

## Migraine – paradigm shift

### *Migrânea – mudanças de paradigmas*

First migraine treatment reports come from the Egyptian medicine in 4000 BC. But it was only in 1918 that Sandoz has isolated ergotamine and the pharmaceutical product was called Gynergene, which was used in gynecology as uterotonic. As from 1925-1927, Gynergene was accepted worldwide to treat migraine crises via muscular or subcutaneous route.

In 1943, oral and parenteral dihydroergotamine was used to treat crises, being less effective, however with less side effects than ergotamine, due to its lower vasoconstrictor power. In 1980 it was indicated as prophylaxis for crises. The idea of prophylaxis appeared by chance in 1966 when Rabkin et al.<sup>1</sup> noticed improvement of migraine crises in patients with angina pectoris treated with propranolol; an accidental discovery. New and very efficient prophylactics were gradually being introduced in the therapeutic armamentarium: amitriptyline, calcium channel blockers, antiserotoninics (pizotifen, methysergide) among others. Since the first scientific approaches to treat and prevent migraine, one paradigm collapsed: “migraine patients shall learn how to live with their crises because this disease has no treatment”.

As from the discovery of sumatriptan by Humphrey et al.<sup>2</sup> and then with the development of other drugs of this class (triptans), such as zolmitriptan, naratriptan, rizatriptan, which are specific and more potent drugs to treat crises than those used to date, there was a trend to a new paradigm shift: migraine crises treatment could be the best approach for patients with severe and incapacitating crises provided they were not very frequent (1 per week).

1. In parallel to therapeutic advances, major progresses in the understanding of the pathophysiology of the aura and the clinical evolution of migraine were announced: In the pathophysiology of the aura = Leao's spreading depression<sup>3</sup>, which is a cellular, neuronal and glial phenomenon predominating in occipital regions.
2. In the pathophysiology of the headache = neurogenic inflammation affecting meningeal vessels causing the demodulation of trigeminal nucleus caudal region and establishing the neurovascular theory of migraine headache<sup>4</sup>.
3. Confirmation that migraine is a hereditary disease = what is inherited is a brain demodulation which, under known triggers (stress, alcohol, odors, female sexual hormones, some foods, etc.), generates a cascade of neurochemical events and the migraine crisis. The announcement of neuronal demodulation / hyperactivity concepts of migraine patients' brains has encouraged clinical trials with different drugs having the property of stabilizing neuronal membranes and so divalproex and topiramate have become the drugs of choice to prevent migraine in recent years.
4. Migraine evolution = some migraine patients evolve to increased frequency and intensity of crises which may become daily or almost daily. Such evolution may be spontaneous, however emotional disorders, stress and excessive analgesics and other headache killers (more than 8 to 10 doses/month) may translate migraine, which is a recurrent disease, into a different disease called chronic migraine and much more difficult to treat. We could compare this transformation to pain in general, considering migraine episodes as acute recurrent nociceptive pain and chronic migraine as Chronic Pain disease.
5. Study of migraine comorbidities = several diseases were identified as migraine comorbidities. Such affections may trigger migraine attacks, may contribute to chronification or may influence the prognosis. It is important to understand the comorbidities of a disease because they have implications in diagnosis and treatment. Most frequent migraine comorbidities are: depression, anxiety, epilepsy, stroke, allergies, irritable colon, peptic disease and essential shivering. The presence of one or more comorbidities should be taken into account when selecting the treatment.
6. Migraine complications = The International Classification of Headache Disorders<sup>5</sup> specifies complications in long term migraine evolution: a) migraine status with severe migraine crises lasting more than 72 hours, uncontrollable

vomiting and dehydration; b) persistent aura without infarction and migraine infarction refer to long standing migraine aura which does not respond to treatment and may evolve or not to brain infarction; c) epileptic crisis triggered during crises of migraine with aura – migralepsy.

Such knowledge has led to other paradigms shift, namely:

- Migraine is a neurological disease (not from the liver, emotional, from temporomandibular dysfunction, etc.) where the major problem is the presence of an inherited central demodulation, which leads to neuronal hyperexcitability.
- Migraine is not a recurrent disease – currently it is considered a recurrent disease which may become daily or almost daily.
- Treatment is no longer limited to analgesics and should be oriented by crises frequency and intensity. Most patients looking for medical assistance need prophylactic treatment and not just a painkiller.
- Very often, migraine has intercritical symptoms, even when crises are not frequent. Migraine patients may have overlapping diseases, which decrease their quality of life and these should also be treated together with the crises.
- In conclusion, migraine is still a benign disease, but which interferes with quality of life and for such it should be adequately treated. Its morbidity is low, but it may occur, thus it should be known by all health professionals. Its evolution to chronic migraine should be prevented. In the medium term, it is expected that the spread of the concepts herein may prevent some migraine patients of having complications of the disease, which can make them a burden for their families and society.

## REFERENCES

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