

# Drug treatment as a cause of hospital admission

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Recently, the health section of the BBC website proclaimed:

## Medicines 'killing 10,000 people'

More than 10,000 Britons may be dying each year because of bad reactions to medication, a study suggests.<sup>1</sup>

The study in question was conducted by Pirmohamed *et al.* in Liverpool, and represents the largest prospective analysis in the UK of ADRs as a cause of admission to hospital.<sup>2</sup>

## BACKGROUND

Previous published work has suggested that the rate of hospital admissions arising as a direct consequence of ADRs is around 5%.<sup>3</sup> In a publication from the USA, Lazarou *et al.*<sup>4</sup> reported a meta-analysis suggesting that ADRs caused over 100,000 admissions annually although heterogeneity of the studies and small biases in the samples may have affected the results. Most UK studies were performed 10–30 years ago and have been relatively small.

## THIS STUDY

Pirmohamed *et al.* undertook a prospective analysis of admissions caused by ADRs in two large UK hospitals to define prevalence and outcome, and to assess causality and preventability. All adults admitted to either hospital over a six month period were assessed to determine if admission had been caused by ADRs. Adverse drug reaction was diagnosed if the cause of admission was consistent with known adverse effects of the drug, if there was a temporal relationship with the start of drug therapy and if investigation excluded other causes. Causality and avoidability were assessed using established methods. The

main outcome measures were the prevalence of admissions due to an ADR, length of stay, avoidability and patient outcome.

## OUTCOME

Over six months there were a total of 18,820 admissions, and 1,225 were related to ADRs, giving a prevalence of 6.5%. Eighty percent of the ADRs were judged to have been directly responsible for the admission. Patients admitted with ADRs (median age of 76 years) were significantly older than patients without ADRs (66 years). The median bed stay for patients with ADR-related admissions was eight days, accounting for 4% of the hospital bed capacity, and the projected annual cost of such admissions to the NHS in England was £466 million. Although most patients admitted with ADRs recovered, 28 (2.3%) died as a result of the index ADR. The overall fatality rate was 0.15%.

## COMMENT

These figures for the prevalence and fatality of admissions due to ADRs are similar to previous findings, and, as the authors point out, it is disappointing that rates have not fallen. While this study has limitations, including the subjectivity of deciding whether an individual admission is drug-related and the difficulty in determining causal relationship, and while it focuses on harm rather than benefit, it serves as a reminder that many aspects of drug therapy require careful consideration and review. Why might this be, and what can be done to improve the situation?

### Individual drugs

The drugs commonly implicated as the cause of ADRs in this study were; non steroidal anti-inflammatory drugs,

diuretics, warfarin, ACE inhibitors, antidepressants,  $\beta$ -blockers, digoxin and opioids. While no drug usage data were available and ADR rates cannot be given, it is worth noting that it is not new drugs that are still causing problems. This is consistent with previous studies.<sup>5</sup> The most commonly implicated drug was aspirin which caused 18% of 1,225 ADR-related admissions, and 74% of patients were taking a small dose (75 mg daily).

#### Avoidability of ADR, including interactions

In this study only 28% of the 1,225 ADR-related admissions were assessed as unavoidable, while 9% and 63% were classified as 'definitely' and 'possibly' avoidable, respectively. One-sixth of admissions were due to drug interactions such as aspirin and warfarin causing GI bleeding, diuretic and ACE inhibitor causing renal failure. Most of these interactions are well-known. Accordingly, measures need to be deployed to improve this situation including:

- Improved education of prescribers. This is vital now that there are new categories of prescribers;<sup>6</sup>
- Regular medication review in primary care; and
- Appropriate use of decision support and information systems.

#### Older people

Older people suffer from age-related illness, and stand to gain much from modern medicines, but they are also at risk from ADRs. This has been confirmed in the present study. There are multiple and complex reasons for the increased frequency of ADRs in these patients, including poor prescribing, polypharmacy, altered drug handling and response, and poor compliance. However, care is required in interpreting what appear to be ADRs. There may, for example, be uncertainty as to when and whether drugs have been taken, and confounding factors include the situation in which a drug reaction and the disease for which the drug has been given cause the same clinical features (confounding by indication). Some simple prescribing guidelines can significantly help to minimise the extent of the clinical problem:

- Strive for a precise diagnosis and avoid giving a drug for each symptom;
- Avoid complex drug regimens;
- Know a few drugs well, including when reduced doses are indicated; and
- Explain the nature and duration of therapy to the patient or carer.

#### Shared responsibility, including patients

The imperative to reduce the number and severity of ADRs is a shared responsibility, presenting a considerable challenge to doctors, pharmacists and nurses. Investment in information technology is needed, for example electronic prescribing systems to support safer practice and powerful integrated drug safety databases to investigate signals giving early warning of drug toxicity. Sharing of safety data by prescribers, the regulatory authority, researchers and the pharmaceutical industry is highly desirable. Patients, as the consumers of medicines, need more easily accessible information about medicines and their side-effects. Better communication between health professionals and patients about the balance between the likely benefits and the potential risks of medicines is essential.

#### KEYPOINTS

- Adverse reactions to drugs have accounted for 5–6% of hospital admissions for many years.
- Most adverse reactions occur in older patients and mortality is low (0.15% in the study discussed), but hospital care is expensive.
- Most adverse reactions are caused by well-established drugs rather than by new drugs.
- Seventy-two per cent of adverse reactions were considered avoidable in this recent study, and one in six was due to well-known drug interactions.
- Preventing adverse reactions includes making a clear diagnosis first; being aware of potential side-effects; avoiding polypharmacy; and giving clear explanations to patients and carers.
- Electronic prescribing systems can make drug use safer, and drug safety databases can give early warning of new drug toxicities.

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