The migraine syndrome is a neurological disorder with a high degree of patient invalidity in biopsychosocial terms and a wide range of medical and psychiatric comorbidities. The clinical and statistical data suggest that affective disorders and anxiety disorders are more common among the patients diagnosed with chronic migraine compared to those with episodic migraine. Also, recent studies suggest that these psychiatric comorbidities constitute a risk factor for chronic migraine [1, 2]. The prevalence of these comorbidities in the general population is 10-12%.

The mechanism of occurrence involves several working hypotheses:
- Migraine and major depressive disorder may be causally interrelated;
- Migraine and depressive affective disorders may share a common genetic and environmental pathophysiology;
- Migraine and depressive affective disorders may be the phenotypic expressions of the same disease (a study by Breslau et al in 2003 reported a bidirectional relationship between depression and migraine, both increasing the risk for onset of each other).

The evolution pattern and the partially overlapped response to treatment of the two conditions provide further evidence to support the hypothesis of the common mechanisms. This bidirectional association observed by Breslau is specific only to depression and migraine, and not to depression and other types of cephalalgia.

Altered interactions between the serotonergic system and other neurobiological systems, probably mediate the symptoms of affective disorders [3]. The changes in both the quantity of serotonin and serotonin metabolites circulating during migraine attacks, the ability of agents that release serotonin in the synaptic cleft to initiate a migraine attack and especially the effectiveness of ligands between serotonin and serotonergic receptors in the improvement of the migraine symptoms, highlights the involvement of this neurotransmitter in the pathophysiology of migraine [4].

Another highlighted bidirectional relationship is between migraine and anxiety disorders, particularly panic disorder. However this relationship appears not to be specific for migraine, this also occurring in other types of cephalalgies with a similar severity [5].

The relationship between migraine and mental disorders represents not only a clinical reality but also an always actual research theme. There are numerous studies that attest to the high prevalence of psychiatric comorbidities in patients with migraine. Thereby among the patients presenting with chronic headaches, there is a 2 to 5 times greater likelihood of developing a mental disorder.

Among the axis I diagnosed psychiatric disorders, the anxiety spectrum (panic disorder, generalized anxiety disorder, phobias, post-traumatic stress disorder) along with the major depressive disorder and bipolar disorder are in a bidirectional relationship with the migraine syndrome.

The high rate of coexistence and the bidirectional relationship between migraine and the psychiatric disorders suggests common etiological mechanisms such as a serotonergic dysfunction, a dysfunction in the hypothalamic-pituitary-adrenal axis and fluctuations in the serum concentrations of the ovarian hormones. Also, recent studies in genetics are showing a common genetic model that could explain these comorbidities.

The psychiatric comorbidities are clinically relevant because of the negative impact on the patient’s quality of life and the increased difficulty of the therapeutic process (a long evolution, an insufficient therapeutic response and an increased risk of polypharmacy).

Pharmacotherapy represents a challenge. In the clinical practice monotherapy does not constitute an effective therapeutic conduct. Thus, among all classes of antidepressants, only the tricyclic antidepressant amitriptyline is effective both as an antidepressant and anxiolytic as well as a treatment of migraine. However, in some cases side effects limit its use. The pharmacotherapeutic attitude requires a separate approach for migraine and comorbidity, taking into account the proper dosages and the potential drug interactions.

Conclusions: Given the high prevalence, the negative impact on the quality of life and the therapeutic challenges, further studies are needed to provide a better understanding of the pathological mechanisms, clinical implications and consequently to develop better therapeutic algorithms for this combination of disorders.

Keywords: Case management, Migraine syndrome, antidepressant, anxiolytics
• the degree of disability caused by the frequency and duration of the migraine attack, the presence or absence of prodrome and postdrome, the occurrence of the so-called atypical migraine syndromes (familial hemiplegic migraine, basilar migraine) [2];

• the presence of comorbidities (hypertension, anxiety disorders, depressive disorders, epilepsy, fibromyalgia etc.) that could cause drug interactions with side effects or low tolerance to acute medication [2].

The main objective of preventive therapy is to reduce the degree of disability and to increase the quality of life. This objective requires on one hand the correct identification of triggers and on the other hand the fast, adequate approach.

Why is it so important to prevent?
The inadequate treatment or under treatment of this condition leads to a chronic state, increased costs, decreased quality of life and possible use of narcotics.

Numerous studies in brain imaging revealed brain lesions in patients with no history of vascular disorders and a normal neurological examination. The changes observed were infarcts in the posterior vascularization - in particular, cerebellum, and white matter lesions especially in women (the occurrence of such injuries is closely correlated with the increased frequency of migraine syndrome) [3].

Medication
From the beta blockers class propranolol is the most widely used.

From among calcium channel blockers verapamil is most commonly used - three double-blind clinical trials have demonstrated the efficacy of verapamil versus placebo in reducing migraine frequency by 18 to 49%.

The use of an angiotensin II receptor blockers (candesartan) resulted in a reduction in the number of days of a migraine episode [8].

Some of the antiepileptic agents used are: topiramate, valproic acid, gabapentin (effective doses of 1800-2400 mg/day), lamotrigine (numerous studies of 3 months with 200 mg/day, with slow titration due to the risk of the appearance of a rash) [9,10].

The valproic acid has been approved for the prevention of migraine. It has been shown to be effective at doses of 500 mg/day to decrease the frequency of migraine episodes [11].

The topiramate, recently approved for the treatment of migraine, has a mechanism of action that is still partially known. Of reference there are two clinical trials conducted in USA, MIGR-001 and MIGR-002 that were well designed and were conducted on a wide scale in the population. The response rate varied from 47% (MIGR-002, 200 mg/day topiramate) and 54% (MIGR-001, 100 mg/day topiramate). The most commonly reported side effects were fatigue, nausea, loss of appetite with a consequent decrease in weight - phenomena occurring particularly at the dose of 200mg/day [10].

Another substance used is methysergide, at doses of 4-8 mg/day, with a response rate of 14 to 30% to improve the clinical condition. However Methysergide requires special precautions since it is associated with pulmonary fibrosis, retroperitoneal fibrosis, and fibrosis of the cardiac valves. A break of 3-4 weeks is recommendable to every 6 months of treatment.

From the antidepressants class the following are recommended: tricyclic antidepressants (amitriptyline is the most well-studied and used), dual antidepressants (SNRI) and SSRIs.

Amitriptyline in effective dosages of 25-150 mg/day enables a reduction of up to 40% of migraine attacks. Side effects include sedation, dry mouth, weight gain, hypotension.

There is less evidence about the efficacy of desipramine, doxepin and nortriptyline.

Regarding SSRIs, studies have led to conflicting data for fluoxetine and concerning sertraline, paroxetine and escitalopram the data for effectiveness in prevention is insufficient.

The use of venlafaxine doses of 37.5 to 300 mg/day significantly reduced the number of migraine episodes per month.

In conclusion, the effective treatment plan is a comprehensive plan that requires an approach to the primary triggers. The control of these triggers such as stress, caffeine, smoking, sedentary lifestyle is very important.

Migraine has high rates of comorbidity with mood and anxiety disorders.

Migraine and psychiatric comorbidity share underlying pathophysiological mechanisms with bidirectional effects.

An effective treatment for migraine and psychiatric comorbidities requires pharmaceutical interventions that target both headaches and the symptomatology of depression and anxiety.