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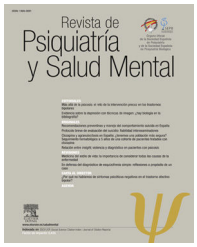

LETTERS TO THE EDITOR

Flexibilization in controlling the use of clozapine: A great opportunity☆

Flexibilización en el control sobre el uso de clozapina: una gran oportunidad

Dear Editor,

The Spanish Association for Medicines and Healthcare Products (AEMPS) recently published an informative note[1] explaining that healthcare professionals are now free of the obligation to send reports containing the analytical results of patients to treatment with clozapine. Nevertheless, the said analytical monitoring must continue, and the same conditions for prescribing and dispensing these medicines must remain.

This change is due to the request by a group of clinical psychiatrists who are experts in the use of clozapine. They met in September 2016 to unify their criteria and exchange experiences in the use of the said drug. The same meeting produced a document containing a range of considerations about 3 main questions: the patient profile of those who could be treated using clozapine, the use of clozapine as a monotherapy or in combined therapy, and the use of clozapine as a second-line antipsychotic drug.[2]

Respecting the first point, it seems to be unanimously accepted that patients who are refractory to conventional treatment are the first candidates for treatment using clozapine. In any case, and correctly, it is said that patients have usually received a large number of treatments and that treatment using clozapine has been delayed for too long. This leads to an increase in refractory responses, and patients are also denied a possible previous improvement. Given the benefits of clozapine, this improvement does not only consist of improved positive psychotic symptoms as negative symptoms also improve. There are benefits in terms of cognitive functioning and a practically zero incidence of extra-pyramidal symptoms (EPS).[3] There is therefore a demand that the term ''refractory response'' be used correctly. I.e., when there is a lack of suitable response after 2 previous attempts to use antipsychotic treatments in monotherapy, at a suitable dose and during a sufficiently long waiting time. Apart from these patients, other groups are proposed such as those at major risk of suicide, patients with aggressive behaviour (without overemphasising the diagnosis), patients with comorbid substance abuse, and some patients with neurological diseases (Parkinson's disease and cases of dementia with severe behavioural alterations).

The importance of the ''setting'' is also mentioned, and it is recommended that specialised clozapine units be created. In this point we consider that it should be pointed out that no all healthcare areas would be able to do so: an alternative in small healthcare areas could be to have a clinic familiarised with clozapine use to take charge of the patients in question. It would also thereby be possible to indicate the treatment during team meetings.

The preference is to use clozapine as a monotherapy, and this seems to be objectively recommendable, even though there are some circumstances when combined strategies would be justified. Such cases would be those with an insufficient or less than optimum response to clozapine, or those in which doubts exist about therapeutic adherence. With the aim of optimising these questions, it is important to monitor clozapine levels, given that as a recent paper by Iglesias García et al.[4] correctly points out, this makes it possible to prevent variations in the dose and minimise potentially undesirable clinical situations. It is of interest in this respect to underline the recent research by Geers et al.[5] into Dried Blood Spot (DBS) analysis as a reliable and new way of carrying out such monitoring. In the same way the said levels could be used as treatment response markers, given the lack of specific biomarkers in psychiatric pathologies, as Meana and Mollinedo-Gajate correctly state in their editorial ''Biomarkers in psychiatry: between myth and clinical reality''.[6]

If it is necessary to add a second antipsychotic drug, it should have a different receptor profile. Amisulpride, risperidone and aripiprazole have all given good results when used in this way.[7]

The combination of clozapine with electroconvulsive therapy (ECT) is also mentioned, and it is said that this may be even more recommendable than antipsychotic polytherapy. Although it is true that this combination has been shown to be more effective than medication alone,[8] it is also true that a certain number of clinics are hardly familiar with its use, so that for them it may be a rather complicated combination to use, given the reluctance that already exists to use clozapine by itself.

Respecting the use of clozapine as a second-line antipsychotic drug, this is the reason why the said collective requests flexibilization of the pharmacovigilance plan, so

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that in this way clozapine could play the role that corresponds to it in treating schizophrenia.

To conclude, we therefore consider that eliminating the obligation to send the reports would be a step forwards in eliminating barriers and increasing the use of clozapine. Given the recent nature of this change, it is still too early to evaluate the effects of this increase in monitoring flexibility. Nevertheless, it is a hopeful first step and a great opportunity to consolidate clozapine as the effective therapeutic tool it has proven itself to be.

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What most influent psychiatry journals do not show☆

Lo que no muestran las revistas de psiquiatría más influyentes

Dear Editor,

For years professional medical publication associations such as the World Association of Medical Editors (WAME),[1] the Committee of Publication Ethics (COPE)[2] and the International Committee of Medical Journal Editors (ICMJE),[3] have underlined that it is obligatory for journals to clearly define conflicts of interests, as well as how to identify and manage them in connection, among other things, with the members of their editorial teams. The ICMJE[3] also recommends that journals publish the conflict of interests policies of their editorial teams. The *BMJ* was the first journal to take this initiative, in 2004,[4] and approximately a decade later only 39% of the 399 high impact biomedicine journals had followed suit.[5]

The interest of society in the United States of America in knowing the financial relationships of prescribing doctors with the biomedical industry (pharmaceutical and healthcare products), led the American Congress to pass a law governing this point. This law came into force in August 2013. Since then, biomedical companies have to publically and annually publish all of the payments made to doctors (and their close family members) for amounts of at least 10 $ or annual payments of at least 100$. These payments may be ''general'', such as for consultancy, expert opinions, travel and meals, or for research (directly or to their institution as the chief researchers).[6] This law has enabled readers to know the payments received by medical journal editorial team members who work in the U.S.A., thanks to the recent publication of 2 works on this specific subject.

Liu et al.[7] analysed industry payments to 713 members of the editorial teams of 52 high impact journals covering 26 medical specialities in 2014. The majority (51%) had received general payments, while one in every 5 had received payments for research. 39% (9/23) of the members of psychiatry journal editorial teams (*JAMA Psychiatry* and the *American Journal of Psychiatry*) had received general payments. This is similar to the figure of 41% in gynaecology and obstetrics journals, although it is far from the 84% in ear, nose and throat journals. In the psychiatry journals the mean general payment (interquartile) was $0 ($0–6394), and the average payment (SD) was $4371 ($7505), in 16th place of 25 specialities. The individual member of a psychiatry journal editorial team who received the highest payment was given $20,600, which is a long way from the almost 11 million dollars received by a doctor in a cardiology journal.

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