

Correspondence

Maintenance doses for clozapine: past and present

We recently completed a quality improvement project for patients on long-term clozapine treatment, with the main aim of assessing the side-effect burden with a view to optimising the treatment. We compared our current clinical practice with one described in a publication 20 years ago in the *BJPsych Bulletin* in 1998 on maintenance doses for clozapine.¹

Murphy *et al*¹ presented findings on 44 patients who had been on clozapine for 6 months or more. Our patient number was 41, and the information was retrieved from electronic case records, although this did not make the job easier as the relevant information was scattered across time and in different sections of the record system.

The patient group in Murphy's study had a mean age of 38 years (21–62 years) with 35 males and nine females, the majority being Caucasian, with a mean duration of clozapine treatment of 38 months (7–69 months). The highest treatment dose prescribed ranged from 300 to 900 mg per day (mean 568 mg), with 50% patients on 500 mg per day or less; only one patient received the maximum dose of 900 mg. The current or maintenance doses of clozapine ranged from 150 to 750 mg per day (mean 460 mg), with eight patients on doses of 150 and 300 mg per day. This was within the British National Formulary (BNF) guidelines at the time (BNF: number 33, March 1997), which clearly differentiated between the higher doses (200–450 mg daily, maximum 900 mg) required initially to stabilise the mental state, and the lower doses (150–300 mg daily) required subsequently for maintenance treatment. The authors found that dosage reductions had been achieved in 29 cases, while there was no attempt to reduce the dose in the majority of the rest of the patients, owing to partial response or less-than-expected symptom control.

Our group included older patients with a mean age of 44 years (29–70 years), who were predominantly Caucasian, with 30 males and 11 females. The mean duration of treatment with clozapine was more than 10 years (range 1–30 years). The dose ranged from 200 to 900 mg per day, with a mean dose of 405 mg per day; 25 patients were on doses between 300 and 500 mg per day, which would have been deemed higher by the BNF guidelines of 1997.

We found that that 80% of patients reported significant side-effects including drooling, sedation/tiredness, gastro-intestinal symptoms, weight gain, urinary incontinence, and

constipation. Also, a significant proportion (50%) were on medication for side-effects, generally in combination. There were significant metabolic problems, with an average body mass index (BMI) of 29.40 and most of the patients (apart from five) having a BMI above 23; two cases were diagnosed with diabetes and on treatment.

We also found that there had been no reduction in clozapine doses in any of the cases over the past 7 years including more recent cases. Of course, one big difference is that there are no current BNF guidelines for maintenance doses for clozapine; BNF (September 2016–March 2017) mentions a usual dose range for clozapine of 200–450 mg per day that one needs to titrate to when starting clozapine.

The side-effect burden on its own should be enough to make clinicians keep dose review on the agenda on a regular basis. Owing to large variations in metabolism, it is hard to predict the optimum dose and plasma level in an individual patient; the manufacturers² advise that once maximum therapeutic benefit has been established, many patients can be maintained effectively on lower doses with careful downward titration. The past BNF guidelines regarding maintenance doses were thought to be not based on evidence,¹ but empirical; it may be time to revisit the past, as patients appeared to be getting a better deal.

Avneet Sharma, Consultant Psychiatrist, Avon and Wiltshire Mental Health Partnership NHS Trust; email: avneet.sharma@nhs.net

1 Murphy B, Long C, Patton C. Maintenance doses for clozapine. *Psychiatr Bull* 1998; **22**: 12–4.

2 Van Beelen AJ, Jollie-Helthuis M. *Zaponex Fact Sheet Clozapine Dosing and Metabolism*. 2013 (Doc.05.SOP.LNL.600.01 Mar 2013).

doi:10.1192/bjb.2018.64



© The Author 2018. This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike licence (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the same Creative Commons licence is included and the original work is properly cited. The written permission of Cambridge University Press must be obtained for commercial re-use.