BJPsych The British Journal of Psychiatry (2009)
195, s5–s6. doi: 10.1192/bjp.195.52.s5

Editorial

Knowledge about antipsychotic long-acting injections: bridging that gap

Tom Burns

Summary
Antipsychotics in depot (or 'long-acting injection', LAI) form are shown in this supplement to be a significant component of clinical practice. They are comparatively underresearched, which may reflect their frequent use witih poorly adherent patients. This supplement clearly demonstrates the need for that research, highlighting the variations in dosing and the absence of established, specific guidelines in their use. Traditional evidence-based approaches to systematic reviews are of limited utility in this area so this supplement's blending of experimental trials with observational research is particularly appropriate and effective. After a brief decline in their use with the introduction of oral atypical antipsychotics, LAIs are regaining a central position in the care of long-term psychosis. This comprehensive review of current knowledge makes a timely contribution.

Declaration of interest
None.

Journal supplements make a real contribution. Their contents are linked together and have a coherence that may be lacking in a typical issue of the main journal. But getting the articles right is not always that easy. There is an obvious risk of repetition and overlap from the contributors, plus the difficulty of achieving a balance when there is simply less to write about some individual topics. Some articles may be very dense, whereas others are rather 'thin' to achieve consistency of structure and length. Obtaining genuinely critical voices is also a problem. Unlike journals, where editors and reviewers respond to submissions individually, supplements are generally composed by a group of like-minded authors who know each other and complement each other's interest in the topic. This is compounded by the relationship with the sponsor (usually, as in this case, a pharmaceutical company) with its commitment to raising interest in the area for legitimate commercial reasons. Together, these two forces can generate a greater sense of consensus in a subject than may be justified.

Drs Patel and Taylor and Professor David have done a good editorial job in avoiding repetition. This supplement has an excellent spread that covers all the major issues relating to depots (referred to throughout as 'long-acting injections'). There are excellent reviews of psychopharmacology by Taylor,[1] research evidence by Haddad *et al* and Fleischhacker,[2,3] and current UK clinical practice by Barnes *et al.*[4]

Take-home messages

The supplement provides some striking and clear take-home messages. Long-acting injections (LAIs) are a significant component of maintenance care in schizophrenia – prescribed from a quarter to a third of patients. Their use dipped somewhat in the late 1990s and early 2000s with the enthusiasm for the new second-generation antipsychotics (SGAs), but is picking up again. This is partly because of a re-evaluation of SGAs and perhaps because of the introduction of the first SGA long-acting preparations. It is immensely helpful to be reminded that LAI side-effect profiles are generally no more burdensome than those of the equivalent oral preparations. Taylor's observations on the enormous inconsistencies in dosage, with the likelihood that LAI-treated patients may often be significantly overdosed, are sobering and stark.[1] They call for urgent attention.

The crucial question of whether there is evidence of improved clinical outcomes is dealt with by Haddad *et al* in a refreshingly undoctrinaire and convincing manner.[2] The limitations of standard evidence-based medicine weightings of evidence (privileging meta-analyses and randomised controlled trials (RCTs)) are well explored for this tricky population. Given that a frequent clinical indication for LAI treatment may be reluctance of the patient to engage (in either treatment or research), RCTs need to be balanced with the broader, non-experimental evidence. Tiihonen *et al*'s figures for the contrasting risks of rehospitalisation associated with perphenazine in its depot and oral forms must outweigh several RCTs given the methodological difficulties in this patient group.[5]

The supplement gives a convincing picture of the extent of LAI usage, at about 30% of schizophrenia patients in high-usage countries such as the UK and Australia. It would have been useful to have had a more comprehensive overview of the international variation: is it due to medical training and culture, the extent of autonomy within multidisciplinary working, or even reimbursement patterns? Collaboration between academics and pharmaceutical companies could add real value here – the companies know the international prescribing patterns in obsessive detail, and in real time.

The authors have kept to their briefs and avoided overlap. Some of the content, however, is fairly peripheral to the focus of the supplement. It might have been better to edit more vigorously and accept that some of the articles would be much shorter. Kane & Garcia-Ribera's wise overview of guidelines is more about antipsychotics generally than about LAIs specifically.[6] This blunts somewhat their powerful message that in effect there are no well-developed 'LAI guidelines' – despite exhortations for their rational use in several broader policies. The historical perspective provided by Johnson ranges far and wide,[7] with surprisingly little attention to the history of the community psychiatric nursing profession, whose growth (at least in the UK) has been strongly associated with the use of LAIs.[8] The medication management paper by Gray *et al* is a remarkable mixture of anatomy, philosophy and some practical guidance which would have benefited by restriction to what its title indicated, even if this meant a much shorter article.[9]

