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NEW ANTIDEPRESSANT DRUGS FOR NEW DEPRESSIONS

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SUMMARY

Although depressive disorders have been known for centuries, drug treatment is relatively recent. It was only in the 1950s, when studyof a drug for tuberculosis, Iproniazid,that its antidepressant propertieswere identified.

After 50 years more selective and specific drugs have been discovered.

The authors review not only new realities in depressive psychopathology, but also the latest innovations of psychopharmacology.

Key words: *depression - antidepressant drugs - psychopharmacology*

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INTRODUCTION

Several statistical worldwide as well as Italian studies, have shown that the use of psychoactive drugs, such as antidepressants, is steadily increasing (Olesen et al. 2012, Kessler et al. 2009).

This figure is linked to the phenomenon of violence against women: from the psychological pressure to physical and sexual violence, to femicide and the involvement of the families of the victims.

The increased demand for antidepressants drugs may be related to inappropriate uses, in that they are prescribed mostly for reactive depression which has little to do with endogenous depression, which is designated as a serious psychological illness.

At the beginning of 60s the so-called "happy pill" began to make a way into the pharmaceutical market: the older tricyclic antidepressants drugs also known as TAD.

During the ages, more drugs were added in order to be more specific and less toxic than the previous molecules. They belong to different chemical classes and interact more selectively with neuronal transmission involved in controlling mood. Thus, scientific research produced the atypical antidepressants drugs (AAD).

It has been reported that there is an improvement of 40-80 % of recovery in people taking these drugs and of these only 30% achieved a complete remission whatever the combination of drugs taken.

Despite the pharmaceutical companies offering a wide range of antidepressant medications, research programs continue in order to create new molecules. The most important achievement is the perfecting of effectiveness of therapeutic response, as it is obvious that no drug is fully effective in determining the complete remission in all patients.

NEW ANTIDEPRESSANT DRUGS

What are the new features of antidepressant treatments? Several antidepressant treatment guidelines emphasize the importance of psychotherapy (APA 2010, NICE 2009) whether related or not to pharmacotherapy, according to the therapeutic indications pointed by Food and Drug Administration (FDA) and Agenzia Italiana del Farmaco (AIFA).

Lately, a new drug, called Vilazodone has been approved. Our attention is focused on how this new molecule differs from those already on the market in terms of safety and efficacy, and how there can be more opportunities for patients. Vilazodone, approved by FDA in 2011 as an antidepressant medication,is derived from SSRI (selective serotonin reuptake inhibitor) class that is used in mood disorders. It increases serotonin levels through inhibition of the re-uptake of the serotonin transporter (SERT), in a similar way to the other molecules belonging to the class of SSRIs. It acts as a partial agonist of 5-HT 1A (5-hydroxytriptamine or serotonin) receptors that play a key role both in antidepressant activity and anxiety. The stimulation of these receptors leads to an initial decrease of serotonergic transmission, inhibition of autoreceptors, and their prolonged stimulation determines the desensitization or down-regulation with consequent increase of the transmission itself.

The range between the inhibition and disinhibition time of serotonergic transmission may explain how long the needed treatments to reduce the symptoms can be.

It can be assumed that this dual mechanism of action can drastically reduce the onset time of therapeutic effect (1 week in some studies) (Rickels et al. 2009), the side effects related to the inhibition of serotonin reuptake inhibitors (nausea, vomiting, sexual dysfunction) and it can provide improvements in anxiety states (Pierz et al. 2014).

At the end of 2013, through FDA support, the European Union has made available the use of a new antidepressant drug: Vortioxetine. This drug interacts with serotonergic transmission, but behaves as a multimodal molecule. Due to its characteristics, Vortioxetine is considered the founder of the new future generation of multimodal antidepressant drugs. In addition to the inhibition of reuptake, it causes different effects on 5-HT receptor subtypes: it is a 5HT7-5HT3 antagonist receptor, 5HT1B partial agonist and 5HT1A agonist (Katona et al. 2014). The drug shows a good efficacy in the treatment of anxious-depressive syn-

dromes in terms of tolerability. Side effects incidence is less severe than the drugs currently used.

At the "Galeno Award" in 2012, one of the highest accolades in the medical-pharmacological field, Agomelatine has been awarded in "Drug Innovation" category. Agomelatine is an antidepressant and anxiolytic drug characterized by an innovative mechanism of action: melanin types 1 and 2 (MT1 and MT2) agonist receptor and 5HT2c serotonin antagonist receptor. Moreover, it promotes a resynchronization of circadian rhythms, altered in depressed patients (Pompili et al. 2013, Bang-Andersen et al. 2011). This mechanism makes it different from other antidepressant drugs that block the reuptake of biogenic amines. As it does not directly affect serotonergic transmission, side effects are markedly limited and the drug can be administered to a group of patients for whom standard treatments are not effective (Plesničar et al. 2014, Henigsberg et al. 2012).

Another important phenomenon in the field of psychopharmacology is the research and commercialization of long-acting and fast-acting compounds. An example is provided by typical and atypical antipsychotics drugs and antidepressants drugs that require the minimum of compliance and an almost instantaneous effect. New pharmaceutical formulations accompanied by phrases such as fast, rapid, act, task, etc. have been introduced.

Cost-benefit and socio-economic-health need to be processed separately. In this context, the efforts of researchers and pharmaceutical companies are necessary to get fast-acting antidepressants. The idea stems from the identification and overview of a new target for depression: the N-methyl-D-aspartate receptors (NMDA). Known for their involvement in memory and learning activities, they appear to be essential for the interaction with the neurotransmitter glutamate, whose levels appear altered in depression. According to several studies, glutamate would be a better target for the direct treatment of depression than serotonin, as it has a longer latency period. Many studies analyse the mechanism of action of ketamine, which is similar to another analogous drug, known as RO-25-6981. These drugs have a good activity on these receptors and they act in a lapse of time between a few hours and a few days (Caddy et al. 2014, FASEB 2014).

CONCLUSION

The nature of depressive disorders determines clinical conditions which are extremely varied. Although psychotherapy is the basis for the treatment of depressive disorders, the search for new antidepressants drugs is necessary for patients for whom standard treatments are not effective. We reviewed the latest molecules placed on the market and their potential advantages. The discovery of new potential medications is developing continuously.

It may take a long time for all of these potential drugs to reach the market, but we may expect a revolution of antidepressant treatment with the introduction of the "instant happy pill".

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