The Association Of Migraine And Recurrent Epistaxis In Adults

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Abstract:
Migraine is common incapacitating disorder with functional disability. We observed frequent complaints, or history of epistaxis in adults with migraine. The aim of this study was to determine whether there is an association between epistaxis and migraine in adults. A detailed questionnaire was used to conduct a study of 186 consecutive patients with migraine, diagnosed according to the 2004 proposed revisions to the International Headache Society criteria; the patients were evaluated in our Neurological Clinic. Control subjects consisted of 200 with non-recurrent headaches, matched as a group for age and sex. 22 (11.83%) of 186 patients with migraine had epistaxis as compared with 2(1%) of 200 control subjects (odds ratio =13.28%). Out of 22 migraine patients 18 (81.82%) with epistaxis below 40 years old. The epistaxis was unilateral in 18 (81.82%) migraine patients, its recurred following throbbing headache in 17 (77.27%) and in the same side of headache in 15 (68.18%) patients. The pain is relived repeatedly following epistaxis in 13 (76.47%) of them and does not change in the others. This study demonstrates a significant association between migraine and recurrent epistaxis in young adults, raising the question of whether epistaxis may represent a precursor and reliving factor of migraine.

Introduction:
Migraine is a common, chronic, incapacitating neurovascular disorder, characterized by attacks of severe headache, autonomic nervous system dysfunction, and in some patients, an aura involving neurological symptoms. In the US more than 23 million
people in the United States suffer from migraine. This roughly corresponds to 17.6% of females and 6.0% of males.\(^{(3–6)}\)

Since 1940s and 1950s, the vascular theory was proposed by Wolff\(^7\) to explain the pathophysiology of migraine headache as an intracranial & extracranial vasoconstriction and subsequent rebound vasodilatation and activation of perivascular nociceptive nerves resulted in headache.\(^{(9,10)}\)

Until now, our understanding of the pathophysiology of migraine is still evolving, and all recent theories trying to explain the vascular and neurological events during migraine headache.\(^{(11-21)}\)

The results of the vascular events is diverse and not restricted to intracranial blood vassals, recent observations demonstrated to have a greater than coincidental association of migraine with ischemic heart disease\(^{22 - 23}\) stroke\(^{24 - 28}\) and endometriosis\(^{29}\).

We observed frequent complaints or history of epistaxis in adults with migraine although epistaxis is a common pediatric problem,\(^{30 - 32}\) Recent evidence discrives an association of migraine and recurrent epistaxis in children.\(^{32,33}\) The incidence of epistaxis declines in adulthood.\(^{33}\) We conduct this study to determine whether there is an association between epistaxis and migraine in adults.

**Background:**

**Pathophysiology of Migraine:** Wolff\(^7\) popularized the vascular theory of migraine, which emphasizes the role of vasoconstriction and vasodilatation leading to oligemia, neuronal disruption and, eventually, aura of migraine and that the subsequent rebound vasodilatation and activation of perivascular nociceptive nerves resulted in headache.\(^{8,10}\)

However, this theory has been challenged for several reasons.

The neural theory of migraine, proposed by Lance,\(^9\) emphasizes the neuronal origins of a vascularly mediated path physiologic cascade that results in headache. PET scanning in patients having an acute migraine headache demonstrates activation of the contra lateral pons\(^{10,12}\) even after medications abort the pain.\(^{(13,14)}\)

Weiler et al\(^11\) proposed that brainstem activation might be the initiating factor of migraine, which reflected to the cerebral cortex, resulting in cortical spreading depression,\(^{15}\) and the release of H+ and K+ ions from the surface of the brain. Activating C-fiber meningeal nociceptors in the pia mater and and plasma extravasations occurs (releasing a proinflammatory soup of neurochemicals eg, calcitonin gene–related peptide).\(^{(16-18)}\)

Therefore, a sterile, neurogenic inflammation of the trigeminovascular complex is present.\(^{(18,19)}\) Once the trigeminal system is activated, it stimulates the cranial vessels to dilate. The final common pathway to the throbbing headache is the dilatation of blood vessels.\(^{(8,12)}\)

The trigeminal vascular hypothesis of migraine, based on the work of Moskowitz and MacFarlane,\(^{(18)}\) focuses on the relationship of the trigeminal nerve and the cerebrovascular system. Antidromic stimulation of the trigeminal nerve (because of a genetic predisposition or triggers acting in the cortex or in thalamic or hypothalamic structures) leads to vasodilatation and release of neuropeptides at the perivascular nerve endings.\(^{(19-20)}\) The affected trigeminal nerve release of substances such as substance P, neurokinin A, calcitonin gene-related peptide, and nitric oxide which interact with the blood vessel wall to produce dilatation, protein extravasation, and sterile inflammation,
stimulating the trigeminocervical complex as shown by induction of c-fos antigen by positron emission tomography (PET) scan. This chain of events is further mediated by mast cells that release histamine and platelets that release serotonin. The release of these chemicals causes inflammation, and what is called peripheral sensitization. This is most likely, what results in the throbbing pain of migraine. Information then relayed to the thalamus and cortex for registering of pain and central sensitization explaining coetaneous allodynia. Involvement of other centers may explain the associated autonomic symptoms and affective aspects of this pain.

Pathophysiology of Epistaxis:

Nosebleed is a common pediatric complaint usually occurs in children aged 2-10 years with uncertain etiology in most cases. Its estimated that approximately 80% to 90% of all epistaxis occurs anteriorly, especially in children and young adults, and arise from the Little area, where the Kiesselbach plexus forms on the septum. The Kiesselbach plexus is where vessels from both the internal carotid artery (anterior and posterior ethmoid arteries) and the external carotid (sphenopalatine and branches of the internal maxillary arteries) converge. Epistaxis that occurs in individuals older than 50 years is more likely to be severe and to originate posterior.

