Anxiety and depressive disorders are mental illnesses with a high prevalence. It is estimated that each year, 38.2 % of the EU population suffers from a mental disorder (164.8 million people affected). According to World Health Organization statistics, it is expected until 2020 unipolar depression to become the second cause of morbidity in the general population, ranking immediately after cardiovascular diseases. It will represent a third of mental illnesses that cause disability.

Recent research conducted in Europe show that depression is one of the most important causes involved in the growth of health care costs. Patients suffering from depression may present anxiety symptoms that cause a worsening of the clinical picture, a prolonged duration of disease and more slowly and incompletely response to treatment. Also, the association of depression with anxiety may occur in suicide and resistance to therapy.

Recent studies, like Sequenced Treatment Alternatives to Relieve Depression demonstrated that depressed patients who had a partial response to treatment administered over a period of six weeks, they had concomitant symptoms from anxiety spectrum that significantly contributed to reducing the percentage of remissions and decrease their quality.

In some cases, anxiety is a residual symptom increasing rate of remissions and affecting the functioning level of the patient. This psychiatric co-morbidity is important due, on the one hand, to increased prevalence of depressive and anxiety disorders, and, on the other hand, due to the emergence of a series of questions, such as:

- which of these disorders is prevalent?
- do they represent different aspects of the same psychiatric condition?

DSM V no longer recognize as entity the mixed anxiety and depressive disorder, and do no longer includes it as nosological entity (independent) nor in depressive disorders section or in anxiety disorders section.

Anxiety and depression are some of the most common psychiatric comorbidities, and at the same time the psychiatric disorders with the highest prevalence in the general population (between 30 % and 50 % of adults diagnosed with major depressive disorder associate an anxiety disorder spectrum, and about 50 % of patients diagnosed with an anxiety disorder also meet the diagnostic criteria for depressive disorder).

Only a few therapeutic strategies address both the anxiety and depressive disorders and the existing ones are far from being satisfactory due to the latency of onset of action, poor tolerability and the potential for addiction phenomena.

Although part of the latest psychotropic class, Agomelatine has demonstrated efficacy on depressive symptoms and associated sleep disorders. Increasingly numerous recent studies demonstrate the anxiolytic effect of Agomelatine, both on depressive disorders associated with anxiety disorders and on anxiety symptoms (generalized anxiety disorder).

Keywords:
The drugs of the class of selective serotonin and norepinephrine inhibitors such as venlafaxine, duloxetine, have been used but they have a number of disadvantages, such as the latency of onset of action and a low tolerance of the patient.

It was observed disorders in circadian biological, psychological and behavioral rhythms in depressive disorders. This desynchronization may explain some cardinal symptoms of depression such dispositional changes and sleep disorders.

Valdoxan (agomelatine) is a new antidepressant, the first melatoninergic antidepressant which acts by resynchronization of altered circadian rhythms in patients with depression and anxiety.

The mechanism of action is multireceptorial, agomelatine acting as an agonist of MT1 and MT2 melatoninergic receptors and as an antagonist of 5-HT2C serotoninergic receptors.

Efficacy of the drug is observed from the first week of treatment and the quickly installed therapeutic action becomes evident both in terms of symptoms seen in this psychiatric comorbidity and in terms of improving the level of functioning and in quality of life indicators.

Valdoxan differs from conventional antidepressants (monoaminergic) to which the onset installation action is observed after an interval of 14 days.

Valdoxan antidepressant efficacy is explained by the specific profile of unique mechanism of action - synergistic action of melatoninergic and serotoninergic receptors.

This synergy is the basis for anxiolytic like activity and was demonstrated in animal models.

Valdoxan antidepressant and anxiolytic effects were evaluated in multicentre, randomized, double-blind studies, using Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), Clinical Global Impressions scales (CGI), in depressed patients who had obvious anxiety symptoms.

In these short-term studies (6-8 weeks) Valdoxan therapeutic effects (in 25-50 mg / day dose) were compared with both placebo and with other antidepressants from different classes (selective reuptake serotonin inhibitors - sertraline, fluoxetine and selective reuptake serotonin and norepinephrine inhibitors - venlafaxine).

It has been shown that Valdoxan in these doses is effective, having an onset of action as early as two weeks and relieving the symptoms of anxiety - anxiety significantly decreasing on anxiety scales.

Meta-analyzes have shown significant clinically differences in favor of agomelatine in comparison with sertraline, fluoxetine and venlafaxine. We emphasize that reducing anxiety scores was seen in the second week of treatment and was maintained long term.

In other studies that have used specific scales to measure the duration and depth of sleep were reported obvious improvements both in early and in the late insomnia. This was reflected in the optimal functioning of patients with depression and anxiety.

Stein DJ et al have shown the effectiveness of agomelatine (variable daily dose of 25-50 mg) in generalized anxiety disorder in a randomized, double-blind trial conducted over 12-weeks, compared with placebo. Anxiety symptoms significantly improved, as evidenced by the scales HAM-A, HAM-D, CGI, Leeds Sleep Evaluation Questionnaire and the Sheehan Disability Scale.

These beneficial anxious spectrum effects were reflected in improved mood, decreased mental and somatic anxiety, improve functionality and quality of life, especially in patients with major depressive disorder and important anxiety.

Mentioned studies show that Valdoxan therapy is effective and produces a rapid and sustained improvement in depressive symptoms associated with anxiety symptoms, increase patient compliance to treatment, produces complete remission, decreases the risk of relapse.

Valdoxan administration as a single agent without the use of other anxiolytic agents (benzodiazepines)
and non-benzodiazepines) can significantly reduce the symptoms of anxiety.

Other Valdoxan advantages are that it does not produce phenomena of dependence and abrupt interrupting of treatment is not manifested by discontinuation symptoms.

It is also observed improved daily functioning due to the unique effects on sleep circuits - resynchronize circadian rhythm leads to the disappearance of sleep disorders without installing daytime sedative effects.

Compared with other antidepressants, Valdoxan has a unique position in the pharmacological approach of depressive comorbid disorders with anxiety disorders, because of good tolerability and better treatment adherence than other anxiolytics.

References
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