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A natural study of the efficacy of replacement medications for the treatment of clozapine-induced hypersalivation

Simon Chu[1,2], Inti Qurashi[2], Niall Campbell[3], Paul Stephenson[2], Ruth Massey[2], Richard Drake[4] and Nusrat Husain[4]

[1]School of Psychology, University of Central Lancashire; [2]Ashworth Research Centre, Ashworth Hospital, Mersey Care NHS Trust; [3]Bowmere Hospital, Cheshire and Wirral Partnership NHS Foundation Trust; [4]Institute of Brain, Behaviour and Mental Health, University of Manchester

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Clozapine-induced hypersalivation is a stigmatizing and debilitating side effect of clozapine treatment that may threaten adherence to treatment [Taylor et al. 2009]. Hyoscine hydrobromide is the most popular treatment for hypersalivation, but has a poor evidence base [Syed et al. 2008].

During autumn 2013, a shortage of hyoscine tablets in the UK (due to production problems) required patients who had been prescribed hyoscine to change to a replacement medication. This provided an opportunity to assess the subjective relative efficacy of hyoscine hydrobromide compared with alternative medications in the treatment of clozapine-induced hypersalivation. We undertook a service evaluation and surveyed patients prescribed clozapine at Ashworth Hospital (Mersey Care NHS Trust) who had been prescribed hyoscine hydrobromide for hypersalivation. Participants were prescribed alternative medication for clozapine-induced hypersalivation by September 2013 and we conducted our survey in November 2013.

Of the 42 consenting participants, 15 were prescribed pirenzepine, 13 were prescribed atropine, and 6 were prescribed a small number other replacement medications (procyclidine, orphenedrine, hyoscine patches) which, owing to small sample sizes, were excluded from our analysis. Eight patients previously prescribed hyoscine were prescribed no replacement medication. In each case, we asked patients to rate on a 7 point scale (1 = much worse, 4 = no change, 7 = much better) their current experience of nocturnal salivation, daytime salivation and a number of other side effects (vision problems, dizziness) compared with when previously prescribed hyoscine.

Table 1. Mean rated changes in side effects according to replacement medication groups.

Group	n	Nocturnal salivation	Daytime salivation	Vision problems	Dizziness
Pirenzepine	15	6.3 (1.0)	5.9 (1.1)	4.4 (0.9)	4.0 (1.0)
Atropine	13	6.6 (0.5)	6.4 (0.6)	4.2 (0.4)	4.0 (0.0)
No replacement	8	4.0 (0.0)	4.0 (0.0)	4.0 (0.0)	4.0 (0.0)

Standard deviation in parentheses.

Mean ratings of subjective relative efficacy in comparison with hyoscine for each of the three medication groups (pirenzepine, atropine, no replacement) are shown in Table 1. Subjective ratings showed that nocturnal salivation improved for both the pirenzepine group and the atropine group, but all patients in the no replacement group reported unchanged scores in night salivation. A one way analysis of variance (ANOVA) showed this to be statistically significant [$F(2,35) = 34.36$, $p < 0.001$], with post hoc Tukey tests suggesting that ratings in the pirenzepine and atropine groups were both higher than in the no replacement group. Similarly, ANOVA confirmed that changes in daytime

salivation for the pirenzepine group and the atropine group were significantly different to the no replacement group which again reported no change [$F(2,35) = 23.4$, $p < 0.001$]. This is unlikely to be a general reporting bias in the pirenzepine and atropine groups because the three groups did not differ in their ratings of changes in vision problems [$F(2,35) = 0.99$, $p = 0.38$] and dizziness [$F(2,35) = 0.0$, $p = 1.0$].

Participants who ceased taking hyoscine and with no replacement medication reported no change in hypersalivation. By comparison, participants who replaced hyoscine with pirenzepine or atropine consistently reported an improvement in salivation (day and night). It should be noted that our service evaluation survey did not implement any randomization to groups and that the data are in the form of retrospective report, both of which limit the interpretation of the outcome. Nevertheless, whilst hyoscine hydrobromide is the treatment of choice for clozapine-induced hypersalivation, a Cochrane Review has indicated that the evidence base is weak [Syed et al. 2008]. There is a broad range of treatment alternatives but these appear equally unsupported in the literature. Thus, clinicians are forced to make pragmatic prescribing judgements in the absence of reliable evidence. Our small scale survey suggests that hyoscine may not be an effective treatment for hypersalivation and there is a clear need for more convincing evidence of the efficacy of treatments to confidently inform clinical practice. Indeed, a feasibility study funded by the UK National Institute for Health Research (NIHR) to investigate glycopyrrolate and hyoscine in the treatment of clozapine-induced hypersalivation is currently being conducted by our clinical team.

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Conflict of interest statement

The authors declare no conflicts of interest in preparing this letter.

References

Syed, R., Au, K., Cahill, C., Duggan, L., He, Y., Udu, V. et al. (2008) Pharmacological interventions for clozapine induced hypersalivation. Cochrane Database Syst Rev CD005579.

Taylor, D., Shapland, L., Laverick, G., Bond, J. and Munro, J. (2000) Clozapine – a survey of patient perceptions. Psychiatr Bull 24: 450–452.