Epistaxis typically occurs when the mucosa is eroded and vessels subsequently break. Various local inflammatory reactions can alter the normal mucosa, causing dryness and crusts permitting the introduction of bacteria and subsequent formation of granulation tissue which characterized by increased vascularity and greater friability of the vessels which is easily bleed.

Patients and method:

The study was undertaken adults with migraine, ages more than 18 years, who were examined consecutively for evaluation for recurrent headaches in the Neurological Clinic in Al- Diwania teaching hospital over a 2 years period from Jul.2005 to Jul.2007. Migraine was diagnosed using proposed migraine revisions to the International Headache Society criteria.

Control subjects consisted of adult patients other than recurrent headache attending the same neurological clinic within the same period, matched as a group for age and sex.

The prevalence of recurrent epistaxis in patients and control subjects was evaluated by means of a detailed questionnaire concerning the presence or absence of recurrent headaches and nosebleeds, the frequency of headaches, age of onset, associated symptoms, hypertension, use of nonsteroidal anti-inflammatory drugs or aspirin, various characteristics of nosebleeds, and relevant family history. The word “migraine” did not appear in the questionnaire. All patients with migraine had complete general and neurological examinations, and appropriate diagnostic testing when necessary. No secondary causes for recurrent headaches were determined in these patients. The patients with recurrent epistaxis were subjected to medical and otolaryngological examination excluding hypertension, bleeding tendency and other causes of epistaxis, patients with identified cause of epistaxis were excluded from the study. Statistical differences for discrete variables between the two groups were evaluated with chi-square and logistic regression analysis. The association between migraine and recurrent epistaxis was
evaluated by odds ratio.

Results:
There were 186 patients with migraine with a mean age 26.3 years, 135 (72.58%) patients under 35 years old, and 52 (27.95%) were male. Control subject consisted of 200 patients of non-recurrent headache there mean age 27.1 years; 58 (27.5%) were males. There was no statistical difference between patients and control subjects with respect to sex and age.

The prevalence of recurrent epitaxis in patients with migraine patients was 22 (11.83%), were its 2 (1%) patients in control group (odds ratio = 13.28%).

- **Epistaxis & migraine**
  - All epistaxis are anterior in both groups. 20 (90.9%) out of 22 migraine patients having history of recurrent epistaxis since childhood. The prevalence of recurrent epistaxis below the age of 40 years old are 18 (81.8%) and 2 (100%) in migraine and control respectively. 28 (15.5%) of migraine patients preceded by aura and 5 (17.85%) of them having recurrent epistaxis, 158 (84.94%) migraine without aura 17 (10.75%) having recurrent epistaxis. (Figure 3)
Out of 22 migraine patients the epistaxis was unilateral in 18 (81.82%), it’s recurred following throbbing headache in 17 (77.27%) and in the same side of headache in 15 (68.18%) of patients. The pain is relived repeatedly following epistaxis in 13 (76.47%) of them and does not change in the others. (Figure 4).

Discussion:
This study reveals that the prevalence of recurrent epistaxis is significantly higher in adults with migraine than in control subjects, pointing to the epistaxis as a precursor of migraine (nausea, vomiting, photophobia and phonophobia in adults\(^{(37-41)}\) and cyclic vomiting, abdominal migraine, and benign paroxysmal vertigo as childhood periodic syndromes) which are listed as criteria by International Headache Society\(^{(4)}\).

The majority of recurrent epistaxis occurred in young adult patients since the prevalence of migraine and epistaxis are higher at this age.\(^{4} 35 42\) There is no significant prevalence of epistaxis with the type of migraine; possible explanation, aura is a neurological and not vascular phenomena.\(^{(15)}\)

The majority of recurrent epistaxis in young adults and originates in the anterior septum from the Kiesselbach plexus. Terminal branches from external and internal carotid arteries coalesce in this area to form an arterial border zone, which is part of the trigeminovascular system. This system is implicated in the pathogenesis of migraine.\(^{10}\) Stimulation of the trigeminal nerve in the mucosa of the nose or Para nasal sinuses, or via a brainstem reflex, has been demonstrated to increase blood flow in the extra cerebral, but not intracerebral circulation.\(^{(43)}\) Another study demonstrated increases in cerebral blood flow with noxious stimulation of nasal trigeminovascular nociceptors.\(^{(44)}\) We speculate
that epistaxis in the migraine patients, results from repeated partial activation of the trigeminovascular system leading to extreme nasal arteriolar dilatation and bleeding. Concurrent timing of epistaxis with the throbbing headache which is the phase of vasodilatation, 8 majority of epistaxis occurred at the same side of headache and the observations by Tunis and Wolff of extra cranial vessels become distended and pulsatile during a migraine attach lend support to such a hypothesis. Epistaxis, possibly facilitated by altered nasal mucosa as a result of recurrent vasoconstriction and sterile inflammatory reaction during migraine attach and Altered hemostasis in migraine.

The migraine headache relived repeatedly following epistaxis in some patients, a result, which can be explained by the response of local vasoconstriction following any bleeding. It is the mechanism of action in some pain abortive medications for migraine.

In summary, this study demonstrates a significant association between migraine and recurrent epistaxis in adults, and raises the question of whether recurrent epistaxis is a precursor to migraine. Advancing our understanding of the comorbidity of migraine and epistaxis and may provide clues to the pathophysiology of migraine and epistaxis. Moreover, it may have diagnostic and therapeutic implications.

References:
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