Antibacterial therapy in general medical wards

D. H. LAWSON
M.D., F.R.C.P.(Ed.)

S. MACDONALD
S.R.N.

Glasgow Drug Surveillance Programme, Western Infirmary and Stobhill General Hospital, Glasgow, Scotland

Summary

Information from a comprehensive drug surveillance programme is analysed to provide details of antibacterial drug use in medical wards. Some 28% of patients received antibacterial therapy, usually for the treatment of respiratory or urinary tract infections. The agents most frequently prescribed were ampicillin, co-trimoxazole and tetracyclines. Overall, 11% of recipients experienced one or more adverse effects of therapy. No significant bacterial growth was obtained from some 40% of specimens of sputum sent from patients. A plea is made for more rational use both of sputum culture in the investigation of patients with respiratory infection and of antibiotics in their treatment.

Introduction

In the past few years considerable attention has been directed towards evaluating drug use in patients admitted to hospital. It has been reported that the average in-patient in a medical ward of an American teaching hospital receives nine drugs during admission (Jick *et al.*, 1970) and that infection is one of the commonest indications for therapy (Miller, 1973). Recently, several workers have expressed concern regarding what they see as the indiscriminate use of antibacterial agents, both in hospital and in out-patient medical practice (Jawetz, 1963; Kunin, Tupasi and Craig, 1973; Jackson, 1974). The present study was carried out in order to investigate the use of antibacterial drugs in four medical wards of two teaching hospitals in the west of Scotland. It provides information on the indications for and hazards attributed to these drugs as they were used in those wards.

Methods

Since 1973, patients admitted to four selected medical wards in two Glasgow teaching hospitals have participated in a study of drug use and adverse drug effects. The methods of this study are those of the Boston Collaborative Drug Surveillance Program, have been outlined previously by Jick and his colleagues (1970) and will be mentioned only briefly here. Consecutive patients are interviewed by trained

nurse monitors who record data from the clinical records, the patient and the attending physicians. Patient characteristics recorded include age, sex, height, weight, admission blood urea, protein and haemoglobin levels, a history of drugs consumed before admission to hospital, and discharge diagnoses. A trained nurse monitor attends ward rounds and collects information on all drugs given to the patient together with a record of whether or not the patient developed an adverse drug reaction (defined as any undesired or unintended effect of therapy). When such a reaction is reported, the event is recorded in some detail. All this information is subsequently edited for completeness and correctness, and transferred for entry on to the computer files of the Boston Collaborative Drug Surveillance Program. For the purposes of the present study, certain additional information was recorded. In all instances where a patient received an antibacterial drug, a record was kept of the specific indication, together with supporting bacteriological evidence where available.

A total of 1717 patients have been monitored to date. Of these 49% were male, and 6.5% died during the study. The mean age of the patients was 56 (s.e.m. 0.5) years and the mean duration of stay in hospital was 13.5 (s.e.m. 0.4) days. The average number of drugs given to patients during their admission was 4.6 and was identical in both hospitals. The primary discharge diagnosis was of cardiovascular disease in 36% of patients, gastrointestinal disease in 12%, respiratory disease in 11%, endocrine disease in 8%, cancer in 7%, and others in 26%.

Results

Antibacterial therapy was given to 480 patients (28%). The proportion receiving these drugs was similar in the two collaborating hospitals (26.5% and 30.1%). Patients receiving antibacterial therapy did not differ from the others with respect to age, sex, prognosis or duration of stay in hospital. The first day of such therapy was within the first four hospital days in 288 patients (60% of recipients) but was not until after the seventh hospital day in 112 patients (23% of recipients). Of the 480 recipients, 356 (74%) received only one, 90 (19%) received two, 24 (5%) received three and 11 (2%)

Correspondence: Professor D. H. Lawson, Clinical Pharmacology Services, Glasgow Royal Infirmary, 84 Castle Street, Glasgow G4 0SF.

TABLE 1. Antibiotics prescribed in medical wards

Drug	Recipients		Adverse reactions*	
	No.	%	No.	%
Ampicillin	251	38.2	36	14.3
Co-trimoxazole	172	26.2	16	9.3
Tetracyclines	66	10.0	6	9.1
Amoxycillin	32	4.9	3	9.4
Cephalosporins	30	4.6	2	6.7
Aminoglycosides	28	4.5	5	17.9
Penicillins	21	3.2	1	4.8
Ophthalmic preparations	17	2.6	0	—
Semi-synthetic penicillins	16	2.5	1	—
Urinary antiseptics	15	2.3	2	—
Antituberculous drugs	6	2.3	0	—
Others	3	0.8	0	—
Total	657	100	72	11.0

* Gives number of patients experiencing one or more adverse reactions attributed to indicated antibiotic.

