

The prevention of adverse drug reactions — a potential role for pharmacists in the primary care team?

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SUMMARY. Medication record cards were kept for 1,366 patients over a three-year period at a neighbourhood pharmacy in north-west London. Eighty-six potential adverse drug reactions were detected. In 53 cases the general practitioner changed the prescription after being contacted by the pharmacist. In a further 15 cases advice intended to reduce the likelihood of an adverse drug reaction was given to the patients by the pharmacist. Seventy-six errors on prescriptions were also detected; these were mainly unintended changes in dose or strength of medication. Pharmacists could have a useful role to play in monitoring for potential drug reactions in general practice. Closer collaboration between the two professions would be of mutual benefit.

Introduction

ADVERSE effects from drugs are thought to affect between 10 and 20 per cent of hospital patients (Seidl *et al.*, 1966; Hurwitz and Wade, 1969; Gardner and Cluff, 1970) and to be responsible for between about three and five per cent of hospital admissions (Hurwitz and Wade, 1969; Caranasos *et al.*, 1974; Miller, 1974). They are also responsible for about one in 40 general practice consultations (Mulroy, 1973). Intensive surveillance in general practice has detected probable or certain adverse drug reactions (ADRs) in about 40 per cent of those given single drug treatment (Martys, 1979). However, many potential ADRs are based on theoretical predictions about interactions which in practice cause little or no clinically detectable effects. A proportion of ADRs may be preventable; the magnitude of this proportion is likely to vary depending

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on the prescribing habits of individual doctors and the characteristics of the population involved. Preventable ADRs may be due to:

1. The prescription of a drug to which the patient has previously been allergic.
2. Using drugs contraindicated by certain disease states, for example non-selective beta blockers in asthmatics or strong sedatives in patients with chronic respiratory failure.
3. Interactions between drugs, for example anti-coagulants and clofibrate or some antibiotics.
4. Errors in dosage or strength.
5. The use of inappropriate dosage, for example in the elderly or in patients with kidney or liver disease.

We suggest that where there is close liaison between the pharmacist and the general practitioner, the pharmacist can help prevent some ADRs, particularly those in categories 1, 2, 3 and 4. In addition, we propose that the development of pharmacist record systems could improve their ability to detect potential ADRs. There have been reports from the UK of the use of a single record card retained by the pharmacist (Dalglish, 1972; *Chemist and Druggist*, 1976). It is often difficult for hospital doctors, general practitioner locums and doctors in deputizing services to obtain an accurate medication history; the use of a patient-held record card may help to improve communication.

Methods

The cards

We (J.I.S. and S.S.) used a two-card record system for three years (1977-80) in our North London pharmacy. The pharmacy is used mainly by the patients of about 15 doctors, and is staffed by two pharmacists and a preregistration pharmacist. One of the cards, retained by the pharmacy, contained the name, age, sex and address of the patient together with the names, strengths, dosages and quantities of any medications,

relevance of some drug interactions. Even in cases when an ADR is thought to have occurred, experienced clinical pharmacologists may fail to agree in about 50 per cent of cases on whether an event is an ADR or not (Karch *et al.*, 1976). The pharmacists in this study usually considered an ADR to be of relevance only when it was supported by clinical case reports in the reference books available and when there appeared to be sound pharmacological reasons for expecting clinical effects.

Prescribing errors

During the study a record was also kept of all errors on prescriptions. An error was defined as a change in the dose, strength or type of medication which was probably not intended by the prescribing doctor. Changes in dose, strength or type were determined from the record of previous prescriptions on the cards and the patient was then asked whether he or she was aware that changes in the medication had been ordered. If not, the general practitioner was contacted and those cases in which the general practitioner had not intended to change the medication in any way were classified as errors. It is possible that errors in first prescriptions were not detected since there was no way of comparing the intended dose or strength of medication with that actually ordered by the general practitioner.

For five months from June 1977, all omissions of dosage and strength (where formulations of different strength are available) were recorded. The extent of multiple prescribing (three or more items simultaneously) was also recorded over the same period.

