The Epidemiology of Serious Adverse Drug Reactions Among the Elderly

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Abstract

Although the incidence and prevalence of serious adverse drug reactions (ADRs) in the elderly cannot be accurately stated, published estimates appear to be unchanged since the earliest reports in the 1960s. Whereas heightened awareness of the problem may weigh in favour of a reduction in ADR frequency, the dramatic increase in the number and availability of therapeutic agents has undoubtedly contributed to the observed high proportion of drug-induced morbidity among acute geriatric hospital admissions. No single drug or drug class is of particular concern since none appears to cause serious morbidity out of proportion with its use.

Although numerous studies have sought to identify risk factors for ADRs, the only truly independent predictor is the absolute number of concurrently used medications. However, other studies indicate that there is poor doctor-patient agreement regarding a patient’s drug regimen, and interventions that aim to...
reduce the incidence of ADRs have failed to demonstrate a positive effect. Thus at present the most rational approach would appear to be to establish an accurate knowledge of the patient’s drug regimens: once this is known one can attempt to rationally minimise the number of medications without compromising therapeutic goals.

Data from the US and the UK indicate that the elderly constitute between 10 and 18% of the population but account for 25 to over 39% of drug prescription costs,[1-6] and for up to 40% of nonprescription drugs dispensed.[7,8] Although drugs contribute significantly to the treatment of diseases prevalent in the elderly, adverse drug reactions (ADRs) also occur more commonly in this age group, and are implicated in 10 to 20% of acute geriatric admissions.[9]

In the 1970s in the US, it was estimated that up to 140 000 deaths per year resulted from ADRs,[10,11] and 1 in 7 of all hospital days was spent caring for patients experiencing drug toxicity.[12] A more recent meta-analysis of ADRs among hospitalised patients in the US estimated that in 1994 over 2 million hospitalised patients experienced serious ADRs and over 100 000 experienced fatal ADRs, making these events between the fourth and sixth leading cause of death.[13] In Australia, it was estimated that ADRs accounted for 20 000 to 26 000 hospitalisations in 1987 to 1988, at a cost of $AU55 million to 69 million.[14] Although some view these claims as exaggerations, caused partly by the lack of ADR causality definitions,[15] they do highlight a significant problem.

Every form of medical intervention, including drug therapy, carries some level of risk, and patients with complicated disease are more likely to have adverse events, if only because their care requires more intervention.[16,17] The elderly are at increased risk because of multiple comorbidities, diminished physiological reserve and increased number of drugs taken. In 1969, attempts were made to quantify drug-related admissions,[18,19] and to identify predisposing factors.[20] Unfortunately, despite numerous other studies over subsequent years, drug-related hospital admissions are still a problem for internal medicine, and the problem has not diminished since the first reports.[21] It has become evident that continual measurement and publication of the prevalence of ADRs does nothing in itself to redress the problem, and despite growing consumer advocacy in recent years, no programme has been developed which demonstrates efficacy in reducing drug-related morbidity.

1. Definitions

An ADR may be defined as ‘any response that is noxious and unintended and that occurs at doses normally used in man for diagnosis, prophylaxis or therapy, and excluding a failure to accomplish the intended purpose’.[10,22,23]

1.1 Types of Adverse Drug Reaction (ADR)

ADRs are classified into 2 main types, type A or type B.[24,25] Type A effects are those to be expected from the pharmacological properties of the drug, such as bleeding when taking warfarin or hyperkalaemia with spironolactone. These reactions occur more often in patients who are unusually sensitive to the known pharmacological properties of the drug. They are not uncommon at normal doses and are dose-dependent. Type A reactions occur in individuals lying at the extremes of dose-response curves for pharmacological effects.

In contrast, type B reactions are the unexpected ones, which, while much less common than type A reactions, are usually associated with a higher proportional morbidity and mortality. Type B reactions are not dose-dependent, are not related to the drug’s known pharmacological properties and do not improve when the dose is reduced; the drug must be withdrawn. These reactions are often immunologically mediated (e.g. anaphylactic shock), or may have a genetic basis (e.g. malignant hyperpyrexia).[24,25]

Additional classifications are type C adverse reactions, which are those associated with long term