

Abstracts: therapeutics symposium 2007

ABBREVIATIONS Blood pressure (BP), British Society for Haematology (BSH), individual care safety report (ICSR), (NMDA), National Patient Safety Agency (NPSA), over the counter (OTC), patient reported outcomes (PROs), significant event analysis (SEA)

SESSION 1 ACHIEVING MAXIMUM CLINICAL EFFECTIVENESS

Chairman: Prof DN Bateman, Director, National Poisons Information Service, Edinburgh Centre, Edinburgh, Scotland

Quality of life, the best measure of effectiveness?

Dr E McColl, Director, Newcastle Clinical Trials Unit, Institute of Health & Society, Newcastle University, Newcastle upon Tyne, England

Email e.mccoll@ncl.ac.uk

Abstract

Background In assessing clinical effectiveness, the measurement of clinical outcomes (e.g. BP, HbA_{1c}) may only tell part of the story. Measuring subjective outcomes of importance to patients provides a further perspective, and in respect of chronic disease management, may be the most relevant measure of treatment effectiveness. Patient reported outcomes include quality of life, but are broader, encompassing also symptom experience, treatment satisfaction, understanding and adherence.

This presentation will highlight key issues in the assessment of patient reported outcomes, in particular, but not exclusively, quality of life. These issues will be discussed in relation to the application of these measures in routine clinical practice, as well as in formal evaluations of effectiveness, in the context of clinical trials.

Methods or Theme The following key themes will be discussed:

- The definition of PROs, and the place of 'quality of life' within this taxonomy;
- factors to take into account in choosing and using PROs;
- the definition, conceptualisation and operationalisation of 'quality of life';
- the pros and cons of generic vs condition-specific measures of quality of life;
- when quality of life should be the primary measure of effectiveness;
- when other PROs and/or clinical outcome measures may be preferred to measures of quality of life.

Conclusions The importance of assessing PROs, including quality of life, is increasingly recognised. However, choosing and using the most appropriate PRO can be challenging, and no single PRO or quality of life measure is appropriate in all situations.

Key words Patient reported outcomes, quality of life, generic measures, condition-specific measures.

Sponsors None.

Declaration No conflict of interest declared.

SESSION 2 THE SAFETY OF DRUGS IN CLINICAL USE

Chairman: D Thomson, Director of Pharmacy, Primary Care, NHS Glasgow

Safety of over the counter medicines: issues for professionals

Prof C Bond, Professor of Primary Care (Pharmacy), University of Aberdeen, Scotland

Abstract

Background Over the counter medicines have been used for many years to treat self-limiting minor ailments. Over the past 15–20 years, a lot more medicines have become available OTC from both pharmacies and general sales outlets, including some highly effective treatments for both acute and long-term conditions.

Like all medicines, effective treatments can have side-effects of varying severity, and may have the potential to interact with other medicines. Research evidence suggests that patients do not always use OTC medicines as directed on the package, and this can contribute to increased risk in their use. Supply of OTC medicines from pharmacies is often made by pharmacy support staff, and other medicines are available by self selection in supermarkets and other non-pharmacy outlets. There is no routine record-keeping of medicines supplied OTC, and where records are kept they are not integrated with other healthcare records such as the GP held record. Thus the potential for drug–drug interactions to be detected or avoided, or pharmacovigilance studies to be conducted, are limited.

It is likely that further potent medicines will soon be available OTC and mechanisms to integrate this route of supply with other health care must be explored.

Sponsors None.

Declaration No conflict of interest declared.

Achieving safety in the marketplace: detecting the drug safety signals that matter

Stanley Davidson Lecture

Chairman: Prof Neil Douglas, President RCPE, Edinburgh, Scotland

Prof R Edwards, Director, WHO Adverse Drug Reaction Co-ordinating Centre, Uppsala Monitoring Centre, Sweden

Abstract

Background There are huge numbers of adverse experiences following medication reported worldwide as ICSRs to regulatory authorities. These, and similar reports or case series in the literature, form the main source of signals of suspected new drug-adverse reaction relationships.