Results

Potential ADRs

Of the 1,366 patients for whom medication records were kept, 33 per cent were aged 60 to 69 and 31 per cent 70 and over. During the three-year period a total of 64,406 items were dispensed on 33,593 NHS prescriptions, of which 52 per cent were for patients who had medication record cards. Potential ADRs are listed in Table 1; there were 86 altogether.

In most instances the doctor was contacted by telephone when the pharmacist was concerned at the possibility of a potential ADR. However, for most of these cases in which the drug prescribed was inactivated, reduced or opposed by concurrent therapy (group 4, Table 1), the patient was merely asked not to take the two medications within two hours of each other.

In the early stages of the study the doctor was telephoned about all prescriptions where other drugs which might interact adversely were prescribed to patients on anticoagulants. However, it soon became apparent that in most instances the doctor was aware of the potential ADR and was monitoring the anticoagulant control with this in mind. On only three occasions had the possible effect of the combination on anticoagulant control not been taken into account.

Some of these potential ADRs were detected without using the card system, for instance prescribing tetracyclines for children. However, 65 of the potential ADRs were detected using the record card retained by the pharmacist. We have no means of determining how many potential ADRs may have been avoided by use of the patient-held card.

The prescription of sugar-containing medications to diabetics has not been recorded in Table 1. It was noted by the pharmacists on 10 occasions in the first year. The amount of sugar may on occasions be sufficient to interfere with diabetic control and the patients were warned of this possibility. In addition, potential ADRs involving over-the-counter medications have not been recorded; all patients making over-the-counter purchases are asked whether they are taking other medications and their cards checked. Hypertensives purchasing sympathomimetics, for instance, are advised to use an alternative. We have also not included in Table 1 diabetics given thiazide diuretics, since although these are known to impair glucose tolerance, they are commonly used and their effect may be compensated for by adjusting the antidiabetic medications. The three diabetics given propranolol were all on oral antidiabetic medication.

Prescription errors

Table 2 shows the errors on prescriptions over the three-year period. Some of the errors were of minor importance, but some might have had serious consequences. For example, one patient who was not a diabetic was prescribed Diabinese instead of Distalgesic; another patient had her insulin changed inadvertently. In most of the cases where the dose was changed in error, the dosage was increased; this could have been potentially dangerous in some cases. For instance, five patients had their digoxin dosage doubled in error, three had their thyroxine dosage increased twofold or more, and one had his dose of debrisoquine doubled.

In all cases in which an apparent error had been made, the doctor was contacted and the prescription changed. In seven of the 50 cases in which the dose appeared to have been altered in error, the general practitioner had intended to change the dose but had not informed the patient. Nearly all of the errors were detected using the card system, although on three occasions the dosages were completely inappropriate for the drug prescribed and would have been detected without the card system.

Omissions of dose

Omissions of dose were very common, particularly on repeat prescriptions, and were only recorded for the first five months of the study. During this period 640 individual items did not have dosage instructions out of a total of 5,906 items for 1,000 patients recorded on the card system.

Adverse Drug Reactions

Table 1. Potential adverse drug reactions over a three-year period.

	Number	Prescriptions changed
<i>Drugs prescribed for patients known to be allergic to them:</i>		
Penicillins	9	9
Tetracyclines	3	3
Sulphonamides	1	1
Others	2	2
<i>Inappropriate prescription of tetracyclines in:</i>		
Children	5	5
Pregnant women	1	1
<i>Prescription for drug known to lead to potentially toxic interaction with patient's concurrent therapy or exacerbate current illness:</i>		
Patients on anticoagulants prescribed drugs likely to affect control	3	3
Patients on MAOI prescribed sympathomimetic	2	2
Hypertensives prescribed sympathomimetics (decongestants or anorectics)	13	5
Asthmatic prescribed propranolol	1	1
Glaucoma patients prescribed anticholinergics	5	2
Post-coronary patient prescribed ergotamine	1	1
Patient prescribed prochlorperazine, reserpine and amitriptyline	1	1
<i>Patients with peptic ulcer prescribed antirheumatic drugs:</i>		
Phenylbutazone	3	1
Indomethacin	1	1
Ibuprofen	1	1
Naproxen	2	1
Aspirin	1	1
Diabetics prescribed propranolol	3	1 (dose reduced)
Diabetics on sulphonylurea prescribed aspirin (2), phenylbutazone (1)	3	2
Patient on high-dose chlorpromazine prescribed metoclopramide	1	1
Penotrane (hydrargaphen) pessaries prescribed to patient with copper IUD	1	1
Alcoholic on disulfiram prescribed alcohol-containing tonic	1	1
<i>Prescriptions for drug whose effect is inactivated, reduced or opposed by concurrent therapy:</i>		
Patients on long-term iron therapy prescribed tetracycline	5	2 3 advised not to take them within 2 hours of each other
Patients on antacids prescribed tetracycline	8	8 advised not to take them within 2 hours of each other
Digoxin and mist. mag. trisilicate prescribed together	4	4 advised not to take them within 2 hours of each other
Dilution of steroid creams with incorrect diluent	3	3
Other incorrect mixtures	2	1
Total	86	53 changed 15 advice given to patient 18 not changed

