Adverse reactions to medication on a coronary care unit

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Summary

In a prospective survey of treatment on a coronary care unit 23.6% of patients who received medication had one or more side effects. In several cases these were severe enough to cause marked deterioration of the patient's clinical status. Whilst antiarrhythmic therapy is an integral part of modern coronary care its potential hazards should be recognized, particularly in the elderly patient.

Introduction

Since the advent of coronary care units (CCU), the hospital mortality from ventricular fibrillation has fallen. This is due not only to rapid defibrillation with direct current shock but also to the treatment of arrhythmias likely to predispose to ventricular fibrillation. However, the constant cardiac monitoring, leading as it does to early treatment with anti-arrhythmic medication, will naturally expose patients to drugs they may not otherwise have received. Whilst this is aimed at benefiting the patient the likelihood of adverse drug reactions will increase. If severe, these may be detrimental to the patient, perhaps in some cases outweighing the benefit of therapy. Despite studies showing a relatively high incidence of side effects of medication in patients in general hospital wards, no similar study has been undertaken in the CCU. The present survey was designed to study the pattern of drug use on such a unit and to record the incidence of adverse reactions to therapy and their effect on the patient.

Patients and methods

All patients with proved acute myocardial infarction admitted to the 6-bed CCU of the Brook General Hospital were prospectively studied. The survey spanned a 6-month period. Myocardial infarction was defined as chest pain with associated enzyme rise and electrocardiographic changes. There was no age limit for admission to the CCU and it was not the policy to give routine prophylactic antiarrhythmic medication. On admission the

clinical condition of the patient was recorded with smoking history, present medication and ECG site of infarction. All antiarrhythmic medication prescribed was recorded as well as the indication for the drug and the patient's response. The latter was divided into 3 categories – no response, desired response (e.g., partial or complete suppression of arrhythmia) or side effects.

Side effects were subdivided as follows:

(a) Mild – non-cardiac with tolerable patient discomfort, e.g. mild dyspepsia, rash.

(b) Moderate – more severe non-cardiac side effects usually necessitating stopping medication, e.g. severe dyspepsia, or transient cardiac effects of a potentially serious nature, e.g. transient bradycardia.

(c) Severe – potentially life-threatening or effects likely further to impair cardiac function, e.g. pulmonary oedema, marked hypotension, severe conduction fusion.

Non-antiarrhythmic therapy and procedures such as temporary transvenous cardiac pacing were also recorded in a similar manner.

Results

Eighty-nine patients with proved myocardial infarction were admitted during the period studied. Fifty-seven (64%) were aged <65 years and 32 (36%) >65 years. The overall mortality during the total hospital stay was 12.4%. All but 2 of those patients died on the CCU. Four patients <65 years old (7.0%) died, compared with 7 (21.9%) aged >65 years. Whilst on the CCU, 42 (47.2%) patients received at least one dose of an antiarrhythmic drug. There was no significant difference in the proportion of younger patients receiving therapy compared with those of 65 years (45.6% v. 50%). A total of 65 antiarrhythmic drugs were given to these patients, a mean of 1.55/patient. Younger patients received significantly fewer drugs than did older patients (1.35 v. 1.88 drugs/patient).

Indications for therapy

Ventricular ectopic beats were treated only if more frequent than 5/min or if they met any of the other Lown criteria (Lown *et al.*, 1967). Lignocaine was the

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drug of first choice and was used in 24 patients, of whom 19 had asymptomatic ectopic activity. If ventricular ectopic activity persisted despite lignocaine, or recurred on stopping the lignocaine at 24–36 hr oral disopyramide was commonly prescribed, 8 patients receiving this drug.

Beta-blocking agents were used in 9 patients, predominantly for regular supraventricular arrhythmias, or persistent sinus tachycardia in the absence of cardiac failure. Digoxin was used in only 6 patients, the indications being atrial fibrillation with fast ventricular response or cardiac failure with cardiomegaly.