Each ICSR is a concern by the primary reporter, who may be a health professional or patient, communicating a negative outcome in an individual patient's treatment. As such ICSRs reflect facts, biases, prejudices, misdiagnoses and impressions. But they also tell us about true, rare events as well as common ones, about drug interactions, unusual patient phenotypes, new drugs, and unusual disease effects. That they are concerns also gives a picture of views about current safety issues of health professionals and the public, so alerting to the need for communication or education.

With large volumes of data, it is necessary to combine quantitative and qualitative methods to find signals which may significantly improve the treatment of individual patients: the needles in the haystack. Knowledge finding, using triage algorithms and data mining, is growing in strength as a preferred method. Moreover, the use of neural networks allows finding of complex patterns in databases of ICSRs.

Individual care safety reports cannot of themselves usually point to more than a suspicion of a drug adverse reaction. Epidemiology and other tools need to be used for confirmation using observational studies and sometimes interventional studies (other pharmacological evidence may be used as well).

Now that computerised healthcare management is common, there is a huge amount of patient information

recorded, particularly prescription information and indications, as well as much other relevant clinical information. Data mining of these databases adds a new dimension to finding drug safety signals. Some bias and confounding may be avoided or become transparent; frequencies of events may be better assessed, and the additional clinical information may be used to define risk situations and risk/benefit balance.

One of the most important needs in the safety of medicines is to communicate the clinically useful information that is already available on medicines from the data already collected. Summaries of product characteristics of medicines do not function as any more than bare bones. We should make much better use of IT systems to provide the meat in a digestible and timely fashion!

For an efficient process from early signal to useful clinical information, many decisions need to be made by regulators and their advisors. These need to be taken with meaningful patient involvement; they should be open to peer review and be transparent, and, above all, subject to follow-up for their effectiveness and impact on public health.

There is a great need for more resources in medicine safety to avoid over-dependence on pharmaceutical industry funding.

Key words ICSRs, regulatory authorities, new drug-adverse reaction relationships, rare events, patient phenotypes, knowledge finding, triage algorithms, data mining, neural networks, databases, medicines safety.

Sponsors None.

Declaration No conflict of interest declared.

SESSION 3 IMPROVING SAFETY OF MEDICINES IN PRACTICE: PROBLEM DRUGS

Chairman: Prof D Webb, Christison Professor of Therapeutics and Clinical Pharmacology, University of Edinburgh, Edinburgh, Scotland

Problem drugs in hospital practice

Dr S Maxwell, Senior Lecturer in Clinical Pharmacology, University of Edinburgh, Edinburgh, Scotland
Email S.Maxwell@ed.ac.uk

Abstract

Background Adverse events related to medicines seem to be increasing. This may be related to a variety of factors including increased numbers and use of drugs in general, higher patient throughput, more complex treatment

CME

regimens and older, more vulnerable patients. Another possible factor is that junior doctors, who undertake much of the prescribing, are not adequately trained to cope with these pressures. Hospitals are putting increased emphasis on avoiding medication problems as part of their clinical governance strategies. An important part of this process is recognition of the drugs most likely to be involved in serious incidents and the circumstances in which they occur. This talk will provide a brief overview of these issues.

Key words Drugs, prescribing, adverse events, medication error.

Sponsors None.

Declaration No conflict of interest declared.

Reducing the risks from insulin

Dr MWJ Strachan, Consultant Physician, Metabolic Unit, Western General Hospital, Edinburgh, Edinburgh

Email Mark.Strachan@luht.scot.nhs.uk

Abstract

Background

The major side-effect of insulin is, of course, acute hypoglycaemia. Despite the substantial advances in insulin therapy and blood glucose monitoring that have occurred in the 80 years since the isolation of insulin, hypoglycaemia remains the most common complication of Type 1 diabetes, and generates as much anxiety in patients as the threat of advanced diabetic complications, such as blindness or renal failure. Few people with Type 1 diabetes escape intermittent exposure and, as a result, hypoglycaemia is the principal limiting factor in achieving good glycaemic control. The magnitude of the psychological consequences of hypoglycaemia cannot be over-estimated and will be considered in this presentation.