Multiple prescribing

Multiple prescribing was recorded for the first five months of the study. During this period, 320 of 1,000 patients (32 per cent) were found to be on three or more different drugs simultaneously and 108 patients (10.8 per cent) were on five or more drugs simultaneously. Over half (196) of the patients on three or more drugs and half (54) of those on five or more drugs were aged over 70 years.

Discussion

We have been able to detect a number of potential ADRs in a neighbourhood pharmacy; the majority were detected by the card system. Although pharmacists do

not have a defined list of patients, many of their customers regularly return to the same pharmacy for their prescriptions. In Holland patients register at pharmacies and this must certainly make it easier to look for potential ADRs (Winters, 1977).

The work of setting up a record system is mainly concentrated in the early months of its operation and tends to decrease after this time—1,000 patients were entered into the card system in the first five months and only 300 subsequently. Even if patients do not always return to the same pharmacy, they can still display their personal record cards at other pharmacies when collecting prescriptions, as well as at hospitals and general practitioner and dental consultations. We acknowledge, however, that such a system may be difficult to organize

Table 2. Errors on prescriptions over three years.

	Number
Repeat prescriptions—strength or dose altered in error	49 (64.5%)
Repeat prescriptions—dose altered by doctor without informing patient	7 (9.2%)
New prescriptions—strength omitted	14 (18.4%)
Wrong drug prescribed	6 (7.9%)
Total	76 (100.0%)

in some inner city pharmacies where there is a rapid turnover of patients and comparatively few of the patients attend the same pharmacy regularly for prescribed drugs.

Some of the potential ADRs detected may be of minor clinical importance; for instance, although beta blockers may affect glucose tolerance in non-insulin-requiring diabetics, this is rarely of clinical importance (Wright *et al.*, 1979). However a highly selective beta blocker such as atenolol may be preferable to propranolol even for non-insulin-dependent diabetics (Deacon *et al.*, 1977). Where the indications for medication are minor, or acceptable alternatives exist, it may be advisable to avoid combinations with a low risk of an ADR. Similarly, there is controversy over the use of antirheumatic drugs in patients with peptic ulcers; although aspirin, indomethacin and phenylbutazone may produce dyspepsia, there is no definite evidence that they cause duodenal ulceration (Levy, 1974). Long-term heavy aspirin consumption may be associated with gastric ulceration and aspirin causes gastro-intestinal haemorrhage without ulceration (Levy, 1974). Many doctors are cautious in the use of antirheumatic drugs in patients with peptic ulceration but the judgement as to what constitutes an acceptable risk in the individual patient can of course be made only by the doctor.

It seems likely that some of the other potential ADRs would have been serious: for instance, the administration of penicillin to patients known to be penicillin sensitive.

Although the total number of potential ADRs detected over three years was a small proportion of the total number of items dispensed (86 out of 64,406), a system such as we have described might have a worthwhile impact on the incidence of ADRs if it were widely used in the 10,000 pharmacies in the United Kingdom, and might result in the prevention of considerable numbers of ADRs every year. In addition, such a system has a potentially important educational role for patients, pharmacists and doctors; it could also help to confirm the importance of the pharmacist as a member of the primary care team.

