The practice of evidence-based medicine in an acute medical ward: retrospective study

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Objective. To review the practice of evidence-based medicine with respect to drug treatment given to medical in-patients.
Design. Retrospective study.
Setting. Teaching hospital, Hong Kong.
Patients. Medical records of 129 consecutive patients who were admitted to the acute adult general medical ward from 1 September 1998 to 30 September 1998 were reviewed.
Main outcome measures. Primary diagnoses, drug treatments prescribed, and the level of evidence (based on a literature search of randomised controlled trials and relevant studies) that supported the treatment given.
Results. For the 129 patients studied, 91 drug interventions had been prescribed on 312 occasions. Treatment that was supported by randomised controlled trials was prescribed in 162 (51.9%) cases. In 121 (38.8%) cases, patients were given standard and commonly used drugs that were not supported by evidence from clinical trials, and in 29 (9.3%) cases, the treatments given had no substantial supporting evidence. The management of some frequently encountered medical conditions was not based on trial data, because the relevant studies had not been conducted.
Conclusion. Basing treatment on comparative efficacy results is a worthwhile goal, but there are limitations in conducting literature searches to identify relevant trials and studies. Evidence-based medical practice is not applicable in a large number of commonly encountered conditions.

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Key words: Acute disease; Clinical medicine; Evidence-based medicine; Randomized controlled trials

Introduction

The past 20 years have seen a dramatic growth in therapeutic advances and in information technology. As health care institutions focus increasingly on the outcomes of medical care, physicians must be able to justify the treatment that they offer to patients. The evidence-based medicine (EBM) movement has become highly influential in medical education and in daily practice.[1-4] The central theme of this movement is the emphasis on medical practice based on the results of randomised controlled trials (RCTs) and meta-analyses, rather than on unsystematic clinical experience. A basic requirement is the existence of efficacy studies. The aim of this study was to review the drug treatment given to medical in-patients of a teaching hospital in Hong Kong over a 1-month period, to determine whether RCT-derived evidence was available for a range of common medical conditions, and to see if the pattern of prescription conformed to the principles of EBM.

Methods

The medical records of 129 consecutive patients who were admitted to the acute adult general medical ward of the Prince of Wales Hospital from 1 September 1998 to 30 September 1998 were reviewed retrospectively. For each patient, we recorded the primary diagnoses that were responsible for their current admission as well as the drugs that were prescribed for those diagnoses. Procedural interventions such as the insertion

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of a chest drain for pneumothorax, or sclerotherapy for oesophageal varices were excluded. We identified the medical condition and searched for relevant RCTs or meta-analyses of trials that supported each intervention from the English literature from 1966 to 1999 by using the *Medline* database. This search was supplemented by manual searches of standard textbooks and non-indexed medical journals. We selected studies that assessed the difference between a treatment group and a control group, and which used random assignment of that treatment. After identifying the pertinent studies, we reviewed the abstract; if the trial demonstrated a beneficial effect, such as reduced mortality and morbidity, the full article was checked. The level of evidence that formed the basis of treatment was categorised into the following three groups, based on the systems devised by Ellis et al[5] and Gill et al[6]:

(1) Intervention that was based on evidence from one or more RCTs;
(2) Intervention that was based on convincing non-RCT evidence that was scientifically plausible. An intervention would come under this category if it were judged that omission of the treatment would be harmful; and
(3) Intervention that was not based on RCTs and which did not meet the criteria set out in (2).

Only conditions for which drugs were prescribed were included; this review did not apply to those patients who were admitted primarily for investigation or who had inactive conditions that did not require drugs. Two examples are given below.

Case 1

An 89-year-old woman was admitted with heart failure. She had pallor and sinus bradycardia. The haemoglobin level was 53 g/L (normal range, 115-155 g/L) and the carcinoembryonic antigen level was elevated to more than 400 μg/L. In view of her frail and dependent status, it was decided not to investigate the cause of her anaemia. No drug treatment was given for the bradycardia and anaemia but frusemide (furosemide) with potassium supplementation was prescribed for her heart failure. A retrospective search of the available evidence for the use of these drugs to treat such a condition was initiated, but no trials that demonstrated efficacy were found. The intervention in this case was thus categorised under group 2.

Case 2

A 48-year-old woman presented with a transient ischaemic attack. She had been taking aspirin for a previous ischaemic stroke. Risk factors included a family history of stroke, hypercholesterolaemia, and intracranial stenoses. She was treated with ticlopidine hydrochloride for the ischaemic attack and simvastatin for the hypercholesterolaemia. A *Medline* search found published trial data that demonstrated clear benefits for these two treatments. They were thus classified as group 1 interventions.

