

Fever: a novelty among the symptoms accompanying migraine attacks in children

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Abstract. – Our casistic of 1787 children with headache, is made up of 943 males (53%) and 844 females (47%) aged 3-14 years. 1724 had primary headache. To make a precise diagnosis of primary headache, all the children have been subjected to a rigorous anamnesis, physical and diagnostic examination (blood, urine test, head x-rays-scans, sight test with cat's eyes). Symptoms that frequently accompany headache are: phono-photophobia, (47%), pallor (43%) nausea (41%) vomit (31%) intolerance to movement (40%) and fever (9%). We especially focused on fever which presented together with migraine in 156 (9%) of the 1724 subjects examined. Headache is an important syndrome and frequent in early childhood. Actually the hypothesis used to explain the etiopathogenetic mechanism is based on a disregulation of the neurotransmitters like serotonin, catecholamine and the prostaglandins.

Key Words:

Fever and migraine, Headache.

Introduction

The recognition that headache is an important and frequent symptom in childhood is especially due to the epidemiological studies conducted by Bille¹ and Sillampa². It has been calculated, in fact, that approximately 20% of the school age population suffers from headache several times a year. Generally, these are migraine crises or muscle tension headaches, although in children such a distinction is rather less neat than adults. Migraine crisis has a diversified clinical expression both because of the characteristics of the pain and the associated symptomatology. Among the accompanying symp-

toms, we condistinguish those that are more frequent (major symptoms) as nausea etc. and those that appear more rarely (minor symptoms) such as fever. Fever here can be secondary to various pathologies, such as – among others – inflammatory, and infectious processes of bacterial and/or viral origin and neoplastic processes, but can also come as an accompanying phenomenon of a cephalalgic syndrome. It has been known for a long time now that fever rises because of the presence of low-molecular weight substances known as "endogenous pyrogens" that penetrate through the hematoencephalic barrier and act upon the thermoregulator centre located in the anterior portion of the hypothalamus. In particular, these substances are cytokines such as interleukins (IL-1-alfa, IL-1-beta), tumor-necrosis factors (TNF-alfa, TNF-beta) and alfa-interferon which are produced by the cells of the host (macrophages, monocytes, endothelial cells, etc.) under the effect of infectious agents, toxins, immune-reaction products, generally known as "exogenous pyrogens". The effect of pyrogen cytokines on the hypothalamus leads to the production of prostaglandin E₂ (PGE₂) responsible for the hypothalamic thermoregulator reset which stimulates peripheral mechanisms in order to reproduce and preserve the heat. The sequel of such events leads to fever³. Aim of our study was to verify a correlation between migraine and fever in children.

Materials and Methods

The study included 1787 children – 943 males (53%) and 844 females (47%) age range 3-14 years, (mean 9.6 years) observed

at the Service of Diagnosis and Treatment of Pediatric Migraine of the University "La Sapienza" of Rome, between 1981 and 1995. On the total of 1787 patients in 1724 the diagnosis was essential headache. The diagnosis of essential headache was formulated after an accurate history with negativity of physical examination, and a series of tests - blood, chemical, and biohumoral exams, urinalysis, visual examination with visual field, X-rays of the skull and paranasal sinuses, sometimes CAT and/or NMR. Furthermore, for all children the cephalalgic risk factors - such as familiar trait, recurrent abdominal pain (RAP), limb pain, cyclic vomiting, kinetosis, sleep disorders, vertigos, and hyperactivity were taken into consideration. We also looked at the distribution of the most important and frequent headache-accompanying symptoms, such as phonophobia and photophobia (47%), pallor (43%), nausea (41%), intolerance to movement (40%), vomit (31%), and fever (9%). The instrumental and laboratory tests carried out did not allow to document any pathologic process responsible for the fever symptomatology. Thus, we may suppose that in a small percentage of subjects examined, a deeper investigation may have highlighted an infectious etiology, most of all viral, in the greater majority of cases. Instead, in most cases the only possible explanation was that the febricula resulted as a frequent accompanying symptom of the headache. Fever always regressed at the end of the crisis and never exceed 38°, with the only exception of a 13 years old subject whose body temperature constantly reached 39°-40° during each crisis. From the age of 9 years, this child had been suffering from a migraine with aura accompanied by fever. All tests performed on him ruled out the possibility that pathological processes could trigger his fever rise.

Results

We especially focused on fever which accompanied migraine in 156 (9%) of the 1724 subjects examined. In 70% of patients¹⁰⁹ fever rose with every migraine crisis whilst in the remaining 30% (47 cases) the association was discontinuous even though well detectable.

Discussion

In pediatric age, the headache-fever association has an unquestionable clinical interest, especially when fever is particularly accentuated. We believe that fever accompanies migraine in a greater percentage of cases the one reported (9%) since a febricula is only occasionally noticed by parents. Beyond its clinical interest, may be the association between headache and fever can help to clarify and strenghten some hypotheses on pathogenetic mechanisms at the basis of this clinical condition⁴. In normal conditions, thermic homeostasis is maintained by the hypothalamic neuronal circuits which process the peripheral incoming messages (heat, cold) and, as a consequence, regulate the mechanisms at the basis of heat production and dispersion⁵. Serotonin, and probably other neurotransmitters as well, modulate the hypothalamic thermoregulatory nervous circuits and, according to most recent and supported theories, it is just serotonin which plays a central role in the pathogenesis of essential headache⁶. We owe especially to Sicuteri et al. the current comprehension of serotonin deficit in the genesis of migraine attack^{7,9}. In fact, serotonin remains the basic determining element of cephalalgia both in central or neurogenous theory. According to this latter theory, migraine pain would be provoked by a deficit of neurotransmitters (serotonin, dopamine, etc.) and of endogenous opioidis (enkephalins, endorphins) and, most of all, of the natural analgesic apparatus at the central nervous system level, denominated, antinociceptive system (ANS). Thus, headache would be the most common example of central dysnociception. Taken into account the role played by serotonin in body-temperature regulation, the appearance of fever during a migraine attack cannot come as a surprise. Moreover, already in 1963 after having observed some cases of cephalalgia accompanied by fever, Wolff¹⁰ put forward the hypothesis that the concurrence of these two symptoms was somehow connected to vasomotory modifications within the thermoregulatory apparatus. Hence, the association fever-headache observed in our group of children can be considered as far from fortuitous, both in reason of its incidence and of the possibility to reconduct

both these manifestations to the same pathogenic mechanism where serotonin has a predominant role.

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