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COMMENTARY

Treatment of acute psychotic agitation: gaps in the evidence base

COMMENTARY ON… MANAGEMENT OF ACUTE AGITATION IN PSYCHOSIS[†]

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SUMMARY

Treatment of psychotic agitation is an area that is very poorly evidenced, principally because research evidence from patients with moderate agitation may not generalise to the more severely agitated patients. There is a significant gap between current treatment recommendations and what is seen in clinical practice. There are also big differences in clinical practice between different units treating seemingly similar patient groups. This commentary considers possible reasons for these findings and also discusses non-pharmacological interventions, which probably contribute more to the management of psychotic agitation than does the choice of one antipsychotic drug over another.

DECLARATION OF INTEREST

None.

Psychotic agitation is clinically important because of the distress experienced by patients and the risks their behaviour may pose to themselves and others. Yet it is an area that is very poorly researched and evidenced, with big differences in everyday clinical practice between different units (Dye 2009; Brown 2010). Justin Schleifer (2011, this issue) provides a useful summary of the literature and evidence-based recommendations for practice, but unfortunately these recommendations are based on poor-quality evidence.

It is almost impossible to conduct ethically acceptable randomised controlled trials of treatment of severe psychotic agitation as most patients will be too unwell to give valid consent to participation. Clinicians are wary of trials which might allocate unwell patients to receive ineffective treatment. Pharmaceutical companies have little incentive to expose their products to scrutiny in situations in which they might perform badly. As a result, the published studies are almost all of oral medication in moderately agitated patients and they leave major doubts about whether the results generalise to more severely agitated individuals.

Research evidence and recommendations

The available evidence can be summarised as follows: antipsychotic drugs are effective in reducing psychotic agitation, treatment can often be usefully augmented by an anxiolytic drug, comparison studies are of poor quality and there is very little convincing evidence of superior efficacy of any particular antipsychotic.

Initial prescribing decisions should be based on the aetiology of the agitation, the adverse effect and risk profile of particular drugs and the patient's medical details and wishes. In acute administration, atypical antipsychotics are probably less risky than typical antipsychotics because of a lower incidence of cardiovascular effects – the common adverse effects of atypical antipsychotics, such as weight gain and metabolic dysregulation, tend to develop with chronic use. Schleifer's recommendations are similar to the latest Maudsley Hospital guidelines (Taylor 2010), other than recommending ziprasidone (albeit with reservations), reserving haloperidol for intramuscular administration and not mentioning the use of buccal midazolam, and in line with the less detailed NICE guidelines (National Collaborating Centre for Nursing and Supportive Care 2005).

Clinical reality

Does clinical practice in UK psychiatric intensive care units, the places where most seriously agitated patients are treated, reflect these recommendations? Well no, not really (Brown 2010). Most patients are prescribed an oral atypical antipsychotic. They are usually also written for haloperidol and lorazepam as required, to be given by mouth or by intramuscular injection at the discretion of the nurse in charge in the event of seriously disturbed behaviour. Thus, an individual who fails to respond adequately to an atypical antipsychotic may receive a number of different drugs, often by several routes.

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[†]See pp. 91–100, this issue.

We do not know why clinicians fail to follow the guidelines. I suspect it is because they are conservative, are not convinced by the evidence for newer drugs, see few adverse drug reactions in their daily practice and have realistic concerns about the risks of under-treatment. Clinicians know that many of their patients are more unwell than those in the studies and perceive the risk of serious assault to be greater than the risk of a serious adverse drug reaction.

An example

Many patients receive one or more intramuscular injections of the medium-acting typical antipsychotic zuclopenthixol acetate, despite a Cochrane review which identified a dearth of evidence supporting its use (Gibson 2004) and a distinct lack of enthusiasm from both NICE (National Collaborating Centre for Nursing and Supportive Care 2005) and the Maudsley guidelines (Taylor 2010). There is enormous variation in the use of this drug between different psychiatric intensive care units with seemingly similar patient profiles (Brown 2010). Whether this represents poor clinical practice or inadequate guidelines is open to debate. Practice is influenced by guidelines but also by individual professional experience. This balance is particularly difficult when the quality of evidence is poor. People have differing views about particular interventions: are the risks and benefits associated with repeated physical restraint and forced intramuscular injection greater or less than those associated with use of a single longer-acting injection? Is the use of seclusion more or less risky and unpleasant than the use of larger doses of medication? We do not know and are unlikely to be able to obtain high-quality evidence to answer these questions.

