemical analysis led to an increase in confidence of attribution of DILI to HDS.
- Chemical analysis data can effectively supplement clinical and historical information in the causality assessment process.
- Further studies are needed to explore its applicability in clinical practice; widespread utilization depends upon retrieving HDS from patients, and the availability of reliable analytical methods.

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