Results

Ninety-one drug interventions were prescribed on 306 occasions (Tables 1-3). Five patients, who had been admitted because of syncope, confusional state, drug overdose, anaemia (no diagnosis on discharge), and dizziness, did not receive treatment. When we considered individual patients who were given drugs, 162 (51.9%) were prescribed RCT-based therapy (group 1),[7-44] 121 (38.8%) were prescribed convincing but non–RCT-based treatment (group 2), and 29 (9.3%) were given interventions without substantial evidence (group 3). The number of patients treated amounted to more than 129, because some had received more than one drug. Of the 91 drug treatments, 35 (38.4%) could be classified into group 1, 42 (46.2%) into group 2, and 14 (15.4%) into group 3.

Discussion

An essential principle of modern health care is that it should have a scientific basis—reliance on assumption or intuition is discouraged.[45] There have been concerns that only a small fraction of medical therapies are supported by objective evidence; two previous articles have addressed this issue.[5,6] In this study, approximately 52% of the patients received drug therapies based on information derived from RCTs. This figure is similar to that obtained by Ellis et al[5] in a similar setting. However, one must bear in mind two points. Firstly, the existence of RCT-based evidence does not necessarily mean that the treatment in question is unequivocally beneficial. For example, although the use of thrombolytics to treat myocardial infarction under appropriate circumstances clearly reduces mortality, other therapies are based on trials that involve smaller sample populations and which thus yield less consistent results. In the case of prescribing β-blockers for portal hypertension or heparin for acute stroke, the results from clinical trials may be conflicting. There is also the question of the methodological quality of the trial: details such as concealment of treatment allocation, blinding of outcome assessment, and handling of withdrawals would influence the size of the therapeutic effect. Secondly, there is a problem in applying average group-derived data

Table 1. Group 1 conditions, which were treated according to evidence based on randomised controlled trials

Condition	Drug	No. of patients treated	References
Respiratory			
asthma	Corticosteroids	4	7, 8
chronic obstructive airway disease	Antibiotic	9	9
	Ipratropium bromide	18	10
	β-Adrenoceptor stimulant	20	11
	Corticosteroid	11	12
	Theophylline	5	13
Cardiac			
congestive heart failure	Nitrates	4	14
	Angiotensin-converting enzyme inhibitor	3	15
essential hypertension	β-Blocker	5	16
	Diuretics	3	16
ischaemic heart disease	Aspirin	6	17, 18
	Calcium-channel blocker	5	19
atrial fibrillation	Warfarin	6	20
	Digoxin	6	21
	Amiodarone hydrochloride	1	22
hyperlipidaemia	Statin	3	23
Rheumatic			
lupus nephritis	Corticosteroid	2	24
	Azathioprine	2	25
rheumatoid arthritis	Hydroxychloroquine	1	26
	Cyclosporin A	1	27, 28
Neurological			
transient ischaemic attack	Aspirin	3	29, 30
ischaemic stroke	Ticlopidine hydrochloride	3	31
	Aspirin	3	32
	Low–molecular weight heparin	7	33
epilepsy	Anticonvulsants	4	34
Gastro-enterological			
peptic ulcer	Proton pump inhibitor	6	35
	Helicobacter pylori eradication	6	36
portal hypertension	β-Blocker	2	37
Miscellaneous			
diabetes mellitus	Oral hypoglycaemic drug	2	38
	Insulin	5	39
	Angiotensin-converting enzyme inhibitor	1	40
pulmonary embolism	Warfarin sodium	2	41
	Heparin	1	42
alcohol withdrawal	Anticonvulsant	1	43
psoriasis	Methotrexate	1	44
Total		162	

to an individual. Randomised controlled trials involve patients from a carefully selected patient group. In practice, however, doctors encounter patients in whom factors such as extremes of age or co-morbidities are not addressed in the original trial.[46] Likewise, we have to judge whether the results of trials performed in Caucasians can be extrapolated to Chinese patients. For example, two studies have suggested that the blood pressure–lowering effect of angiotensin-converting enzyme inhibitors is lower in Chinese diabetic hypertensive patients.[47,48]

This study shows that around 39% of common therapeutic decisions were made in the absence of data from RCTs. This finding highlights the practical limits of EBM, as there are conditions for which there are no RCTs or meta-analyses to guide treatment. For group 2 interventions such as potassium supplementation to treat hypokalaemia, no RCT data will be available in the foreseeable future, as the benefits appear to be so self-evident that it would be considered unethical to conduct a trial. Without evidence-based information, physicians still have to make therapeutic decisions and rely on their clinical judgement. Factors such as an underlying disease, the prognosis, patient preference, and psychosocial background are considered before a course of action is determined.