The cost of the two-card system is about 2p per patient; the completion of a card required on average about five minutes at the first visit and much less, probably one or two minutes, on subsequent visits. The

card system does raise problems of confidentiality, since the pharmacist records the major conditions from which the patient claims to suffer. However, patients are quite free to withhold information if they wish to, although only five patients in three years declined to participate in the record system when its purpose had been explained. Pharmacists already encounter many situations, such as pregnancy testing, contraceptive purchase and enquiries from patients about their treatment, in which confidential information is exchanged, and the pharmacist's code of practice includes instructions on confidentiality. Patients may not always be accurate in giving their diagnoses, but the majority of important medical conditions are well known to the public and we have not encountered problems due to misinformation.

As presently constituted, retail pharmacy has a large commercial element which does affect the relationship between pharmacist and patient and makes it somewhat different from the relationship between other health professionals and patients. It may be that if retail pharmacists wish to assume a more professional and paramedical role, they will have to relinquish some of the more commercial aspects of retail pharmacy. This is a matter for debate within the pharmaceutical profession.

Other pharmacists in this country have also found dispensing records useful, although they have used a single-card system in which the card is retained by the pharmacist; this is obviously quicker and cheaper than using a two-card system. However, some potential adverse reactions may be missed when the patient attends another pharmacy or a hospital. Further studies are required to compare the effectiveness of the one- and the two-card systems. The cost of implementing such a system seems likely to be small compared with the cost of the NHS drug bill, which was £796 million in 1979 (DHSS). It is possible that such a system would ultimately pay for itself by encouraging more rational prescribing and reducing demands on the health service due to ADRs.

In the state of New Jersey, USA, pharmacists are now required by law to record all medications dispensed by prescription and to review the medication record on each occasion prior to dispensing (Stewart *et al.*, 1977). Although it seems unlikely that this country will follow suit in the near future, this legislation has established a precedent which may be copied in time by other states and countries.

Dosage omissions might be reduced by having a box for dosage for a maximum of, say, four items on each prescription. Information which has been collected on multiple prescribing in 1,000 patients suggests that it is widespread, often involves the elderly and is particularly likely to lead to ADRs and mistakes in dosage (Melmon, 1971). However, the pharmacist cannot easily intervene in this area and further emphasis on the problems of multiple prescribing is required in both undergraduate and postgraduate medical education.

Experience with our system suggests that communication between general practitioners and pharmacists could be improved with benefit to both parties. Previous studies have shown that only 3.9 per cent of a sample of 453 general practitioners used pharmacists to check potential adverse effects and contraindications to drugs (Eaton and Parish, 1976) and that many pharmacists believe that their skills are under-used (*Chemist and Druggist*, 1974). Although there have been suggestions that the pharmacist should play a more active and direct role in patient care (Gatherer, 1974; Barrett and Vere, 1979), there has been little change in the role of the retail pharmacist in recent years.

Although initially there was some resistance by a few doctors to being informed by the pharmacists of a potential ADR, over the three years in which the monitoring has been in progress the pharmacist's role appears to have been accepted by the local general practitioners and a good working relationship has been established.

Local meetings between general practitioners and pharmacists could help to further mutual understanding between the two professions. In addition, the education of trainee general practitioners and medical students should include contact with pharmacists so that doctors develop a better understanding of the improvements in patient care which could follow a closer working relationship between the two groups.

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Alcohol and mortality: a U-shaped curve

In a longitudinal study of civil servants, 1,422 men were classified according to their average daily alcohol intake. Over 10 years of follow-up, the mortality rate was lower in men reporting moderate alcohol intake than in either non-drinkers or heavier drinkers (>34 g alcohol per day). Cardiovascular mortality was greater in non-drinkers and non-cardiovascular mortality was greater in the heavier drinkers. The heavier drinkers had higher mean blood pressures and contained a greater proportion of smokers. A multivariate analysis showed this U-shaped relationship between reported alcohol consumption and subsequent mortality to be largely independent of differences in smoking, blood pressure, plasma cholesterol and grade of employment.

Source: Marmot, M. G., Shipley, M. J., Rose, G., *et al.* (1981). Alcohol and mortality: a U-shaped curve. *Lancet*, **1**, 580-583.