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Migtera® in the Treatment of Migraines

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[1]Shokhida Gazieva, [2]Satima Kuranbaeva, [3]Gulchehra Usmanova, [4]Umida Shamsieva, [5]Sevara Kalandarova, [6]Dilnoza Yusupova
Tashkent Medical Academy

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migraine, VAS scale, MIDAS scale, triptans, zolmitriptan, Migtera, Rapimig.

Abstract
The evidence base of the use antimigrenous drug of Migtera® (a.i. zolmitriptan) in the management of patients with migraine attacks, evaluation of its effectiveness in comparison with the used antimigrenous drug Rapimig (a.i. zolmitriptan) is considered. The results of studies of the treatment of these patients using antimigrenous drug Migtera® showed its equivalent efficacy and tolerability compared to patients taking basic therapy with antimigrenous drug Rapimig.

According to the classification of the International Headache Society, all headaches are divided into primary and secondary. Primary headaches include migraines without and with aura, cluster headaches, and tension headaches. Secondary headaches are those that occur as a result of some other disorder, for example, brain tumors, rhinosinusitis, diseases of intracranial and extracranial vessels. Migraine is a chronic neurological disorder. It is characterized by recurrent moderate and severe headaches, often accompanied by nausea, vomiting, photophobia and phonophobia. This is one of the most frequent neurological disorders, manifested in 12.6% of the population (6% of men, 18% of women) [20]. Among them, the most frequent are the so-called circadian types, expressed by the appearance of pain at certain times of the day or oscillatory. The paroxysmal nature of migraine is a distinctive feature of this disease [10]. The frequency of seizures and pain-free intervals vary from patient to patient [12]. Some patients may experience an increased frequency of seizures at certain times of the year [9] or towards the end of the week [21], while others report daily variations in the onset of a migraine attack [22]. The mechanisms underlying the oscillatory nature of migraine are unknown.

Despite the fact that migraine therapy is well developed (according to the American Association for the Study of Headache, the effectiveness of proper treatment can reach 95%), more than 70% of patients are not satisfied with the result of treatment [17]. In part, this is the fault of the patients themselves, who do not go to the doctor, self-medicate, and ignore the recommendations received. However, in many cases, the low effectiveness of therapy is the result of inadequate medical care. Some doctors continue to treat patients with migraine, based on outdated information, without taking into account the possibilities of modern methods of treating migraines. However, the difficulty of treating headaches is not only due to the "correctness" of the choice of the drug. Migraine is a complex neurobiological disorder with a multifactorial pathogenesis, and the problem of its treatment cannot be solved with the help of any one, even a new and effective medicine. To achieve success, it is necessary to take into account a number of aspects, both purely medical and psychological [2].

The results of a survey of patients with migraine showed that the majority are not satisfied with the drug used for the treatment of a migraine attack due to a long waiting period for the onset of action (87% of patients), incomplete analgesic effect (84%), inconstancy of the effect (84%), recurrence of headache (71%) and side effects (35%) [18.]. Among the reasons for the ineffectiveness of migraine attack therapy is the use of painkillers with low clinical efficacy; taking insufficient, inadequate doses of drugs [5,6]. Triptans proved to be the most effective in relation to painkillers of other pharmacological groups [6]. Thus, 9-10% of patients were satisfied with the effect of taking simple and combined analgesics, NSAIDs – 25-27%, ergotamines – 31-39%, triptans – 62-66% of patients [19].

Triptans are specific antimigrenous drugs that have a selective agonistic effect on serotonin 5-HT 1b-, 1d-, 1f-receptors. 5-HT 1b receptors are located in the wall of the vessels of the meninges. The effect of triptans on these receptors causes narrowing of vessels dilated during migraine attack and reduces perivascular neurogenic inflammation.

5-HT 1d and 1f receptors are located on the presynaptic ends of the trigeminal nerve fibers, the activation of which

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prevents the release of vasoactive proteins that dilate blood vessels [5,8].

Triptans are used to relieve migraine attacks and should not be used for the treatment of other types of headache, except for cluster headache. To date, there are 7 types of triptans: sumatriptan, zolmitriptan, naratriptan, risatriptan, almotriptan, eletriptan and frovatriptan [13]. The effectiveness of triptans has been proven in large placebo-controlled studies and has the highest level of evidence for the treatment of a migraine attack [13, 14, 23]. In 60% of migraine patients who had not previously responded to NSAID therapy, triptans were effective [11].

