JOINT MEETING OF THE PULA CONGRESS WITH ALPS-ADRIA NEUROSCIENCE SECTION: DIAGNOSIS AND MANAGEMENT OF PAIN

MIGRAINE

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Migraine is a primary recurrent headache manifesting in attacks lasting 4-72 hours and affects 2-20% of world population. Women are more often affected, mostly during reproductive years. The migraine effects quality of life and has negative impact on working capability.

Studies have showen that migraine is a common primary headache, but is not adequately diagnosed. Migraine is diagnosed in only 41% of women and 29% of men. Over 50% of patients with headacaches do not consult their medical doctors and among those who do, most of them do not go on check-ups.

Also, migraine is an expensiv disease. A number of studies so far have evaluated the costs due to migraine. The costs can be divided into direct costs which include visits to the general practitioner and the emergency departments, costs of hospitalization and farmacotherapy. Indirect costs comprise 2/3 of total costs and include absence from work and costs due to reduced productivity.

The exact mechanism of patophysiology of migraine hasn't been established yet. The current state of knowledge in this field suggests that a primary neuronal dysfunction leads to a sequence of changes intracranially and extracranially that account for migraine, including the three phases of premonitory symptoms, aura, and headache.

Central and peripheral sensitization are thought to play a role within individual migraine attacks and in the transformation of episodic migraine to chronic migraine. Sensitization refers to the process in which neurons become increasingly responsive to nociceptive and non-nociceptive stimulation: response thresholds decrease, response magnitude increases, receptive fields expand, and spontaneous neuronal activity develops.

The once popular vascular theory of migraine is no longer considered viable in its original form.

While the exact mechanism of serotonin action remains obscure, there is evidence that a low serotonin state results in a deficit in the serotonin descending pain inhibitory system, facilitating activation of the trigeminovascular nociceptive pathways in conjunction with cortical spreading depression.

The calcitonin gene-related peptide (CGRP) may also play a central role in migraine pathophysiology. CGRP may mediate trigeminovascular pain transmission from intracranial vessels to the central nervous system as well as neurogenic inflammation.

Elevated CGRP levels are normalized in patients with migraine following administration of the serotonin 1b/1d receptor agonist sumatriptan [34], suggesting that triptans may act to control migraine at least in part by reducing CGRP levels.

Pharmacologic modulation of CGRP activity offers the promise of future treatment options for acute migraine attacks.

The abortive (symptomatic) therapy of migraine ranges from the use of simple analgesics such as nonsteroidal antiinflammatory drugs (NSAIDs) or ac-

etaminophen to triptans or the less commonly used dihydroergotamine.

The serotonin 1b/1d agonists (triptans) are considered to be "specific" therapies for acute migraine since, in contrast to analgesics, they act at the pathophysiologic mechanism of the headache. All of the triptans inhibit the release of vasoactive peptides, promote vasoconstriction, and block pain pathways in the brainstem. Triptans inhibit transmission in the trigeminal nucleus caudalis, thereby blocking afferent input to second order neurons; this effect is probably mediated by reducing the levels of calcitonin gene related peptide (CGRP). Triptans may also activate 5-HT 1b/1d receptors in descending brainstem pain modulating pathways and thereby inhibit dural nociception.

The available triptans include sumatriptan, zolmitriptan, naratriptan, rizatriptan, almotriptan, eletriptan, and frovatriptan. In Croatia are available only three triptans (sumariptan, zolmitriptan and rizatriptan). Sumatriptan can be given as a subcutaneous injection (usually admi-nistered by autoinjector in the thigh), as a nasal spray, or orally. Zolmitriptan is also available for both nasal and oral use. The others are available for oral use only.

Prophylactic therapy is recommended when migraine attacks are frequent, are long-lasting, acute therapy is not efficient or the side-effectc are serious. Several groups of prophylactic medications can be recommended. Beta blockers are the first line for prophylaxis in patients who are normo- or hypertensive.

Among antidepressants, the most efficient seems to be the tricyclic antidepressant amitriptyline, while selective inhibitors of serotonine reuptake (SSRI) seem to be less efficient. In the antiepileptic group, the most efficient is the valproat acid, gabapentine and topiramate.

Many studies pointed out the acupuncture to be effective in prophylaxis of migraine headache.