PROTOCOLS

Adverse drug reactions – Serious and life-threatening

Principal investigator

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Background

It is simply impossible to identify all the unintended consequences of drugs before they are marketed. This is due to the inherent limitations of pre-market clinical trials, the individuality of drug effects in humans and the unlikelihood that rare adverse drug reactions (ADRs) will be detected in patients studied before a drug is approved. The economic cost of drug-related morbidity and mortality in the United States has been estimated to be between $30 billion and $130 billion annually.[1]

Of particular concern is the alarming lack of understanding of ADRs in children, as only a few reports have described the problem in this population.[2-4] Pre-marketing trials often do not include children who may be at risk for unique ADRs, or an increased frequency of ADRs compared with the general population.[5] According to Health Canada and the United States Food and Drug Administration, less than 25% of marketed drugs can be advertised as safe and effective for use in infants and children.[6] A Boston collaborative study recently confirmed that, statistically, the potential adverse drug event rate is significantly greater in paediatric patients compared to adults.[7] Other factors, such as the inability of many children to evaluate and express their own response to medications, also increase the risk of ADRs in children.[8]

Clearly, more accurate information is needed to understand both the scope of the problem and the true incidence of adverse reactions that affect paediatric patients in Canada. Individually, unexpected and serious ADRs are relatively uncommon. Collectively however, they can number in the hundreds or even thousands and are an important cause of morbidity and mortality. In the United States, it is estimated that fatalities due to ADRs are the fourth to sixth leading cause of death in American hospitals.[9] While there is no national data regarding the problem of adverse drug reactions in Canadian hospitals, some information is available from British Columbia's Children's Hospital.

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The Canadian and American health-care systems have relied steadfastly on the idea of a voluntary surveillance system for the identification and reporting of serious ADRs. A major criticism of voluntary surveillance systems by health-care professionals has been the high level of under-reporting. Health-related accreditation bodies estimate as many as 95% of all adverse drug events are not reported, supporting the need to stimulate reporting on a large-scale basis.[10,11] In 2011, the Canada Vigilance Program received 28,675 domestic reports of suspected adverse drug reactions for all ages. Of these reports, 1,612 (approximately 6%) were paediatric.[12]

The degree of under-reporting is even more impressive, given that in the year 2000, children aged 0-19 years made up 25.5% of the total Canadian population.[13] Through the Canadian Paediatric Surveillance Program (CPSP), directed at paediatricians and paediatric subspecialists, the number of reported ADRs will increase. This study will use the CPSP active surveillance methodologies to generate cases from a large and geographically diverse paediatric population to derive meaningful data, address related public health concerns and improve our understanding of the scope of the ADR problem in this population.

Methods

Case ascertainments and reporting: Paediatricians and subspecialists who report cases through the CPSP monthly survey will receive this ADR protocol, including the surveillance case definition below, and will be asked to complete detailed reporting forms for all identified cases. Reports will be forwarded to the Marketed Health Products Directorate (MHPD) on a regular basis.

Case definition

Serious and life-threatening adverse drug reactions (ADRs)* in an infant or child 18 years or less, associated with the use of prescription, non-prescription, biological (immunoglobulins) products, complementary medicines (including herbals), and radio-pharmaceutical products.

Report even if you are not certain if the product caused the adverse reaction or you do not have all the reporting details.

Exclusions: Do not report reactions due to medical devices, blood products (platelets, red cells, single donor plasma), vaccines, poisonings or self-administered overdoses.

*** Noxious and unintended severe** response to a drug which occurs at any dose and results in emergency observation, hospitalization, persistent or significant disability, or death.

Adverse drug reactions – Serious and life-threatening (continued)

Objectives

- To identify the products most frequently causing ADRs in children, the type of reactions encountered, as well as the characteristics of those affected.
- To identify serious and life-threatening paediatric ADRs not currently captured by Health Canada's Canada Vigilance Program.

Duration

Starting date: January 2004 (continuing project).

Expected number of cases

The maximum expected number of cases is 500 per year.

Ethical approval

University of British Columbia Behavioural Research Ethics Board

Analysis and publication

Data will be analysed by the principal investigator, and annual reports (along with quarterly updates) will be distributed to CPSP participants. *"CPSP Tips of the Month"* will also provide ongoing feedback information about the project.

The results of this prospective surveillance study will be presented at Canadian conferences as well as international meetings. Data will also be published in peer-reviewed paediatric journals.

References

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