The most effective drug from the group of triptans is zolmitriptan (Zomig), which has a pronounced dual mechanism of action and high selectivity to serotonin receptors 5NT–1D and 5NT–1B type. Zomig affects the stem nucleus of the trigeminal nerve, inhibiting the conduction of pain impulses, dilation of cerebral vessels and neurogenic inflammation, causes vasoconstriction, inhibits the release of neuropeptides (vasoactive intestinal peptide, substance P, etc. [3]. Comparative analysis of triptans showed the early onset of the action of zolmitriptan (Zomiga), its stable effectiveness in attacks and various forms of migraine [1].

Zolmitriptan (Zomig) is administered orally (1 tablet – 2.5 mg) during a migraine attack, regardless of food intake. The action begins in 15-20 minutes and reaches a maximum within 1 hour. In almost 80% of patients, headaches significantly decrease or completely disappear within an hour. If necessary, after 2 hours, you can take a second tablet of zolmitriptan. The need for repeated use of zolmitriptan occurs in no more than 20% of patients [1]. When treated with the drug, along with the reduction or complete cessation of headache, nausea, photophobia, phonophobia significantly decreases [4]. Zomig is highly effective in the complex treatment of migraine status, migraine attacks lasting 2-5 days. Eliminates menstrual migraine. With prolonged use of zolmitriptan, its clinical efficacy does not decrease.

The need for such effective drugs contributed to the development by the pharmaceutical company FE "Nobel Pharmsanoat" LLC (Uzbekistan) of the drug Migtera® (a.s. zolmitriptan) and the presentation on the market of medicines with their availability and at the same time high quality in this group of triptans.

Objective: To evaluate the efficacy and tolerability of the drug "MIGTERA®" 2.5 mg, 5 mg coated tablets manufactured by FE "Nobel Pharmsanoat" LLC, Uzbekistan in patients with migraine attacks in comparison with a group of patients with identical pathology taking the drug "RAPIMIG" 2.5 mg, 5 mg coated tablets manufactured by Actavis Ltd, Malta, to identify the possibility of implementing the import substitution program and, accordingly, to recommend the drug for wider clinical use in the Republic of Uzbekistan.

1. Materials and Methods:

The registration of indicators was carried out immediately after receiving the data of clinical and laboratory studies, which included monitoring of the general condition, assessment of symptoms, upon admission, echoencephalography, rheoencephalography were removed to clarify the diagnosis, pain was assessed on the VAS scale (Visual analogue scale) and migraine severity assessment on the scale of MIDAS (The Myocardial Infarction Dimensional Assessment Scale - MIDAS).

Data of indicators by which the effectiveness of the drug was judged

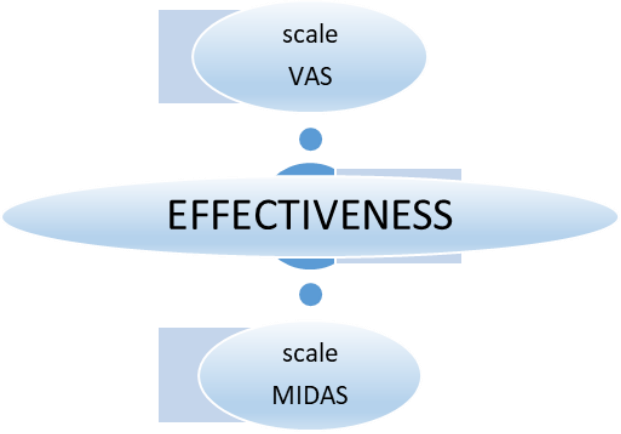

Figure 1 Performance indicators

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Professor Richard Lipton and Dr. Walter Stewart proposed a fundamentally new approach to the treatment of migraine attacks, which was first published in Pain in 2000. It was developed as a faster and more effective way to determine the level of disability in migraine, without relying on a headache diary [16]. This approach is based on the assessment of the effect of migraine on the patient's daily activity simultaneously with the diagnosis of migraine. This initiative was called MIDAS (Migraine Disability Assessment) from the English disability-a violation of daily activity. The essence of the method is that the patient is asked to answer 5 simple questions about the loss of time due to headaches in three main areas of his life: study and work, housework and family, sports or social activity [15]. The information expressed in the form of quantitative indicators was subjected to statistical processing, including using special software products. The method of variational statistics was used with the derivation of the main parameters according to the Student.

The study included 60 patients with symptoms of a migraine attack. The patients were divided into two groups: group A - 30 patients who took MIGTERA® 2.5 and 5 mg manufactured by FE "NOBEL PHARMSANOAT" LLC (Uzbekistan) and group B - 30 patients who took RAPIMIG 2.5 and 5 mg manufactured by Actavis Ltd, Malta.

