Guidance on switching away from Piportil Depot® (pipotiazine palmitate) injection

Piportil Depot (pipotiazine palmitate) injection was globally withdrawn in March 2015 because of a shortage of the active ingredient. There are no generic versions available and pipotiazine is not available in an oral formulation. Therefore, clinicians will need to switch to another antipsychotic as existing stocks run out. In Scotland alone, about 410 patients are currently prescribed Piportil Depot, which translates to roughly 5000 recipients UK-wide (if that figure is generalisable). We present our suggestions for managing the antipsychotic switch.

1 Treatment decisions should be made on an individual basis, in discussion with the patient, their carers (if the patient agrees) and the treating team.

2 An early decision is whether a long-acting injection (LAI) or depot is still required or whether a switch to oral medication should be considered. This decision should take account of the patient’s views, the risk and likely consequences of a relapse and the risk of covert nonadherence with oral treatment. The main advantage of LAIs is that adherence is transparent. The patient’s psychiatric history will be informative in making this decision.

3 With the exception of clozapine, there are no major differences in efficacy between individual antipsychotics, although they vary markedly in their risk of side-effects. Consequently, the patient’s past experience of antipsychotics, and their views on potential adverse effects, will be important considerations guiding the choice of a new antipsychotic.

4 If it is decided to switch to another LAI, then appropriate guidance, including that in the summary of product characteristics of the new LAI, should be followed regarding the details of the switch. If the patient has not previously received the new antipsychotic then a test dose is required before starting the LAI. In the case of first-generation antipsychotic LAIs, this takes the form of a low dose of the LAI, but with second-generation antipsychotic LAIs, it takes the form of a few days’ treatment with the oral form of the same antipsychotic.

5 Acquisition costs vary considerably between first- and second-generation antipsychotic LAIs, but this should be only one of a range of factors considered in the selection of the new antipsychotic.

6 The long half-life of Piportil Depot makes withdrawal effects unlikely. Illness relapse is likely to be the most common clinical concern after switching. We advise clinicians to be vigilant regarding relapse for at least 12 months after the switch, and the patient’s specific relapse signature should be discussed and borne in mind. Further details on the kinetics and switching of LAIs are given elsewhere.

The long half-life means that any existing adverse effects, for example extrapyramidal symptoms or hyperprolactinaemia, are likely to persist for some months after the switch. If an anticholinergic agent has been necessary to treat extrapyramidal symptoms during Piportil Depot treatment, it may be necessary to continue it for several months after the switch, before gradually withdrawing it. Similarly, hyperprolactinaemia may continue for up to 6 months after stopping Piportil Depot, even if the new antipsychotic is not associated with raised prolactin levels. Carry-over effects need to be considered when evaluating the tolerability of any replacement antipsychotic.

Undergraduate psychiatry teaching should happen in primary care

Abed & Teodorczuk1 make a valid point in their article, but their proposed solution has been advocated for some time and, while it may be a necessary condition to improve undergraduate psychiatric teaching, it is unlikely to be sufficient.2 Training (and psychiatry is not alone in this) is heavily dependent on service configuration for its delivery. As psychiatry has become more community based, it has also become more fragmented. The answer to this lies partly in making educational contracts more transparent, but surely we need a more radical solution. Given that the vast majority of psychiatric morbidity and care occur in primary care and given that most of our medical students will work in non-psychiatric settings, there is an urgent need for most if not all of undergraduate psychiatric education to take place in primary care.

There is an opportunity to deliver this fundamental shift through the changes recommended in the Shape of Training review.3 The key themes of making medical training more flexible and focused on generalist training, and getting the balance between service provision and training right to ensure that patient needs drive medical training, should lead to a shift of undergraduate psychiatric teaching to primary care. An added benefit of this may be that, for once, the change in the educational tail may wag the service-provision dog, leading to more integrated services at the primary/secondary care interface.

Correspondence

Authors’ reply: We broadly support Dr Dave’s point concerning the need for closer working with primary care. Invariably, this will help prepare medical students for the reality of clinical practice post-qualification and additionally expose them to a less complex patient group. However we fall short of agreeing with the radical solution proposed.

The purpose of the editorial1 was to draw attention to the challenges faced by clinical psychiatry teachers in the context of the changing educational landscape and pressures. We have not suggested that the solutions proposed are sufficient alone. Rather, we contend that increasing transparency of funding, specifically developing learning opportunities in community teams and innovating undergraduate curricula, are especially timely and relevant given the ongoing challenges facing undergraduate psychiatry education delivery and its central importance as a ‘shop window’ for our profession.

Today’s psychiatrists increasingly work in a supervisory capacity with team members, for example in community teams, and hence we propose there is an essential need to include undergraduate education within the design of new service delivery arrangements. Organisations with a focus on learning perform more effectively in terms of patient experience outcomes2 and, therefore, bringing undergraduates into our psychiatry team settings may ultimately benefit not only students, but also mental health trusts and patients. Creating an expansive learning culture with an emphasis on undergraduate teaching can only be positive.

