Pharmacovigilance is for everyone

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The publication earlier this year of the Royal Pharmaceutical Society’s paper on “The contribution of pharmacy to making Britain a safer place to take medicines” is a welcome push to make pharmacists a key component of drug safety.

However, recommendations concerning pharmacovigilance in the report could be counterproductive. The report recommends that the “new professional body for pharmacy works with the Medicines and Healthcare products Regulatory Agency (MHRA) to establish a national pharmacovigilance network of hospital pharmacists in key hospitals to document and report the early use and effects of new medicines”. Our alternative view is that pharmacovigilance should not be treated as a specialist, potentially leading to a reduction in reporting base, and pharmacy should address the major burden of adverse drug reactions that rests on hospital inpatients and those in the community.

Burden

The burden of adverse drug reactions (ADRs) on the UK population has been examined in two large prospective studies in the UK. One showed that around 6.5 per cent of all admissions to hospital are drug-related, with older patients and women the most affected. The more recent one showed that 14.7 per cent of patients within hospitals suffered ADRs. Both studies showed that the overwhelming majority of drugs were not new therapeutic agents with provisional safety records. They were established drugs whose safety issues were well described in the literature. For example, non-steroidal anti-inflammatory drugs and diuretics caused almost 60 per cent of ADR-related admissions to hospital, and diuretics and opioid analgesics were most frequently implicated as causative drugs post-admission. A recent systematic review of the literature also found that antiplatelet agents, diuretics, NSAIDS and anti-coagulants were the most frequent causes of preventable harm, and recommended that “interventions on these drug groups could reduce appropriately the number of preventable drug-related admissions to hospital from primary care”.

Pharmacists should focus on reducing the burden of these prevalent and serious ADRs, which are costing the NHS an estimated £657m per year in hospitals alone and £1 billion overall.

The National Patient Safety Agency’s patient safety alert on managing anticoagulant therapy is a good example of how national initiatives can address the causes of common preventable ADRs on both sides of the primary and secondary care interface. The impact of the alert will be difficult to measure, but the awareness it has raised is undoubtedly valuable. However, national initiatives should be secondary to the need for individual pharmacists to take responsibility for improving the monitoring of drug therapy. Although the evidence base for monitoring drug therapy can be limited outside straightforward cases, such as clozapine monitoring, pharmacists could improve standards of care and minimise ADRs by ensuring timely monitoring, encouraging rational prescribing by prescribers and the rational self-adoption of medicines by patients.

The signal detection of new ADRs in new drugs is crucially important. Clinical trials provide provisional safety data on drugs before licensing. Clinical trials cherry-pick participants, often missing out groups taking concomitant medicines or with co-morbidities, and physiological vulnerabilities that make them more prone to ADRs. The most stringently conducted trials are compromised by the number of patients recruited. Statistical power to detect efficacy does not translate to the power to find rare serious reactions. Mathematically, the rule of three states that if “n” patients are treated with a medication and offers a particular ADR, then the incidence of that ADR will, with a likelihood of 95 per cent, lie between 0/n and 3/n. New medicines have on average only been used in trials involving no more than 3,000 patients, meaning adverse drug reaction with a frequency of 1 in 1,000 may be missed.

For this reason, spontaneous reporting schemes for ADRs, such as the yellow card scheme, will continue to be important. An analysis of 21 drugs withdrawn in France between 1998 and 2004 showed that 19 withdrawals were linked to spontaneous case reports. A similar analysis of 11 products withdrawn in the UK showed evidence from spontaneous reports supported the withdrawal of eight products.

Specialised pharmacovigilance pharmacists within hospital may not be effective at improving this situation. First, much of the prescribing of new drugs occurs in primary care, partly due to the nature of the new drug launches in the UK, and of medicines by the formulary control that pharmacists are involved in. Secondly, if pharmacovigilance pharmacists are only based in “key hospitals” as suggested, the basis of drug use, which such pharmacovigilance pharmacists can draw from, is reduced.

Far from being a specialist activity, pharmacovigilance is a fundamental professional competency of pharmacy practice. Those areas with specific drugs of interest, such as biologics, or a specific patient-group focus, such as paediatrics, are correctly identified by the report, but the real solution is missed. Pharmacovigilance should not be an add-on service from specialist networks, but should be integrated into existing hospital pharmacy services. Pharmacist specialists in such fields as HIV treatment, rheumatology and intensive care must make greater use of the existing yellow card scheme.

Local ADR reporting schemes have acted as unnecessary filters, with pharmacy assessment of causality and completeness of a yellow card delaying submission or preventing ADR reports. A 1998 survey found that only 70 per cent of local ADR reports were forwarded on the yellow card scheme, and a survey of chief pharmacists found a widespread view (67 per cent) that yellow cards from hospital pharmacists should be screened by pharmacy departments before submission. There are anecdotal experiences of local medicines information services delaying batches of yellow cards for several months before submission. An early local ADR reporting scheme describes how, after examining 79 suspected ADRs, 35 were not submitted to the yellow card scheme after “it was considered that the patient’s drug history did not coincide with the onset conclusion of the reaction, or the documentation and clinical history were inadequate to incriminate the suspected drug”. These decisions can only be made by medical assessors at the MHRA.

Despite some evidence of a lack of confidence in pharmacist ADR reporting within the profession, and a continuing need for training, the reports to the MHRA have been of high quality. There is no evidence that greater specialisation is needed, instead, greater participation is required. The successful extension of ADR reporting to patients in the UK underlines the drive to widen the reporting base.

Change in approach needed

In contrast to the recommendations of the making Britain a safer place to take medicines report, we suggest fundamental changes in the approach of pharmacists to pharmacovigilance. Pharmacovigilance training at the undergraduate level should be strengthened, the incorporation of ADR reporting into the professional routine of all pharmacists and promoting of chief pharmacists should be a key part of revalidation. The Society could also help strengthen pharmacovigilance by encouraging the establishment of regional yellow card centres throughout the UK by the MHRA.

Additionally, we suggest that focusing on strategies to improve the prescribing and monitoring of established drugs and supporting research that aims to explore new interventions to reduce the ADR burden would have a greater effect on the health of the nation.