Approximately 15% of all drug treatments were classified under group 3—that is, these interventions

Table 2. Group 2 conditions, which were treated according to convincing evidence that was not based on randomised controlled trials

Condition	Drug	No. of patients treated
Cardiorespiratory		
asthma	β-Adrenoceptor stimulant	3
	Ipratropium bromide	1
pericarditis	non-steroidal anti-inflammatory drug (indometacin [indomethacin])	1
pneumonia	Antibiotic	14
tuberculosis	Antituberculous drugs	3
congestive heart failure	Diuretics	12
unstable angina	Nitrate	9
Gastro-enterological		
gastro-enteritis	Antibiotics	3
pseudomembranous colitis	Antibiotics	2
cirrhosis	Vitamin K	2
constipation	Stimulant laxative (senna)	1
	Osmotic laxative (lactulose)	2
	Bulk-forming laxative	4
diarrhoea	Antispasmodic (co-phenotrope)	2
spontaneous bacterial peritonitis	Antibiotics	2
Neurological		
vasculitic neuropathy	Corticosteroid	1
	Carbamazepine	1
peripheral vertigo	Cinnarizine	1
tuberculosis arachnoiditis	Corticosteroid	1
brain oedema	Dexamethasone	2
alcohol withdrawal	Thiamine (vitamin B_1)	2
Parkinson's disease	Antiparkinsonian drugs	2
ischaemic stroke	Warfarin sodium	1
Others		
Grave's disease	Antithyroid drugs	2
	β-Blocker	1
iron-deficiency anaemia	Iron supplement	3
macrocytic anaemia	Folic acid	1
rheumatic heart disease	Warfarin sodium	1
deep vein thrombosis	Warfarin sodium	2
Raynaud's syndrome	Calcium-channel blocker	1
	Antiplatelet drug	1
pemphigus	Corticosteroid	2
pain control	Morphine	1
	Paracetamol	10
	Analgesic	6
	Opiate (buprenorphine)	1
hypokalaemia	Potassium chloride	10
gout	Colchicine	1
	Allopurinol	1
urinary tract infection	Antibiotics	3
benzodiazepine overdose	Oral activated charcoal	1
	Flumazenil	1
Total		121

were not based on objective evidence. Although this figure is disappointing, the drugs in this category were mostly inexpensive and relatively non-toxic. There was no justification for many of the interventions in this category (eg the use of antibiotics in cases of uncomplicated asthma). Ideally, such treatments should be discouraged and subject to periodic audit. Drugs that have a narrow therapeutic window or potentially significant side effects—for example, immunosuppressive agents or anticoagulants—were generally prescribed with caution.

Although 61.6% (groups 2 and 3) of the drug interventions were not supported by trial data, this figure does not necessarily indicate irresponsible prescribing behaviour. Many of the interventions were classified under group 2—namely, conventional treatments for which there is no RCT support. The implication for medical practice is that EBM is not applicable in a large number of commonly encountered conditions. Whether this suggestion holds true for other disciplines or other settings requires further investigation. Furthermore, drug therapy is just one aspect

Table 3. Group 3 conditions, which were treated by interventions without substantial evidence

Condition	Drug	No. of patients treated
Chest pain (atypical)	Antacid	2
	Histamine H_2-antagonist	2
Unspecified	Multivitamin	6
Prohylaxis, gastro-intestinal bleeding	Antacid during corticosteroid use	1
Acute upper respiratory tract infection	Antibiotic	3
	Antitussive	1
Chronic obstructive airway disease	Expectorant	2
Asthma	Antibiotic	1
Congestive heart failure	Aspirin	2
Demyelinating neuropathy	Multivitamin	1
Pruritus	Histamine H_1-antagonist	2
Dyspepsia	Antacid	2
	Histamine H_2-antagonist	2
	Proton-pump inhibitor	2
Total		29

of patient management: the diagnostic process, good nursing care, counselling, improving compliance, and dietary control are also crucial; however, these aspects are more difficult to quantify.

In conclusion, basing treatment on comparative efficacy results is a worthwhile goal, but—as shown in this study—there are limitations in conducting literature searches to identify relevant trials and studies. There are also clinically important situations, as in the words of Sir Douglas Black, "whose complexity makes them, for the present, 'insoluble' by the RCT route."[49] Evidence-based medical practice will not provide answers to every clinical problem.

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