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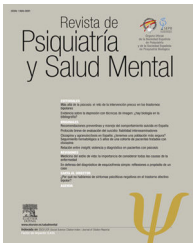

LETTER TO THE EDITOR

Tianeptine: New description of the mechanism of action and change of technical data sheet☆

Tianeptina: nueva descripción del mecanismo de acción y cambio de ficha técnica

Dear Editor:

We are very pleased to be able to inform you of the positive effect a recently published article in the journal ''REVISTA DE PSIQUIATRÍA Y SALUD MENTAL'' has had on our clinical practice.

The article *Tianeptine, an atypical pharmacological approach to depression*, by professor Alamo et al.,[1] is a historical review of antidepressant medication which then focuses on tianeptine, an antidepressant which is classified as atypical because it does not fit into any of the major pharmacological groups of this type of medicine.

Tianeptine has recently been marketed in Spain (2015), although it had already been marketed in the 1990's in other European countries. At that time, the hypothesis expounded was that tianeptine was a tricyclic antidepressant (but different to the traditional ones), with a serotoninergic mechanism of action.[2] However, thanks to the advance of research techniques over the last few years in the field of neuropsychopharmacology, this hypothesis has had to be recently modified due to numerous articles which were published after its authorisation and they have had to advance in the knowledge of its mechanism of action and pathways where it exercises its antidepressant effect and other effects, such as anxiolytical and improvement in cognitive function, and which is magnificently summarized in the before-mentioned article.

The first key to the article of Alamo et al. was to clarify that although tianeptine has a heterocyclic structure, with 3 cycles, it cannot be classified as an antidepressant of the tricyclic pharmacological group due to its clear structural differences which present both in the actual rings and in the lateral chain, that distinguish it from other antidepressants. This structure conditions its pharmacological and clinical profile, which is differential to other antidepressants.

The essential part of this cited article is dedicated to the review and updating of all the new evidence resulting from experimental studies and published in recent years on tianeptine and its pharmacological idiosyncrasies. It demonstrates the enormous data processing work performed with the 127 references included in the article, the analysis of which leads to the conclusion that the action of tianeptine is essentially based on the modulation of glutamatergic functionalism. Experimental knowledge of this system is advancing rapidly and today we are aware that apart from its involvement in depression it also participates in other cognition and memory functions. From a clinical perspective the characteristic of tianeptine of presenting an antidepressant action, is accompanied by an additional anxiolytic effect, without provoking sedation and an improvement in cognitive component.

Apart from the scientific dissemination achieved thanks to the article by Alamo et al., advances in the knowledge of tianeptine's mechanism of action has had a ''normative'' effect. Thus, last September the Spanish Medicines and Health Products Agency authorised an updating of the technical data sheet of the product Zinosal® (the only drug to contain tianeptine in Spain). In its new version[3] the technical data sheet currently describes that ''tianeptine is an antidepressant with a glutamatergic mechanism of action'', correcting the existing error in the previous version of the technical data sheet which mentioned that ''tianeptine is a tricyclic antidepressant.

As a result, analysis of new accumulated scientific evidence has coincided in time in the form of scientific communication in a Spanish journal (and in Spanish) with a regulatory change that reflects the viewpoint of the health authority.

We believe that it also results in a patient benefit, since Spanish doctors now have greater knowledge of the pharmacological mechanisms of tianeptine, since when it acts with a glutamatergic modulator that is different to the other antidepressants up until now available there is a new perspective in the Spanish antidepressant arsenal. This is a promising event in several situations (e.g. in the case of patients who lack the benefit of other antidepressants or those who may have the added benefit of it providing an additional anxiolytic effect.

Conflict of interests

Both Jaime Algorta (medical director) and Aurora Dominguez (records director) work for Exeltis Healthcare SL, the laboratory which markets tianeptine in Spain.

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Comment on ''Psychoneuroimmunology of mental disorders''☆

Comentario sobre "Psiconeuroinmunología de los trastornos mentales"

The area of psychoneuroimmunology has received increasing interest during the last generation. A major reason for this is due to our improved understanding of the dynamics between visceral responses and affective states. Saying this, our knowledge of the complexity of these processes is incomplete. A significant finding in psychoneuroimmunology is the role of inflammatory processes in mental disorders. This is a very broad topic which has been discussed by Soria et al.[1] Firstly, I commend the authors for focussing on the diagnostic and therapeutic aspects of mental disorders in relation to psychoneuroimmunology. The authors provide a concise and insightful overview of major mental disorders and the involvement of cytokine activity in their etiology. As the authors note, previous studies draw a strong correlation between cytokine induced inflammation and schizophrenia, depression, bi-polar disorder and PTSD.

In their discussion the authors make two comments which I will expand on. Firstly, is the need to expand research into inflammatory markers beyond the current variables. I would also include ethnicity, exposure to psycho-physical trauma and enteric gut microbiome (EGM) makeup. These are also important variables in inflammation and mental disorders. For example, some studies indicate that gut bacteria play a key role in modulating endocrine function and stress response. Furthermore, various gut bacterial species are vital in neurotransmitter production,[2] and neurotrophin modulation during neo-natal development.[3] It has been shown how administration of the bacterial species *Bifidobacteria infantis* into immature rats reduces pro-inflammatory response of IL-6, TNF-α, and IFN-γ cytokines.[4] Several gut bacterial species may even create neurochemicals whose molecular structure are analogous to those produced by the host's CNS. Consequently, we need to further explore whether EGM engineered biomimicry may contribute to mental disorders.

Moreover, the authors are rightly concerned on the use of anti-inflammatory drugs in treating severe mental disorders. So far studies on anti-inflammatory drugs as a potential treatment have been small and inconclusive. We need to be cautious. Anti-inflammatory drugs have not been authorised as a viable alternative to anti-depressant or anti-psychotic drugs. However, this may not deter some physicians from prescribing them. In developing countries where I have lived, many physicians are reluctant to prescribe anti-depressant or anti-psychotic drugs to patients due to their expense. In contrast, anti-inflammatory drugs are relatively cheaper. This may prove to be a decisive factor in prescribing their use.

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