Physical complications associated with insulin-induced hypoglycaemia are much less common. Permanent neurological damage and death can occur following prolonged, profound hypoglycaemia. This is usually in the setting of concurrent alcohol excess or deliberate insulin overdose. There are instances when insulin has been used as a murder weapon.

Injection site problems are relatively uncommon and take the form of lipohypertrophy and local allergic reactions. Improving safety from insulin requires clear protocols in hospital for prescription, particularly when dealing with intravenous insulin. Subcutaneous insulin should be prescribed on a daily basis. As ever, better patient education remains paramount, but the risk of hypoglycaemia will be ever-present until better methods of detection are developed.

Key words Insulin, acute hypoglycaemia, blood glucose monitoring, glycaemic control, psychological consequences, neurological damage.

Sponsors None.

Declaration No conflict of interest declared.

Safer practice with anticoagulants

Professor D Cousins, Head of Safe Medication Practice, National Patient Safety Agency

Email David.cousins@npsa.nhs.uk

Abstract

Background Anticoagulants are one of the classes of medicines most frequently identified as causing preventable harms and admissions to hospitals. Managing the risks associated with anticoagulants can reduce the chance of patients being harmed in the future.

This patient safety alert has been developed in collaboration with the BSH and a broad range of other clinical organisations and individual clinicians, patients and patient groups.

Methods or Theme In a patient safety alert planned for publication in March 2007, the NPSA will be recommending that NHS and independent sector organisations in England and Wales take steps to make the use of anticoagulants safer, thus:

1. Ensure all staff caring for patients on anticoagulant therapy have the necessary work competences.
2. Review clinical protocols for anticoagulant services to ensure they reflect safe practice.
3. Audit anticoagulant services using BSH/NPSA safety indicators as part of the annual medicines management audit programme.
4. Ensure that patients prescribed anticoagulants receive appropriate information. There is an updated patient-held information (yellow) booklet.
5. Promote safe practice with prescribers and pharmacists to check that the INR level is safe before issuing or dispensing repeat prescriptions for oral anticoagulants.
6. Promote safe practice for prescribers co-prescribing one or more clinically significant interacting medicines for patients already on oral anticoagulants.
7. Ensure that dental practitioners manage patients on anticoagulants according to evidenced-based therapeutic guidelines.
8. Amend local policies to standardise the range of anticoagulant products used, incorporating characteristics identified by patients as promoting safer use.
9. Promote the use of written safe practice procedures for the administration of anticoagulants in social care settings.

Conclusions The National Patient Safety Agency plans to launch these safer practice recommendations in March 2007, and the NHS in England and Wales will be required to implement and evaluate these recommendations by 31 March 2008.

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Key words Anticoagulants, warfarin, heparin, NPSA, preventable harms, medication errors.

Sponsors None.

Declaration No conflict of interest declared.

Avoiding problems with opioids

Professor DN Bateman, NPIS Edinburgh, Royal Infirmary of Edinburgh, Edinburgh, Scotland

Email nick.bateman@luht.scot.nhs.uk

Abstract

Background The management of pain remains an area where present treatments are often sub-optimal. The increasing use of opioids as drugs of abuse has resulted in significant limitations on physicians and pharmacists. While the search for newer, more effective, analgesics continues, there have also been advances in the use of substitution therapy for addicts.