Achieving balance in supplements

There are two areas that are dealt with in what appears to be an overly optimistic and rather one-sided manner. Waddell & Taylor's contention that the 'low' rate of LAI prescribing relates to an

https://doi.org/10.1192/bjp.195.52.s5 Published online by Cambridge University Press

'image problem' is unconvincing.[10] The quoted research that many psychiatrists considered them old-fashioned was conducted at the height of the enthusiasm for the SGAs (when almost anything else seemed 'old-fashioned', not just LAIs). Many clinical psychiatrists (strongly biased towards LAIs, like this one) will need more convincing that current usage is lower than it should be (and we would want it to be) mainly because of our attitudes and inadequate knowledge. There is the very real issue that most people are uncomfortable about the prospect of taking long-acting drugs – particularly drugs that can profoundly change how one feels, with no way of reversing these effects for several weeks. Of course this resistance *can* be overcome – where patients fully agree with their doctors, and understand and accept the risks and benefits of the treatment. Unfortunately this is not always the case in schizophrenia, where ambivalence about the treatment (and even about the diagnosis or the existence of an illness at all) is more often the rule than the exception. That some studies have found that patients established on LAIs prefer them adds little.

Similarly, Fleischhacker's otherwise excellent review of the second-generation LAIs skates too lightly over the problems with the new olanzapine LAI.[3] It seems rather disingenuous simply to state neutrally that it requires 3 h of observation because of the risk of a potentially serious post-injection syndrome. Despite the impression arising from the collective enthusiasm of the authors in this supplement, LAIs are still most frequently used with patients who are poorly committed to their treatment. This is confirmed by Lambert *et al*'s demonstration of their association with community treatment orders.[11] Even for those of us who do try to introduce long-acting formulations early, they are at their most indispensable for patients who may not want contact with the mental health services at all. Such patients consider an LAI to be the lesser of two evils. They accept it because it limits our engagement, not as an introduction to 3 h of interaction and observation. This obligation to stay around for such a long period is likely to be a massive disincentive and practical challenge in a significant proportion of patients receiving LAIs. A supplement like this gives the authors the space to explore such issues more thoroughly.

Everybody involved in this supplement – editors, sponsors, authors (and myself) – clearly thinks that LAIs are essentially a 'good thing'. The result of this conviction is a collection of articles that concentrate and deepen our understanding of this important, common and underresearched component of clinical practice. Despite this, there are many uncertainties involved in the use of these medications, and there is the lingering suspicion that there may be more negatives than positives still to learn. Nevertheless, this is a sound beginning and deserves to be widely read.

Tom Burns, DSc, FRCPsych, Department of Psychiatry, Warneford Hospital, Oxford OX3 7JX, UK. Email: tom.burns@psych.ox.ac.uk

References

1 Taylor D. Psychopharmacology and adverse effects of antipsychotic long-acting injections. *Br J Psychiatry* 2009; **195** (suppl 52): s13–9.

2 Haddad PM, Taylor M, Niaz OS. First-generation antipsychotic long-acting injections *v.* oral antipsychotics in schizophrenia: systematic review of randomised controlled trials and observational studies. *Br J Psychiatry* 2009; **195** (suppl 52): s20–8.

3 Fleischhacker WW. Second-generation antipsychotic long-acting injections: systematic review. *Br J Psychiatry* 2009; **195** (suppl 52): s29–36.

4 Barnes TRE, Shingleton-Smith A, Paton C. Antipsychotic long-acting injections: prescribing practice in the UK. *Br J Psychiatry* 2009; **195** (suppl 52): s37–42.

5 Tiihonen J, Walhbeck K, Lönnqvist J, Klaukka T, Ioannidis JP, Volavka J, et al. Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder: observational follow-up study. *BMJ* 2006; **333**: 224–7.

6 Kane JM, Garcia-Ribera C. Clinical guideline recommendations for antipsychotic long-acting injections. *Br J Psychiatry* 2009; **195** (suppl 52): s63–7.

7 Johnson DAW. Historical perspective on antipsychotic long-acting injections. *Br J Psychiatry* 2009; **195** (suppl 52): s7–12.

8 Wooff K, Goldberg DP. Further observations on the practice of community care in Salford. Differences between community psychiatric nurses and mental health social workers. *Br J Psychiatry* 1988; **153**: 30–7.

9 Gray R, Spilling R, Burgess D, Newey T. Antipsychotic long-acting injections in clinical practice: medication management and patient choice. *Br J Psychiatry* 2009; **195** (suppl 52): s51–6.

10 Waddell L, Taylor M. Attitudes of patients and mental health staff to antipsychotic long-acting injections: systematic review. *Br J Psychiatry* 2009; **195** (suppl 52): s43–50.

11 Lambert TJ, Singh BS, Patel MX. Community treatment orders and antipsychotic long-acting injections. *Br J Psychiatry* 2009; **195** (suppl 52): s57–62.

https://doi.org/10.1192/bjp.195.52.s5 Published online by Cambridge University Press