Alternatives to drug treatments

My principal reservation about Schleifer's article is the disparity between the five pages given over to the discussion of drug treatments and the half-page discussion of other interventions. Evaluating psychosocial interventions in psychotic agitation is even more difficult than evaluating drug treatments, because of problems in defining an intervention and providing adequate controls. Nevertheless, the importance of the physical environment, therapeutic activities, staff numbers, training and attitudes, and the involvement of patients in treatment decisions cannot be overemphasised. Discussion of these issues constitutes much of the content of both the Department of Health (2002) recommendations on psychiatric intensive care units and low secure services and the standard textbook on psychiatric intensive care in the UK (Beer 2008).

The design of a unit is important – it must be safe (secure, good lines of sight, fittings that patients cannot used to harm themselves or others) but should also be pleasant and therapeutic. Patients should have easy access to friends and family. Therapeutic activities are vital, as boredom can be a trigger of agitation. Units need a full complement of suitably trained and experienced staff, effective leadership and clear guidelines about managing common clinical situations. Different disciplines bring particular insights and techniques. Clinical management of agitated behaviour should be by negotiation rather than confrontation, understanding and addressing the immediate cause of the patient's distress and involving them, as far as possible, in decision-making. There must be enough staff to provide personalised care and to deal promptly and effectively with any emergency. Staff must be properly trained in de-escalation techniques: skilled practitioners are often able to de-escalate difficult situations without extra drugs or to persuade a patient to accept oral medication, thereby avoiding confrontation and forced intramuscular treatment. Nevertheless, treating teams sometimes will have to use interventions such as forced intramuscular medication, physical restraint or seclusion. None of these procedures is pleasant, none is entirely safe. The relevant safety procedures must be followed at all times.

Using and improving the evidence base

The treatment of severe psychotic agitation is an area which needs further research. The undoubted difficulties in conducting good randomised controlled trials should not stop clinicians from undertaking the good naturalistic studies which would greatly improve the quality of evidence in this area. In the meantime, it is important both that clinicians and managers understand the limits of the current evidence-based guidelines and that they reflect carefully before stepping outside them.

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Excerpts from *The Letters of Dostoyevsky to His Wife*, by Fyodor Dostoyevsky

IN OTHER WORDS

Selected by Sanju George

In 1867, just two months after their marriage, Dostoyevsky and his wife Anna Grigorievna fled to Dresden, to escape his gambling debts. From there he went alone to Homburg to play roulette. The excerpts below are from his letters to Anna written from Homburg.

Sunday 19 May. 10 a.m.
'Yesterday was a very horrid day for me. I lost far too heavily (judging relatively). What am I to do my angel? Gambling is not intended for a man with nerves like mine. I played for about ten hours, and ended by losing. I lost during the day and won again. […] as soon as I begin to win, then immediately I take risks. I cannot control myself […].'

Monday 20 May. 10 a.m.
'The main thing about it all is, that it is so senseless, stupid and vulgar and yet I cannot tear myself away from my idea, i.e. I cannot leave absolutely everything and return to you. […] Can you believe me? I lost everything yesterday, everything to the last kopeck, to the last gulden, and in the end I decided to write to you at once to ask you to send me some money for my journey home. But I remembered *my watch* and I went to the watchmaker either to sell or to pawn it; it is a terribly common practice here, i.e. in a gambling town.'

24 May. 10 a.m.
'Anya my dear, my friend, my wife, forgive me […]. Can you, will you respect me now? And what is love without respect? Our very marriage is shaken by this. Oh! My friend, don't condemn me completely! I loathe gambling, not only now, at this moment, but yesterday, and the day before yesterday I cursed it […]. Our circumstances are bad enough as it is, and yet I have wasted money on this journey to Homburg and lost more than 1000 francs – nearly 350 roubles. It is a crime!'

Fyodor Mikhailovich Dostoyevsky (1821–1881), widely regarded as one of the best 19th-century Russian writers, is perhaps less known for his gambling addiction. Dostoyevsky battled this addiction, or 'cursed monomania' as he called it, for several years. He eventually recovered, but not before it had strained his marriage, finances and psychological health. The excerpts here are from *The Letters of Dostoyevsky to His Wife* (translated from Russian by Elizabeth Hill & Doris Mudie), Constable & Co, 1930.

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