For bradyarrhythmias, atropine was the drug of first choice. All 11 patients who received atropine had symptomatic bradycardia (<55/min) due to heart block or sinus bradycardia, with a systolic blood pressure below 90 mmHg.

Other antiarrhythmic drugs used occasionally as second-line agents included mexiletine, verapamil and phenytoin. The specific indications for therapy in individual patients experiencing side effects are recorded in Tables 2 and 3.

Effect of therapy

Thirteen of the 65 drugs (20%) produced side effects. Thirty-one (47.7%) led to improvement in the patient's condition and 21 (32.3%) had no effect. A comparison of the 2 age groups (Table 1) shows

the similarity of response in both groups. The side effects of antiarrhythmic medication are shown in Table 2. Seven patients experienced adverse reactions to other medication as shown in Table 3. Combining the data of Tables 2 and 3, 21 side effects occurred in 17 patients—an incidence of 19.1% of all patients. Excluding the 14 patients who received no medication in any form whilst on the CCU, the incidence of side effects becomes 23.6% of those patients receiving some form of drug treatment. Reference to the tables shows that whilst the older patients were not subject to a higher incidence of side effects, those that they did experience tended to be more severe.

Discussion

Despite the higher mortality of elderly patients in this study, the incidence of side effects was no higher than younger patients when considered in relation to the total number of medications prescribed.

TABLE 1. Results of antiarrhythmic therapy in the 2 age groups. Figures in brackets indicate percentage

	< 65 years	> 65 years	Total
No benefit	10 (28.6)	11 (36.6)	21 (32.3)
Improved	18 (51.4)	13 (43.4)	31 (47.7)
Side effect	7 (20)	6 (20)	13 (20)
	35	30	65

TABLE 2. Side effects of antiarrhythmic medication

Patient No.	Age	Drug	Indication	Side effect	Classification
(a) Over 65					
2	72	Isoprenaline	Heart block bradycardia	Ventricular tachycardia	Severe
3	72	Digoxin	Atrial fibrillation	Severe, prolonged vomiting	Moderate
3	72	Propranolol	Uncontrolled atrial fibrillation	Intractable left ventricular failure	Severe
3	72	Lignocaine	Frequent ventricular ectopic beats	Coma	Severe
6	75	Disopyramide	Ventricular ectopic beats	Left ventricular failure	Severe
6	75	Mexiletine (oral)	Ventricular ectopic beats	Severe gastrointestinal disturbance	Moderate
53	65	Lignocaine	Ventricular ectopic beats	Hypotension and vomiting	Moderate
(b) Under 65					
22	62	Verapamil	Supraventricular tachycardia	Hypotension and left ventricular failure	Severe
41	52	Disopyramide (oral)	Ventricular ectopic beats.	Persistent systolic BP below 100 until drug stopped	Moderate
57	54	Digoxin	Cardiac failure	Bradycardia and Wenckebach phenomenon	Moderate
67	56	Disopyramide	Frequent, multifocal ventricular ectopic beats.	(a) Acute retention (b) Hypotension and severe left ventricular failure	Severe
73	62	Propranolol	Persistent chest pain	Nausea	Mild
84	52	Lignocaine	Ventricular ectopic beats	Slurring of speech	Mild

TABLE 3. Side effects of other treatment prescribed on coronary care unit

Patient No.	Age (years)	Treatment	Indication	Side effects	Classification
(a) Over 65					
31	69	Glyceryl trinitrate	Chest pain	Faintness and transient hypotension	Moderate
35	72	Temporary pacing wire	Sinus node dysfunction	Staphylococcal septicaemia	Severe
65	70	Frusemide	Cardiac failure	Skin rash	Mild
72	71	Thyroxine	Newly diagnosed myxoedema	Confusion, severe arrhythmia	Severe
(b) Under 65					
17	44	Frusemide	Cardiac failure	Hypokalaemia ($K^+ = 2.2$) → ventricular ectopic activity	Moderate
64	57	Glyceryl trinitrate	Chest pain	Sinus arrest → syncope	Severe
82	52	Glyceryl trinitrate	Chest pain	Marked but transient hypotension (60/?)	Moderate

However, since elderly patients received more drugs their chances of experiencing an adverse reaction were higher. Coupled with the tendency for more severe reactions to occur in the older group it may be stated that these patients are at a greater risk of moderate and severe side effects. Nevertheless the younger patients were not immune and the overall incidence of adverse reactions of 23.6% indicates the need for particular care on the part of the physician when prescribing on the coronary care unit.