With this in mind, we cannot support the radical solution proposed to transfer the majority of, if not all, undergraduate psychiatric education to primary care. Ultimately such a move would do medical students a disservice as they enter mental health rotations with a keenness to learn about psychiatry.

A primary-care-focused approach has the potential to undermine psychiatry as a profession by reinforcing stereotypes about the role of the psychiatrist being separate from medicine. Furthermore, undergraduate psychiatry attachments have been shown to be influential in improving medical students’ attitudes and career intentions regarding psychiatry.3 It is unclear from published a paper on this issue.3 Between 1 January 2000 and 30 June 2012, 621 individuals with bipolar disorder were admitted to three general Manchester hospitals. All mental and physical comorbidities with a prevalence > 1% were compared with those of 6210 randomly selected and group-matched hospital controls of the same age and gender, regardless of priority of diagnoses. Comorbidities that increased the risk for hospital-based mortality (but not mortality outside of the hospitals) were identified using multivariate logistic regression analyses. The study was intended to determine which specific mental and physical comorbidities contribute to later in-hospital deaths in individuals with bipolar disorder, and whether the risk factors for hospital-based mortality differ for individuals with bipolar disorder in comparison with hospital controls.

In our view, our study has the advantage that a more representative and more relevant control sample was used and that the most relevant outcome from comorbidity – mortality – was addressed. In partial agreement with Forty et al, we found that excess comorbidity in individuals with bipolar disorder was caused by asthma and type 2 diabetes mellitus (T2DM). In addition, T2DM in individuals with bipolar disorder represented

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Comorbid medical illness in bipolar disorder

Forty et al2 investigated whether the presence of physical comorbidity in individuals with bipolar disorder is associated with a more severe bipolar illness course that may contribute to the worsening of the mortality gap between individuals with bipolar disorder and the general community. Forty et al claimed this to be the first study on this issue in a UK clinical sample: that is, the first study that assessed rates of physical comorbidity in individuals with bipolar disorder and made direct comparisons with unipolar and control samples. The study is done statistically carefully.

While the results concerning the self-remembered physical comorbidities over the lifespan in the unipolar sample and the bipolar sample are clear, we have reservations concerning the composition of the control sample. Specifically, Forty et al used mixed samples of treatment-seeking individuals with unipolar and bipolar disorders that were originally recruited in genetic studies from psychiatric clinics, hospitals, general medical practices and self-help groups, as well as volunteers responding to media advertisements.2 The observed odds may be falsely calculated as the younger control sample is chosen, at least to a substantial proportion, from a specialised community sample that is representative neither of the general population nor of treatment-seeking individuals of the general community.

The reader might be interested to know that we recently published a paper on this issue.3 Between 1 January 2000 and 30 June 2012, 621 individuals with bipolar disorder were admitted to three general Manchester hospitals. All mental and physical comorbidities with a prevalence > 1% were compared with those of 6210 randomly selected and group-matched hospital controls of the same age and gender, regardless of priority of diagnoses. Comorbidities that increased the risk for hospital-based mortality (but not mortality outside of the hospitals) were identified using multivariate logistic regression analyses. The study was intended to determine which specific mental and physical comorbidities contribute to later in-hospital deaths in individuals with bipolar disorder, and whether the risk factors for hospital-based mortality differ for individuals with bipolar disorder in comparison with hospital controls.

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a major risk factor for general hospital-based mortality with excess mortality due to acute T2DM, as well as other diabetes-related complications. Our study gives support for an aggressive multidisciplinary approach to identify and treat T2DM to prevent diabetic, respiratory and vascular complications in all individuals with bipolar disorder.

**Authors’ reply.** We agree with Schoepf & Heun about the importance of control-sample characteristics in case–control comparisons and the need to consider the possibility of biased or unrepresentative findings. That is why, in our study, we used age as a covariate to take account of the younger age of controls compared with our mood disorder cases. We also discussed the potential limitations on generalisability caused by using a voluntary sample from a single ethnic group.

Schoepf & Heun describe a different methodology (with its own strengths and limitations) to examine a different issue, namely the influence of comorbidity on mortality. It is encouraging that the findings from the two different approaches are consistent in highlighting the clinical importance of comorbidity of physical illness with bipolar disorder. Psychiatrists and mental health services must ensure that patients with bipolar disorder have access to appropriate, high-quality physical, as well as psychiatric, care.

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3 Schoepf D, Heun R. Bipolar disorder and comorbidity: increased prevalence and increased relevance of comorbidity for hospital-based mortality during a 12.5-year observation period in general hospital admissions. *J Affective Disorders* 2014; 169: 170–8.

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