The average age in the group receiving the studied drug was 33÷1, 1 years, of which men – 27.6%, women – 72.4%. In the group receiving the drug of comparison, the average age was 33.9÷1.1 years, of which men – 20%, women – 80%.

The study did not include patients with:

— uncontrolled hypertension;
— IBS;
— angiospastic angina pectoris (Prinzmetal angina pectoris);
— disorders of cerebral circulation or transient ischemic attacks in the anamnesis;
— combined use with ergotamine or its derivatives, or other 5HT1B/1D-serotonin receptor agonists;
— WPW syndrome or arrhythmias associated with other additional pulse pathways;
— hypersensitivity to the components of the drug.
— over the age of 65.

Patients of both groups took medications at a dose of 2.5 mg orally, 1 tablet, to relieve a migraine attack. Patients were warned that if a repeated dose is necessary, it should be taken 2 hours after the first one. If the patient did not experience relief after taking the drug at a dose of 2.5 mg, subsequent migraine attacks were recommended to be stopped with the drug at a dose of 5 mg. And also a recommendation was given to use the drug as early as possible after the onset of a migraine headache attack.

It was specifically pointed out that the tablet should be placed on the tongue, where it dissolves and is swallowed with saliva, that is, there is no need to take the tablet together with the liquid. This avoids nausea and vomiting that may accompany taking tablets with liquids. After taking the medication, it was recommended to lie down in a quiet, dark room until relief comes. The trial period lasted 20 days.

Other drugs with a similar effect were excluded. The basic therapy preparations necessary for the treatment of the underlying disease and other medications compatible with zolmitriptan were used. Patients participating in the study could also receive drugs that are constantly used to treat concomitant diseases.

2. The Results of the Study:

According to the dynamics of changes in clinical symptoms on the VAS and MIDAS scale, pronounced, significant improvements in the indicator are visible. At the same time, it should be noted that there is a synchronous, identical change in the direction of improvement in both groups:

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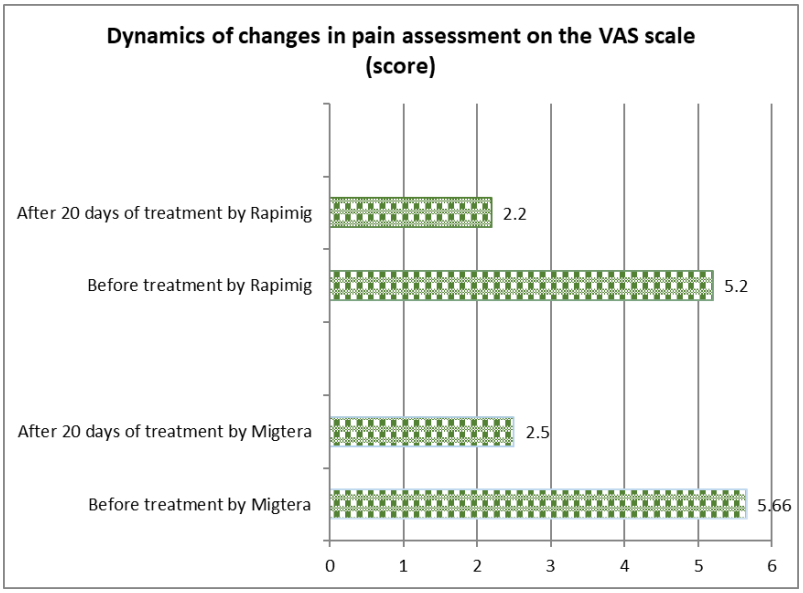
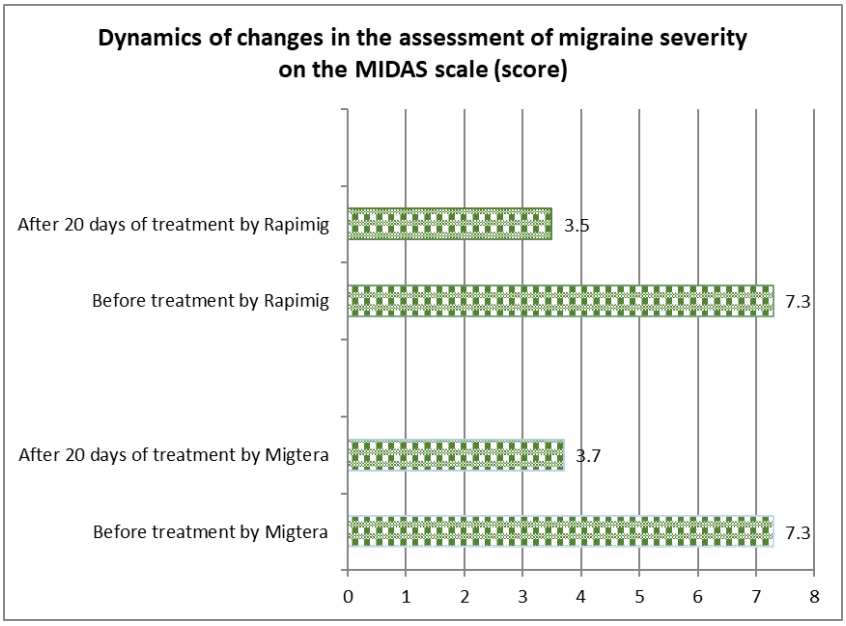