TABLE 2. Relationship between bacteriological studies and antibacterial therapy

Bacteria found sensitive to drug							
			before therapy started	after therapy started	No specimens cultured	No pathogenic organisms cultured	Bacteria resistant to drug after therapy started
Diagnosis	Drug	Numbers	(%)	(%)	(%)	(%)	(%)
Respiratory tract infection	Ampicillin	172	14 (8)	13 (8)	29 (28)	72 (42)	23 (13)
	Co-trimoxazole	101	35 (35)	5 (5)	17 (17)	41 (41)	3 (3)
	Tetracycline	52	19 (37)	4 (8)	8 (15)	20 (39)	1 (2)
Urinary tract infection	Ampicillin	40	15 (37)	15 (37)	2 (5)	5 (13)	3 (7)
	Co-trimoxazole	62	37 (60)	11 (18)	3 (5)	8 (13)	3 (5)

received four or more antibacterial agents, the total number of exposures being 657.

The indications for antibacterial therapy were bronchopneumonia 37%, exacerbation of chronic bronchitis/emphysema 28%, urinary tract infection 20%, and others 15%. No specimens were sent for bacterial culture in 23% of patients with respiratory tract infection (RTI) and in 5% of those with urinary tract infection (UTI) ($\chi^2=10.7$, $P<0.01$). In a further 42% of those with RTI and 13% of those with UTI, no bacteria were isolated from the specimens which were sent ($\chi^2=32$, $P<0.01$). Bacteria sensitive to the chosen drug were isolated in 29% of those with RTIs and in 76% of UTIs ($\chi^2=57$, $P<0.01$), however resistant bacteria were equally prevalent in both groups (7% of patients). Thus, there was a complex relationship between bacteriological studies and the clinical diagnosis of respiratory and urinary tract infections.

The antibacterial drugs most commonly prescribed in these wards are shown in Table 1. Between them ampicillin, co-trimoxazole and tetracycline accounted for 75% of all antibacterial drug exposures. The commonest group of antibiotics prescribed, the penicillins and their semi-synthetic analogues, accounted for 49% of exposures.

Ampicillin was the single most commonly used antibacterial drug in the study: of the 251 recipients, 91% received it as the antibiotic of first choice. Comparable figures for co-trimoxazole and tetracycline were 70% and 64% of recipients respectively. Two-thirds (67%) of the ampicillin recipients received only this one antibiotic. Comparable figures for co-trimoxazole was 60%, and for tetracycline, 47%. The mean duration of treatment with these drugs was 7.7, 7.1 and 9.1 days respectively.

The relationship between the bacteriological studies and the drugs commonly chosen to treat the two most frequent conditions, respiratory and urinary infections, is indicated in Table 2. In patients with respiratory infections, bacterial cultures often failed to grow pathogenic organisms. When pathogenic bacteria were obtained, resistance to ampicillin was reported more frequently than to either co-trimoxazole or tetracycline. This observation requires to be interpreted cautiously, however, since it almost certainly reflects the observed tendency to commence therapy with ampicillin before the results of culture became available, in contrast to the habit with the other drugs. Moreover, the reported resistance patterns of the organism did not correlate

well with the clinical response of the patient to these drugs. By contrast in patients with urinary infections, cultures were sent from the majority and were rarely reported as producing no significant growth. In both ampicillin and co-trimoxazole recipients resistant bacteria were equally prevalent, however, and ampicillin recipients were significantly less likely to have a sensitive culture report available before treatment commenced than were co-trimoxazole recipients.

The frequencies of adverse reactions attributed by the medical staff to each of the commonly used antibacterial agents are shown in Table 1. Overall, 11% of antibacterial drug exposures were associated with some form of reported adverse reaction and of those, 50% led to discontinuation of the drug in question. Details of the adverse reactions attributed to the commonly used drugs were as follows:

Ampicillin

Of the 251 patients given ampicillin, 36 (14.3%) developed a total of forty-seven adverse reactions. Drug rashes were seen in twenty-two patients (8.8%), gastrointestinal upsets in twenty-one (8.4%), super-infection (oral moniliasis) in two (0.8%) and injection site complications in two (0.8%).

Co-trimoxazole

Of the 172 co-trimoxazole recipients, sixteen (9.3%) developed twenty-two adverse reactions. Drug rashes were seen in five patients (2.9%), gastrointestinal upsets in fifteen (8.7%), super-infection (oral moniliasis and drug fever) in one patient each (0.6%).

Tetracyclines

Of the sixty-six patients given oxy- or chlor-tetracycline, six (9.1%) developed nine adverse reactions. Drug rashes were attributed in three patients (4.5%) and gastrointestinal upsets in six (9.1%).

Other antibiotics

The only other group of antibiotics associated with significant numbers of adverse reactions were the aminoglycosides and, of these, the most commonly prescribed in these wards was gentamicin. Of the twenty-one gentamicin recipients, four developed a total of seven adverse reactions. Renal dysfunction attributed to gentamicin was reported in five patients, injection site complications in one and severe gastrointestinal upset in another. In none of the patients was renal impairment of major severity, or ototoxicity, attributed to gentamicin.

One of the major factors leading to discontinuation of antibacterial therapy before completion of the intended course was drug rash. This occurred in

8.8% of 251 ampicillin recipients, 6.2% of thirty-two amoxycillin recipients, 4.7% of twenty-one penicillin recipients and 2.9% of 172 co-trimoxazole recipients. In the entire series of 1717 patients, drug-attributed rashes occurred in 1.1% of those who were exposed neither to the above antibiotics nor to blood or blood products. Of considerable interest is the finding that no patients in this study developed serious super-infection (e.g. colitis, septicaemia) as a consequence of exposure to antibiotics. The only manifestation of super-infection reported was the occasional oral monilial infection which responded readily to removal of the original antibacterial agent and appropriate therapy with nystatin.