Although no similar previous survey of medication on the CCU is available there have been several studies of side effects of medication in different hospital environments. Hurwitz and Wade (1969) found that 10.2% of all hospital patients receiving medication experienced drug reactions and they considered 80% of these to be of moderate severity, necessitating treatment and/or prolonging hospital stay by at least one day. Patients on medical wards constituted approximately half their total patient population and the incidence of adverse reactions in this group was 16.4% compared with only 3.2% of surgical patients. Despite this high incidence, the authors conclude that 'such an incidence of reactions to drugs may pass almost unnoticed in the hospital community unless a special survey is undertaken'. A similar statement is made by Buchanan and Cane (1978) who studied drug utilization in a general intensive care unit and found the mean number of drugs prescribed per patient was 7. There was an overall mortality of 24.5%. They point out the vast potential for drug interactions in such circumstances and comment that although several cases of iatrogenic diseases were noted, probably many more such instances passed unnoticed. The CCU probably lies somewhere between the general medical ward and the intensive care unit with respect to drug utilization and severity of illness, and hence to adverse reactions. Allowing for the difference in patient composition and prescribing habits between a

general medical ward and CCU, the incidence of adverse reactions in the present study is in the range one might expect from the work of Hurwitz and Wade.

Whilst most of the side effects in the CCU patients are related to hypotension, cardiac failure or non-cardiac manifestations, one should be aware of the potential paradoxical effects of antiarrhythmic medication. In a study of cardiac patients undergoing acute drug testing with a variety of oral antiarrhythmic drugs (Velebit *et al.*, 1979), 12% had an exacerbation of their arrhythmia. These patients predominantly had either chronic ischaemic heart disease or non-ischaemic heart disease. In the setting of acute myocardial infarction where rhythm disturbances tend to fluctuate more than in the chronic stage, the physician may attribute a deterioration in the patient's rhythm following therapy to the natural progression of the arrhythmia coupled with a failure of treatment, rather than seeing the therapy as the causative factor in the deterioration. A careful assessment of the situation will aid in deciding whether to continue with drug therapy or to discontinue and utilize alternative therapy. The negative inotropic effects of many antiarrhythmic medications may cause diuretic-resistant cardiac failure in the susceptible patient which may be wrongly attributed to cardiogenic shock (Resnekov, 1978). Withdrawal of disopyramide in case number 6 (Table 2), led to rapid resolution of left ventricular failure previously poorly responsive to high dose diuretics.

It has been argued that if the benefits of modern drug therapy are to be exploited, the occurrence of adverse reactions to drugs has to be accepted (Hurwitz and Wade, 1969). However, one should constantly attempt to reduce the incidence of such reactions in order to reduce patient morbidity and, possibly, mortality. Despite the fact that no patient in the present study had a reaction which could be unequivocally related to their subsequent death,

those patients who have severe reactions are at risk of extending their infarct size owing to the hypotension or arrhythmia provoked by the drug. Since this study did not examine mortality after hospital discharge, one cannot determine the long-term effects but they are likely in some cases to be detrimental.

A prime duty of the physician is 'to do no harm' but at times he will have to weigh up the potential good of a drug against the harm it may cause. Necessary therapy should not be withheld from the patient on the coronary care unit, but caution should be exercised particularly when prescribing for the elderly. Perhaps, by bearing this in mind, the trend towards the ICCU (intensive coronary care unit) will move towards the CCCU (the conservative coronary care unit).

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