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GENERAL REVIEW

Toxicodynetics: A new discipline in clinical toxicology

Toxicodynétique : une nouvelle discipline en toxicologie clinique

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Summary
Objectives. — Regarding the different disciplines that encompass the pharmacology and the toxicology, none is specifically dedicated to the description and analysis of the time-course of relevant toxic effects both in experimental and clinical studies. The lack of a discipline devoted to this major field in toxicology results in misconception and even in errors by clinicians.
Material and methods. — Review of the basic different disciplines that encompass pharmacology toxicology and comparing with the description of the time-course of effects in conditions in which toxicological analysis was not performed or with limited analytical evidence.
Results. — Review of the literature clearly shows how misleading is the current extrapolation of toxicokinetic data to the description of the time-course of toxic effects.
Conclusion. — A new discipline entitled toxicodynetics should be developed aiming at a more systematic description of the time-course of effects in acute human and experimental

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poisonings. Toxicodynetics might help emergency physicians in risk assessment when facing a poisoning and contribute to a better assessment of quality control of data collected by poison control centres. Toxicodynetics would also allow a quantitative approach to the clinical effects resulting from drug—drug interaction.

MOTS CLÉS
Pharmacocinétiques ;
Pharmacodynamie ;
Toxicocinétique ;
Toxicodynamie ;
Toxicodynétique ;
Surdose ;
Intoxication

Résumé
But/objectif. — L'étude des différentes disciplines participant à la définition de la pharmacologie et de la toxicologie montre qu'aucune n'est spécifiquement dédiée à l'analyse et l'étude de l'évolution dans le temps des effets toxiques aussi bien dans les études expérimentales que dans les études cliniques. L'absence d'une telle discipline est à l'origine d'erreurs conceptuelles avec retentissement clinique.
Matériels et méthodes. — Revue des différentes disciplines qui composent la pharmacologie et la toxicologie médicale et comparer la description des effets toxiques apportée par la toxicodynétique à celle apportée par les études toxicocinétiques en privilégiant l'étude de cas où l'analyse toxicologique n'a pas été faite ou de façon incomplète.
Résultats. — La revue de la littérature montre les erreurs résultant de l'extrapolation à la clinique de données pharmaco/toxicocinétiques.
Conclusion. — Une nouvelle discipline appelée toxicodynétique, néologisme provenant de la contraction de l'étude cinétique d'effets toxiques, permet une systématisation de la description des intoxications aiguës dans un contexte expérimental ou clinique. La toxicodynétique est une méthode d'évaluation de risque qui serait utile au médecin urgentiste prenant en charge des intoxications. Elle contribuerait aussi à évaluer la qualité du recueil des informations collectées par les centres antipoison. Elle permet aussi une approche quantitative du résultat clinique des interactions médicamenteuses.

Introduction

The clinical status of the patient is paramount, and mathematical formulas and equations can never substitute for evaluating the patient!
Mary Ann Howland [1].

In modern medicine, consistent efforts have been made to harmonize data collection in order to clarify definition of diseases, grading severity, and facilitate comparisons between centers and countries. This effort was done in a number of medical specialties including emergency medicine with the description of events occurring during the onset of cardiac arrest using the ''Utstein style'', and cardiology. In pharmacovigilance, efforts were made to harmonize and improve the quality of case reports to increase the likelihood of causation of adverse drug reactions, including drug—drug interactions [2—4]. Interestingly, the time-course of effects is of paramount importance when looking at the causation of a drug in any adverse reactions. In clinical toxicology, a number of efforts were done regarding the out-of-hospital management of a number of poisonings. Clear information is required to refine the time-course of the events of each recorded case with a particular attention paid to the delay between exposure and the moment of phone call. Differences in collecting data have been consistently reported suggesting the need for National guidelines to reduce variations in poisoning management [5]. Guidelines were recently published for reporting case studies on extracorporeal treatments used during the course of poisonings [6]. According to authors' recommendations, these guidelines aimed at improving the completeness and transparency of published case reports allowing the systematic aggregation of information from case reports. For this purpose, no less than 114 items were considered mandatory for case study reporting. However, we are not aware of such an effort to report on more basic poisonings not requiring extracorporeal treatments.

In clinical toxicology, while the effects of toxic substances are well described, the time-course of the effects are described in only a limited number of poisonings, including paracetamol [7], colchicine [8], iron [9], organophosphates [10], and corrosive [11] ingestion. In contrast, in current practice in acute poisonings, the quality of reports of the time-course of effects depends on the phase of poisoning. In emergency medicine, and initial call to the PCCs, the time of ingestion (time zero), the supposed ingested drugs, the delay in onset of signs and symptoms, the rapidity of worsening and the magnitude of maximal