Options in managing alternatives to hyoscine in clozapine-induced hypersalivation: a survey of secure services consultants

Clozapine-induced hypersalivation is socially embarrassing and potentially life threatening. It can lead to poor medication adherence, which is of concern for patients in secure settings.

Hyoscine hydrobromide is widely used as a first-line treatment, despite little available evidence.[1] Alternatives are limited, but 19 different agents are listed in the *Maudsley Prescribing Guidelines*,[1] including antipsychotics, antidepressants and other drugs with antimuscarinic properties. There are few meaningful trials. Within the north-west of England, obtaining hyoscine has been difficult at times due to supply shortages and so alternatives have been sought.

Partnerships in Care have over 50 consultant psychiatrists nationwide caring for over 1000 in-patients, mostly within secure conditions, with a fair proportion prescribed clozapine. To examine prescribing alternatives to hyoscine, all consultants with clinical responsibilities were contacted regarding their prescribing practices and experiences. Responses were sent back in the form of a patient non-identifiable response via email.

Just under 50% of consultants replied (n=23). In the absence of hyoscine hydrobromide, there was overall little confidence in alternatives, but clinicians tended to advocate one or two. Atropine, either sublingually or via eye drops was relatively popular and the 8 clinicians that supported its use had some confidence in it. Four clinicians each supported the use of amitriptyline, pirenzepine and trihexyphenidyl. All the medication recommendations received were in the latest *Maudsley Prescribing Guidelines in Psychiatry*, except for procyclidine. Most options consisted of drugs with antimuscarinic properties such as pirenzepine and trihexyphenidyl. Dose reduction of clozapine was recommended by 1 consultant. The author and another two consultants have had some success with glycopyrrolate syrup, but this is a very expensive option.

Clozapine-induced hypersalivation is a condition potentially difficult to manage. The wide range of options and lack of evidence does not support clinicians in their attempts to continue treatment. In circumstances where patients do not respond to hyoscine, the most popular choice was sublingual atropine. National guidance and further trials are required. The shortage of hyoscine raises legal and ethical questions for patients subject to certification by second-opinion doctors and whether clinicians are likely to request further certification for alternative classes of drugs for hypersalivation.

1 Taylor D, Paton C, Kapur S (eds) *The Maudsley Prescribing Guidelines in Psychiatry, 11th Edition*. Wiley-Blackwell, 2012.

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Cardiovascular monitoring in patients prescribed clozapine

Wilson *et al*[1] highlight the ongoing issue of poor physical health monitoring in patients prescribed clozapine. We recently presented a survey which investigated standards of physical health monitoring in adult patients (n=98) prescribed clozapine against standards set out by *Maudsley Guidelines* in which we found similarly high rates (53%) of clozapine augmentation and antipsychotic polypharmacy (details available from the authors on request). Moreover, cardiovascular monitoring was poor with only 30% of patients having had a baseline electrocardiogram prior to initiation of clozapine. Similarly, only 28% had yearly electrocardiogram monitoring performed once clozapine therapy had been established. Of those patients established on clozapine therapy, 34% were found to have asymptomatic sinus tachycardia, which was more commonly seen in patients prescribed additional antipsychotic medication than those prescribed clozapine alone (P<0.001). Clinical actions in response to asymptomatic sinus tachycardia varied enormously, with only 12% of cases having been discussed with local cardiology services.

These findings are of great concern when one considers that clozapine is associated with potentially life-threatening adverse cardiovascular conditions such as myocarditis and cardiomyopathy.[2] While tachycardia is commonly seen during the early stages of clozapine treatment, occurring in up to 50% of patients, sustained tachycardia, defined as a heart rate >100 bpm for more than 6 months, can precipitate cardiomyopathy and appears to be an independent risk factor for sudden cardiac death.[3] Reducing clozapine dose and the use of rate-limiting drugs such as beta-blockers have been suggested as potential solutions to this problem,[4] although these options may not always be clinically appropriate and there appears to be a broad range of approaches in dealing with this.

In response to these findings we have introduced a system whereby initiation of clozapine therapy and its continued prescription by our pharmacy department is contingent on evidence of baseline and continued cardiovascular monitoring. We have also developed a shared care pathway with our local cardiology department ensuring that cardiac monitoring is optimised in this vulnerable patient group and that management of sustained tachycardia is jointly managed by both psychiatric and cardiology services. Information on this shared care pathway is available from the corresponding author.

1 Wilson S, Hamilton R, Callender J, MacManus A, Howitt S, Okpo B. Clozapine antipsychotic polypharmacy: audit of use and patient monitoring. *Psychiatrist* 2013; **37**: 322–5.

2 Kilian JG, Kerr K, Lawrence C, Celermajer DS. Myocarditis and cardiomyopathy associated with clozapine. *Lancet* 1999; **354**: 1841–5.

3 Shinbane JS, Wood MA, Jensen DN, Ellenbogen KA, Fitzpatrick AP, Scheinman MM. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies. *J Am Coll Cardiology* 1997; **29**: 709–15.

4 Young CR, Bowers MB, Manure CM. Management of the adverse effects of clozapine. *Schizophrenia Bull* 1998; **24**: 381–90.

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