Adverse medication events in a psychiatric practice: a naturalistic study

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Aims and method To document the number and type of adverse medication events in a psychiatric sector service. Significant new adverse events were collated by the author and team over 30 months. Intervention to prevent any adverse event was enacted as soon as any were noticed or anticipated.

Results Thirty-six significant events occurred including three deaths and nine near misses. Corrective action was taken immediately any adverse event occurred. Inadequate communication between various hospital clinics, general practitioner practices, psychiatric clinics and pharmacies was the biggest avoidable cause of adverse events.

Clinical implications Awareness of adverse drug events is essential in psychiatry. Clear, transparent pathways of prescribing are a key requirement to reduce avoidable adverse medication events. Psychopharmacology is a core module for psychiatric training.

Declaration of interest None.

The average psychiatric sector service has approximately 350 patients. Very few of these patients do not take medication, and the older they are the more medication they are prescribed. Medication may come from psychiatry, general practitioners (GPs), other clinics, may be obtained over the counter, from the internet, from a homeopathic practitioner, the street, relatives, etc. Multiple doctors, health services and medications increase the risk of adverse drug reactions.[1–3] The more complex the pathway for medication delivery, the more likely it is that mistakes will happen. A patient being discharged from hospital may have four routes to acquire medication – the hospital discharge script, the GP script, the clinic script and the pharmacy. There is a widespread literature documenting the prevalence of adverse drug reactions and drug–drug interactions and they confirm these patterns of risk.[4,5] To quantify the extent of such events in our service we prospectively monitored all adverse reactions and drug–drug interactions over 2.5 years.

Method

Medication safety was promoted as a theme for the multidisciplinary team over 2.5 years (30 June 2009 to 31 December 2011). An alerting initiative was conducted with 30 local pharmacies via a questionnaire and doctor visits, to enable user-friendly communication between the pharmacies and the team. Any new adverse symptoms or complaints thought to relate to medication were related to the author (E.G.B.). Events were assessed through history and investigation of all medication the patient was taking, and the degree to which medication adverse reaction or interaction was responsible was decided. Many such events were confirmed as drug-related by subsequent improvement in the patient after stopping, changing or reducing the medication. Data were gathered prospectively by documenting emergent events as they occurred.

It is important to state that this study was undertaken as part of routine clinical care and adverse effects were dealt with immediately. It may be seen as a debacle of 'carry on doctor' proportions when read in the cool light of journal club moral high ground, but the glaring 'Oh My God!' interactions and adverse effects were the doing of the other actors, namely GPs, physicians and patients themselves. It highlights what is actually happening in a tertiary referral university hospital setting when there are multiple players and less-than-perfect communication. These results are shocking but no worse and probably better than in most services.[6] The beginning of improvement is establishment of a baseline.

Results

In total, 36 significant drug-related events occurred over the 2.5 years of the study. There were 3 deaths, 9 near misses and 23 adverse events or drug–drug interactions. Each significant event was discussed in a team meeting. All three deaths were related to multiple carers – GP, medical clinic and psychiatry. The first person was a man in his 80s who developed lithium toxicity of 2 mmol/l in the context of

recently instituted captopril by a physician and eventually succumbed to multi-organ failure. The second was a man of 32, who died suddenly, and a post-mortem reported an enlarged heart of 450 g and a cardiac arrhythmia as a probable cause of death; he was taking three medications recognised to cause prolonged QT: haloperidol, methadone and clozapine, all of which were within therapeutic blood levels and no prolonged QT was seen on electrocardiograms (ECGs). The third person was a man of 54 who was taking warfarin for pulmonary emboli related to olanzapine and who died from a cerebral bleed.

There were several near-miss events. A 73-year-old lady went into respiratory failure and reduced consciousness following use of an opiate patch for pain, and recovered on removal of the patch and naltrexone injection. A 73-year-old man collapsed and was resuscitated in hospital following mixing up his medications which included a tricyclic antidepressant. Two patients were discharged from the medical wards on both a tricyclic and duloxetine: one developed weakness and the other did not manifest symptoms but the combination was unnecessary and not evidence based. A 30-year-old woman developed pulmonary emboli while taking olanzapine; this settled on warfarin treatment and stopping olanzapine. A 55-year-old man developed a pituitary tumour with visual field defects and prolactin of 64 000 units while taking haloperidol decanoate depot 25 mg every 2 weeks; on stopping haloperidol and instituting olanzapine instead, the tumour regressed and prolactin returned to normal levels over 6 months. An 88-year-old lady was inadvertently put on venlafaxine 225 mg and escitalopram 20 mg after hospital discharge and suffered no ill effects, but the escitalopram was discontinued. A 50-year-old lady was taking tramadol and sertraline without event: the tramadol was stopped (risk of serotonin syndrome). A 65-year-old lady developed extreme agitation while taking clonazepam; she sustained a broken ankle after a fall and almost wandered on to a busy road, but she recovered on stopping the clonazepam.

We also discovered other adverse drug events, as follows.