Methods or Theme In the management of pain, opioid drugs present a number of problems to the prescribing doctor. They have a higher incidence of adverse effects than other analgesic groups, and significant numbers of patients stop treatment because of this. Approximately one in four patients suffers nausea, one in five constipation and drowsiness, and one in six, vomiting and dizziness. Analgesic efficacy is often unpredictable, complicated by the variations in metabolism of

commonly used opioids such as codeine. Development of tolerance is a problem for some patients. Evidence that switching from one drug to another in this group is an effective strategy is weak, particularly since individual susceptibility to analgesic effect is not well correlated between one drug and another. Active metabolites of morphine are renally excreted, thus making accumulation likely in patients with impaired renal function and in the elderly. Standard fixed dose combinations of opioids with paracetamol are problematic, since the quantity of opioid may be too little in some preparations and too great in others. Recent withdrawal of co-proxamol has focused attention on this area.

Opioids with secondary pharmacological properties, including methadone, tramadol and dextropropoxyphene further illustrate the complexity of using these agents. Methadone acts on NMDA receptors and has slower onset and offset than other opioids. Highly effective as an analgesic, its use in drug addiction management has altered its place in therapy. Tramadol effects 5HT receptors, its metabolism is variable, and in clinical trials it causes nausea at least as frequently as other opioids. Efficacy is therefore also somewhat unpredictable, and in some studies less than standard paracetamol opioid combinations. Dextropropoxyphene (co-proxamol) has sodium channel-blocking properties. These three drugs in overdose are particularly hazardous, methadone causes QT prolongation at high-dose, tramadol fits, and co-proxamol sudden death, probably from ventricular arrhythmia.

Conclusions Opioids remain a widely used group of compounds but individual titration, and a knowledge of the pharmacology of these drugs are key to optimum use in the patient.

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Key words Analgesia, opioids.

Sponsors None.

Declaration No competing interests. Professor Bateman has published papers used to support the withdrawal of co-proxamol.

SESSION 4 IMPROVING SAFETY OF MEDICINES IN PRACTICE: MEDICATION ERRORS AND STRATEGIES FOR PREVENTION

Chairman: Dr A Timoney, Consultant in Pharmaceutical Public Health, NHS Tayside

Significant event analysis: enhancing the safety of patient care through reflective learning

Dr P Bowie, Associate Advisor, A Power, Assistant Director of Pharmacy, NHS Education for Scotland, Glasgow, Scotland

Email paul.bowie@nes.scot.nhs.uk

Abstract

Background In general practice, it is estimated that prescribing related incidents account for 25% of litigation cases,¹ and that error may occur in up to 11% of all prescriptions.² An average incidence of 18 errors per 100,000 items dispensed has been reported in hospital pharmacy.³ Investigating and learning from 'significant' events including medication errors are strongly promoted in the NHS.

Significant event analysis is promoted as a team-based mechanism for learning and change. It involves the structured analysis of an event deemed to be 'significant' by the healthcare team. The emphasis is on establishing why an event happened, highlighting learning needs and facilitating necessary change. In Scotland, providing evidence of SEA is part of GP appraisal and the new GP contract. The pharmacy and dental professions have embraced SEA, while it is recommended as part of training for foundation doctors.

We describe a voluntary and confidential model of external peer review to facilitate educational feedback on SEA performance. Selected findings from a series of related studies are also reported.⁴⁻⁹

Methods or Theme Participants submitted an SEA report in a standard format to be reviewed by trained peer assessors using a content valid instrument⁷ to facilitate educational feedback. Of 833 SEA reports submitted, 541 (65%) were judged to be 'satisfactory' by peer review (95% CI: 32-72%).

- A range of learning issues were identified by peer review for SEA judged to be 'unsatisfactory'.
- Peer review is valued by participants as it enhances the validity of their efforts.
- The evidence base for the effectiveness of SEA is limited.

Conclusions Most practitioners are able to analyse a significant event to a satisfactory standard. A significant

minority require educational input. Where a standard structured method of SEA exists, there is potential to facilitate learning from safety incidents including medication errors.