Chart 1

At the same time, a decrease in the value of pain on the VAS scale among group A patients with the highest frequency was observed in 10 patients by 50% and in ten more by 66.7%. In four patients, the pain decreased by 40%, in three by 60%, in one by 42.9% and in another by 75%. On average, the pain decreased by 55.8%.

Among the patients in the group with the highest frequency, pain reduction was observed in 14 patients by 60%, in six patients by 50%, in five by 66.7%, in three by 75% and in one by 16.7%. On average, pain in this group decreased by 53.7%. The average values of the scores before and after the treatment are given in the chart 1.

An identical synchronous change in dynamics was observed in both groups and in the effectiveness indicator on the MIDAS migraine severity assessment scale – in group A, the decrease in migraine severity was 49.3%, in group B it decreased by 52.1% (chart 2.).



The tolerability of the drug was assessed on the basis of subjective symptoms and sensations, which the patient reported independently and taking into account objective data obtained by the doctor. The dynamics of laboratory parameters, as well as the frequency and nature of adverse reactions were taken into account. The assessment of the tolerability of the studied drug

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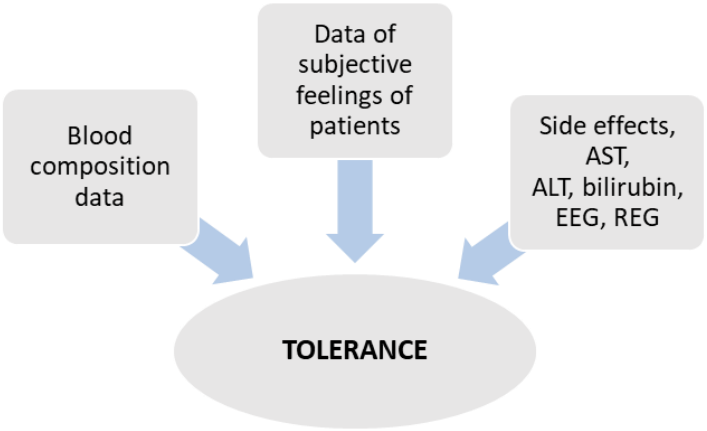
was carried out on the basis of the above criteria in points on a scale from 0 to 4 points:



The conducted studies have not established any significant changes in these indicators, with the exception of one case when a patient from group A was forced to leave the group due to an individual allergic reaction in the form of a rash.

There were no significant changes in the dynamics of changes in the level of hemoglobin, the number of erythrocytes and leukocytes, ESR.

Other indicators of laboratory studies, such as the activity of ALT, AST enzymes, and the level of bilirubin in the blood, also remained within physiological fluctuations. The EEG and REG indicators, apparently due to the short observation period, also did not show any interrelated changes.

The drugs were well tolerated; there were no subjective complaints about changes in the state of health on the part of patients.

3. Conclusion

The use of MIGTERA® tablets in migraine therapy produced by FE "NOBEL PHARMSANOAT" LLC (Uzbekistan) has shown its equal comparability in efficacy and tolerability and can completely replace the imported drugs of similar action used.

The widespread introduction of this drug, market saturation and availability is one of the important factors in the timeliness of treatment and, accordingly, the reduction of this problematic factor in reducing the quality of life.

At the same time, a doctor who is faced with the treatment of migraines should not be a simple performer of the proposed algorithms. In order for therapy to be effective and safe, it is necessary to be more creative in choosing methods, taking into account the individual characteristics of patients. At the same time, it is very important to create trusting and at the same time business relationships with the patient, his training and active involvement in the process for more effective achievement of the treatment goal.

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