Correspondence

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Regarding: The impact of a change in prescribing policy on antipsychotic prescribing in a general adult psychiatric hospital: a response to Osman & McCauley

Dear Editor,

We thank Osman & McCauley, (2014) for some astute observations on the results of our recent audit (Kelly *et al*. 2014), which illustrated the benefits of adopting a new antipsychotic prescribing policy to limit multiple antipsychotic prescribing. Mugtaba & McCauley, 2014) draw attention to the omission of the route of administration of antipsychotics in our study and cite some common difficulties that can lead to under-investigation of long-acting injectable (LAI) antipsychotic preparations in studies aimed at estimating the extent of multiple antipsychotic prescribing. These include the difficulty in calculating the total daily antipsychotic dose percentage and the location of the section for prescribing the LAI preparation in the medication sheet. Neither of these factors influenced our report and indeed, during the study, we did record LAI antipsychotic use and we thank Mugtaba and McCauley for the opportunity to now report them.

Before the intervention, four patients (2.5% of total prescribed antipsychotics) were prescribed LAI antipsychotics, all of which were first-generation antipsychotics (FGAs). Of these, three were prescribed the LAI antipsychotics in combination with regular oral FGA antipsychotics, and two fulfilled criteria for high dose, accounting for 15% of the total high-dose prescribing. After the intervention, two patients (1.5% of total prescribed antipsychotics) were prescribed second-generation antipsychotic (SGA) LAIs, and both were prescribed regular oral SGAs, though neither fulfilled criteria for high dose. We also note that the total daily antipsychotic dose percentage including the LAI antipsychotic dose was calculated using British National Formulary (BNF) maximum licensed dose, as in the Paton *et al*. study (Paton *et al.* 2008). Our study design also mitigated against the risk of data omission by assigning two researchers to independently and carefully check the medication sheets. The main reason for not reporting this in the original submission pertains to the low rate of LAI antipsychotics prescribing in our study (Kelly *et al*. 2014) and the fact that LAI antipsychotics were included in the total daily antipsychotic dose percentage. The reasons for this low rate, in the light of Mugtaba and McCauley's anecdotal account of high LAI antipsychotic use in their own practise, is unclear.

We agree that combined LAI and oral antipsychotics can be one of the major routes to multiple antipsychotic prescribing. Between a quarter and a third of people with schizophrenia are prescribed LAI antipsychotics and approximately half are also prescribed an oral antipsychotic (Barnes *et al*. 2009). The National Audit of Schizophrenia, which excluded as required (PRN) prescribing, showed that 15.9% of community-dwelling patients were prescribed multiple antipsychotics of which 7% can be attributed to combined oral antipsychotic (excluding clozapine) and LAI antipsychotic prescribing (Patel *et al*. 2014). It has been established that multiple antipsychotic prescribing increases the risk of high-dose prescribing (Barnes & Paton, 2011). There is no evidence to show that oral and LAI antipsychotics should be combined in the long term, however, in the short term during periods of titration after relapse, combining an LAI antipsychotic with an oral antipsychotic, preferably the same agent, may increase plasma levels more rapidly compared with the use of an LAI antipsychotic alone (Kane *et al*. 1998).

Mugtaba and McCauley look for guidance on managing behavioural disturbances without subjecting patients to the risk of exceeding the daily antipsychotic dose limit. This will depend on several factors such as the availability of de-escalation and seclusion, training competencies, admission procedures and ward staffing compliment. Pharmacological options to achieve a lower dose of antipsychotic in the short term include benzodiazepines (lorazepam) or sedating antihistamines (promethazine) (Huf *et al*. 2009). However, even with these agents, adhering to combination and high-dose guidelines while managing an acute behavioural disturbance in those on maintenance LAI antipsychotic is challenging, and in our view exceeding such limits in the short term is often unavoidable. Although the National Institute for Health and Clinical Excellence (NICE) schizophrenia guidelines contain two explicit exceptions to combination and high-dose prescribing: cross titration during switching from one antipsychotic to another and those requiring augmentation of clozapine (NICE, 2009, 2014); the NICE guidelines related to the management of severe behavioural disturbance state 'there may be certain circumstances in which the current BNF uses and limits may be knowingly exceeded'. In such cases a 'risk–benefit analysis should be recorded in the case notes and a rationale should be recorded in the care plan' and 'where the risk–benefit is unclear, advice may be sought from clinicians not directly involved in the service user's care' (National Collaborating Centre for Nursing and Supportive Care, 2005).

Prevention of long-term prescribing of combined oral and LAI antipsychotics is clearly highly desirable and one which warrants further consideration. Although there is no standardized definition, periods of >6 weeks cannot be considered short term (Miller, 2005). It is noteworthy that Correll *et al*. (2011) found that psychiatrists inherited most of their combined antipsychotic cases and were reluctant to convert patients to a single antipsychotic. Residual psychotic symptoms have been identified as the most frequently documented reason for multiple antipsychotic prescribing (Grech & Taylor, 2012). In this scenario, rather than combined or high-dose antipsychotic prescribing, provided there has been an adequate dose, duration and plasma level of the initial antipsychotic, and provided intervening medical, substance abuse and cytochrome P450 interactions/polymorphisms have been considered, switching the antipsychotic to one with a different receptor binding profile may be a more viable option (Dold & Leucht, 2014). Of course, depending on prior treatment failures, certain subgroups of patients that relapse on LAI antipsychotics may fulfil criteria for treatment refractory schizophrenia (TRS), for which clozapine, the only licensed treatment (Taylor *et al*. 2012) is clearly superior (Leucht *et al*. 2013). In TRS cases where clozapine is contraindicated (history of prior clozapine-induced agranulocytosis or myocarditis), options are limited and the evidence base is weak (Beck *et al*. 2014). Augmentation options at this stage include lamotrigine (Kremer, 2004; Sommer *et al*. 2012), eicosapentaenoic acid (Puri & Richardson, 1998; Porcelli *et al*. 2012) or anti-inflammatories (Sommer *et al*. 2014). However, the lack of sufficiently powered randomized double blind placebo-controlled trials preclude routine clinical use of these medications.

Faced with such a scenario and in order to prevent long-term prescribing of initially necessary combinations of oral and LAI antipsychotics, it is ultimately the responsibility of the treating team to ensure that additional medications prescribed during periods of behavioural disturbance are monitored, reduced and discontinued at the earliest possible opportunity. In the light of our original results, the benefits of a change in prescribing policy on the actions of the treating team should not be underestimated and offers at least one route towards superior patient management in this context.

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