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Key words Patient safety, significant event, clinical audit, peer review, feedback.

Sponsors None.

Declaration No conflict of interest declared.

Preventing medication errors: how errors occur and how they might be prevented

Professor RE Ferner, Director, West Midlands Centre for Adverse Drug Reaction Reporting, Birmingham, England

Email r.e.ferner@bham.ac.uk

Abstract

Aetiology and definitions All human action is error prone. A medication error is a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient. Errors can be made in the planning of an action (mistakes) because of poor rules or inadequate knowledge, or in carrying out an action (slips and lapses). Violations are conscious acts that contravene accepted rules.

Incidence Medication errors are common, and their consequences potentially serious. They are hard to detect, so their incidence is uncertain. Estimates for error rates vary one hundredfold, up to 4% of all US deaths.

Prediction and Diagnosis

Prophylaxis There has been very little predictive work, although methods exist. Root cause analysis – finding out what happened, and what allowed it to happen – could help diagnosis.

Poor rules can be improved. Treatment can be made safer if a nomogram is used for warfarin dosing, or patients whose thiopurine-methyltransferase activity is low are identified prior to azathioprine treatment. Adequate plans require knowledge of the basic principles and so teaching these should be a priority. Clinicians also need details of the relevant drugs, patient, and clinical context. Computerised prescribing and decision support can help, but need care: too little information, and patients are put at risk; too much, and clinicians ignore it. Slips and lapses are unavoidable, but we can reduce the probability that they will occur by less reliance on human action, by altering the conditions under which actions are performed, and increased checking. Castigation is counterproductive.

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Key words Medication errors, error prevention, human factors, medication safety.

Sponsors None.

Declaration No conflict of interest declared

PAST PRESIDENTS

John Rutherford (1695–1779)

He was the twenty-second President of the College, serving from 1752–1756, his son Daniel, following in his footsteps in 1796–1798. At one time, a portrait in the College purported to be of John was later found to be of Daniel and notes thought to be of John's lectures were found to be Daniel's. John was a son of the manse, his father being Minister in Yarrow in the Scottish Borders. At the age of 14 he matriculated at Edinburgh University to study philosophy and mathematics before going on to medicine, neither his age nor his choice of subjects being at all unusual in those days. After studying anatomy, surgery (very limited in those days) and *materia medica* he went to London, Paris and Leyden (studying under Boenhaave), gaining his MD at Rheims. (In those days it was possible, indeed common, to gain

a degree without having studied in that university.)

In 1721, he returned to Edinburgh and, with Andrew St Clair, Andrew Plummer and John Innes, gained permission from the Town Council to use a house they had bought as a chemical laboratory and teaching centre for students, much as the Hunter brothers did in London when no fewer than 26 such private 'medical schools' were in operation there. They were permitted to grow medicinal plants on some unused ground adjoining the house, selling some produce to local apothecaries and using the rest in their practice and teaching. So impressive was their venture, that in 1716 Rutherford was appointed Professor of the Practice of Medicine (lecturing in Latin), a post he held until retiring in 1765 when he was succeeded by John Gregory. It might be thought that being professor would give him the right to teach students in the Royal Infirmary, but that honour

was only bestowed on him in 1748. His Saturday morning classes were highly popular. Patients were invited to come before the students, describe their symptoms and then be diagnosed and discussed by Rutherford, before being sent home with appropriate medications. In 1750, such was the success and impact of his teaching, that he was given clinical charge of a ward. So began the famous pattern of medical care and clinical teaching in Edinburgh's Royal Infirmary, which is continued to this day.

He was married twice. Anne, the daughter from his first marriage, was the mother of Sir Walter Scott, a relationship Scott describes with some pride in his autobiography.

Like many other famous men in Edinburgh, he is buried in the Kirkyard of Greyfriars Church.

Derek Doyle
Obituaries Editor, The Journal RCPE