A total of 175 patients (10.2%) received an antibiotic immediately before admission to hospital and, of those, 66% received further antibiotic therapy during admission. The drugs most commonly used before admission are shown in Table 3. Four antibacterial agents, ampicillin, co-trimoxazole, tetracycline and oral penicillin accounted for 90% of those preparations. No patient was admitted to the ward as a result of an antibiotic-attributed adverse reaction.

TABLE 3. Antibiotics prescribed before admission

Drug	No. exposed	Proportion of total population
Ampicillin	92	5.4
Co-trimoxazole	25	1.5
Tetracycline	22	1.3
Penicillins	22	1.3
Semi-synthetic penicillins	6	0.4
Cephalosporins	4	0.2
Others	4	0.2
Total	175	10.2

Discussion

It has recently been reported that overall drug usage is substantially lower in the Scottish medical wards under study than in comparable American medical wards (Lawson and Jick, 1976). The present report confirms this observation with regard to antibacterial drug use. Some 28% of Scottish patients received such drugs as compared with 42% of comparable patients in Boston and 37% of patients in a large hospital in Florida (Caldwell and Cluff, 1974).

The commonest indication for antibacterial therapy in the Scottish wards was a respiratory tract infection, either bronchopneumonia or an exacerbation of pre-existing chronic respiratory disease. In 66% of these patients there was no bacteriological evidence to support the use of an antibiotic. By contrast, 80% of the patients receiving antibacterial therapy for urinary tract infections had bacteriological evidence of an infection either before therapy commenced or shortly thereafter. This difference

clearly implies that the diagnosis of respiratory infection is usually made on clinical grounds and that empirical antibacterial therapy is the rule rather than the exception, whereas the diagnosis of urinary tract infection is usually made both on clinical and bacteriological grounds leading to more rational use of antibiotics.

This study raises large questions about the relevance of sputum culture in the management of patients with acute chest infections superimposed upon chronic obstructive airways disease. Over 40% of the specimens sent for culture from such patients were found not to grow pathogenic organisms. This figure is in close accord with that reported by Philp and Spencer (1974) who studied a group of subjects who developed secondary respiratory infections whilst in hospital. These workers also reported a negative association between prior antibiotic therapy and the likelihood of detecting the causal organisms in the sputum. In the present study no such association was found although there was a trend in that direction which did not attain statistical significance: the frequency of failure to detect pathogenic organisms in sputum cultures being 46% in those receiving previous antibacterial therapy as out-patients and 39% in those who did not receive such treatment. If the studied wards are typical of other medical wards in this respect, clearly a large amount of time and effort on the part of the bacteriological services is being wasted. It seems a better policy to treat such patients empirically in the first instance and reserve examination of the sputum by culture for those who do not respond to initial therapy or in whom there is an additional problem, for example diabetes mellitus. A similar plea has recently been made by Tager and Speizer (1975) who reported that in America the annual cost of drugs used in the treatment of chronic bronchitis (mostly antibiotics) was over 300 million dollars. They reviewed the literature on the place of antibiotic therapy in acute exacerbations of chronic bronchitis and concluded that a radical reassessment of management of such patients was required.

In general it was customary to commence treatment with antibiotics before the results of cultures became available. This habit would seem justified were it not for the relatively high frequency of undesired effects attributed to these drugs. Overall, 11% of antibacterial drug exposures were associated with an undesired effect and although the majority were of only minor long-term significance, the discomfort associated with, for example, an ampicillin rash was often as great as the potential benefit likely to accrue from the use of the drug in the first instance.

The frequency of drug rashes attributable to ampicillin in this study was 8.8%. This is similar to

that reported from the American hospitals contributing to the Boston programme (Shapiro *et al.*, 1969) and has subsequently been confirmed in a multicentre study in Britain (Collaborative Study Group, 1973). Unfortunately the number of amoxycillin recipients was insufficient to compare the frequency of rashes attributable to this drug with that of ampicillin. The frequency of rashes attributable to co-trimoxazole was lower than that of ampicillin. Overall, the adverse reactions attributed to co-trimoxazole were sufficiently mild to encourage this drug's increasing use as an antibacterial agent of first choice in the therapy of respiratory and urinary tract infections. However, in view of the vast expenditure on antibiotics in the Health Service and the vast cost of performing numerous, clinically meaningless, bacterial cultures, particularly of sputum, the time has come to look in a more critical way than hitherto both at our prescribing habits of these expensive and widely abused drugs, and at our investigating habits particularly as they relate to sputum culture.

Acknowledgments

We are grateful to the Scottish Home and Health Department for a generous grant towards the cost of this investigation and to Professors G. M. Wilson and A. Goldberg for providing access to patients under their care, and to Dr H. Jick of the Boston Collaborative Drug Surveillance Program, for analysis of some of the data presented here.

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