- Two patients with high clozapine levels (1.2 mg/l and 1.4 mg/l), one of whom developed dysarthria. The levels were possibly due to slow metabolism or to inhibition by concomitant escitalopram or clarythromycin.
- Ataxia, memory loss and confusion in a man taking valproate and lamotrigine; the symptoms ceased on halving the lamotrigine dose (recognised interaction).
- Two Chinese patients developed marked sedation on small doses of quetiapine (25 mg) and olanzapine (5 mg) (the Chinese are known to have a higher percentage of slow metabolism (up to 20%) compared with other ethnic groups).
- Assessment for QT interval in a man on aripiprazole and tamsulosin (an alpha blocker), both of which prolong QT; ECG was normal.
- A man on methadone 70 mg/day needed an increase in dose to 140 mg after commencing rifampicin (induction).
- Mental confusion and sedation in a man taking risperidone 7 mg when ciprofloxacin was started, and recovery after the antibiotic was stopped (inhibition).
- Interaction of grapefruit juice and escitalopram causing agitation in a 46-year-old man; resolved on stopping the juice (inhibition).
- Fivefold increase in liver function tests in a man taking lofepramine after quetiapine was added and reduction to twice normal levels on stopping quetiapine (pharmacokinetic additive impact on liver function tests).
- Allergic reaction in a 45-year-old woman newly commenced on quetiapine extended release 100 mg requiring emergency department attendance with skin rash, agitation, respiratory distress and neck stiffness; the situation resolved on stopping quetiapine.
- A young woman was trying to conceive while taking valproate, which was substituted by an antipsychotic.
- Several falls in a blind lady taking 125 mg of lamotrigine plus other medications, and the falls stopped on halving the dose of lamotrigine.
- Rebound mania after stopping lithium in a lady who developed renal impairment (recognised effect).
- Increased clozapine levels in a man who stopped smoking (recognised effect).
- Four ladies developed non-specific dysphoria and anxiety while taking orlistat plus their usual psychiatric medication; symptoms resolved on stopping orlistat (no information in literature or drug company data reporting interaction of orlistat and psychiatric medication).
- Persistent sinus tachycardia (110–130 beats/min) in a 35-year-old woman on zuclopenthixol 200 mg every fortnight despite cardiac investigation (recognised effect of drug).
- Petit mal episodes in a 30-year-old man taking paroxetine 50 mg and quetiapine 400 mg, which resolved on reducing both medications (lowered epileptic threshold).
- Institution of propranolol 40 mg three times daily in a lady with severe anxiety, unaware she also had significant asthma. The pharmacist alerted the carer and the propranolol was not dispensed (pharmacodynamic event).
- Exacerbation of anxiety in a 25-year-old woman when clarithromycin was added to escitalopram; anxiety resolved on stopping the antibiotic.
- Clarithromycin was also associated with visual hallucinations and agitation in a 60-year-old woman taking venlafaxine and tramadol 100 mg three times daily and the situation settled on stopping the antibiotic and opiate.

Discussion

It is well recognised that physical illness due to medication adverse events is common in psychiatric practice, and contributes substantially to morbidity and mortality.[7,8] An intervention that reduces these risks is to be welcomed, especially if it is cost-neutral and does not require more resources, as in this study.

The list of adverse drug events reported here is not unusual. They encompass the signature drug events that are highlighted in the drug–drug interaction and adverse drug reaction literature.[9] The antibiotic-related events are

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common, and QT interval prolongation is an important adverse event with many psychiatric medications. The orlistat events require further study to see whether there is a relationship between it and psychiatric medication malabsorption. The observation in four patients and the mechanism of action of orlistat, namely gut lipase inhibition, make the association plausible. The list of toxicities of lithium, lamotrigine and clozapine highlights the ongoing need for vigilance with these agents. The intervention of pharmacists in alerting the doctor to potential or active medication events was welcome. The occurrence of thromboembolic phenomena with anti-psychotics is well known, and the hazard of warfarin treatment is always a risk especially in elderly patients or those with reduced insight. Multiple prescribers were a significant issue in many events, and require vigilance and cognisance of this ongoing risk. The role of medications for non-psychiatric illnesses in the morbidity of drug events in this population was notable, and underlines the importance of having up-to-date information about the more common medications used in general medicine.

The expected prevalence of different drug-related events varies from practice to practice and region to region, and the overall benchmark for expected adverse drug event numbers in any given practice would be a very useful guide but does not exist to date.[10] A gold standard for good drug management in a standard psychiatric practice is yet to be established. This would be expected to depend on a number of factors which we experienced in this study. They include the level of competence of the doctors and their knowledge of drug metabolism and pharmacokinetics; the educational level of the patients and their understanding of medication; the simplifying of medication dispensing, as the lowest the number of doctors, hospitals and chemists involved, the safer the pathway; a list of all the medications a patient is taking from whatever source, preferably from one dispensing pharmacy.

Having a study protocol that is part and parcel of daily work practice is a great help in providing a service, and has benefits of making a multidisciplinary team focused and alert also to other areas of patient safety and well-being. The concept of an integrated psychiatry service which delivers all the care to a patient, both mental and physical, is gaining currency and is shown to improve outcomes.[7,8]

About the author

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