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Tension-Type Headache and Women: Do Sex Hormones Influence Tension-Type Headache?

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Abstract Most of the world's population has suffered from a tension-type headache (TTH) at some point in their lives. The pathophysiology of this disease is not well understood, but TTH shares many features with migraine, leading to the belief that TTH and migraine may be on different ends of the same disease spectrum. There are many shared triggers between migraine and TTH, menstruation being one of them. Does menses being a trigger for TTH make TTH more like migraine, or does the role of sex hormones in TTH give us insight into the unique pathophysiology of this disease? This article will review TTH, concentrating on the role of sex hormones as a trigger for TTH.

Keywords Tension-type headache · Episodic tension-type headache · Sex hormones

Introduction

Tension-type headache (TTH) is the most common headache subtype in the world. It is defined as a headache that is bilateral, pressing or tightening in quality, mild to moderate in severity, with possible light or sound sensitivity, but not both (Table 1) [1]. It is not aggravated by physical activity, nor associated with vomiting. TTH is experienced at some time in the lives of 30% to 80% of the population; the lifetime prevalence of TTH is 69% in men and 88% in women, with a male-to-female ratio of 4:5 [2, 3].

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The pathophysiology of most headache disorders still is unclear, and for TTH, is poorly understood. While it may share features with migraine, such as some similar triggers for headache and an occasional response to triptans, TTH has some unique properties of its own. The male-to-female ratio is much closer than in migraine headaches [4••]. Myofascial trigger points play some role in episodic TTH, implying a peripheral mechanism being involved in the pathophysiology of TTH, whereas in migraine, central mechanisms are primarily involved. There may be a link between TTH and migraine in the form of female sex hormones. For some women, menses is a trigger for TTH, and both pregnancy and menopause may affect their TTH. If hormonal fluctuations actually can trigger TTH, this may imply central mechanisms involved in the pathophysiology of the disease.

The purpose of this article is to discuss how episodic TTH affects women, particularly how TTH can be influenced by changes in sex hormones, and to discuss if the relationship between TTH and sex hormones gives us insight on the pathophysiology of episodic TTH.

Prevalence

TTH is considered a "normal" headache by most people, frequently relieved by over-the-counter medication. The headache can vary in both frequency and duration, from short episodes of mild pain, to frequent, long-lasting, or continuous severe pain. Often, patients do not report TTH to physicians. Though 59% of patients with TTH feel that the headaches interfere with their activity, only 16% of patients consult their physicians for the headache [5, 6]. Studies have shown that 5% of the employed population from ages 25 to 64 years is absent 4 days per year due to

Table 1 International Headache Society criteria

Diagnosis	Criteria
Episodic tension-type headache (frequent)	A. At least 10 episodes occurring on 1 but <15 days per month for at least 3 months (≥ 12 and <180 days per year) and fulfilling criteria B–D;
	B. Headache lasting from 30 min to 7 days;
	C. Headache has at least two of the following characteristics:
	1. Bilateral location
	2. Pressing/tightening (nonpulsating) quality
	3. Mild or moderate intensity
	4. Not aggravated by routine physical activity such as walking or climbing stairs
	D. Both of the following:
	1. No nausea or vomiting (anorexia may occur)
	2. No more than one of photophobia or phonophobia
	E. Not attributed to another disorder
Migraine without aura	A. At least 5 attacks fulfilling criteria B–D
	B. Headache attacks lasting 4–72 h (untreated or unsuccessfully treated)
	C. Headache has at least two of the following characteristics:
	1. Unilateral location
	2. Pulsating quality
	3. Moderate or severe pain intensity
	4. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
	D. During headache at least one of the following:
	1. Nausea and/or vomiting
	2. Photophobia and phonophobia
	E. Not attributed to another disorder
Menstrual migraine	Attacks, in a menstruating woman, fulfilling criteria for migraine without aura.
	Attacks occur exclusively on day 1±2 (ie, days –2 to +3) of menstruation in at least two out of three menstrual cycles and at no other times of the cycle
Menstrually related migraine	Attacks, in a menstruating woman, fulfilling criteria for migraine without aura
	Attacks occur on day 1±2 of menstruation in at least two out of three menstrual cycles and additionally at other times of the cycle

(*Data from* The Headache Classification Subcommittee of the International Headache Society. [1])

headache, and 2% are absent for 20 days per year due to headache [3].

The prevalence rates of TTH vary, with studies showing lifetime prevalence rates of anywhere from 34.8% to 75% of the population [3, 7]. This range could represent the infrequent reporting of symptoms by patients to their physicians. It also may represent the rare episodes many patients have, causing a lack of recall about their infrequent headaches.

The annual incidence for TTH is 14.2 per 1,000 person-years for frequent TTH, with a male-to-female ratio of 5:4 [8••]. Unlike migraine, TTH is only slightly more prevalent in women compared to men. Disability related to TTH is greater than that of migraine, likely related to the higher prevalence of the disease [8••]. Prognosis of TTH has not been analyzed to a great extent. One 12-year longitudinal study from Denmark found that in patients with frequent episodic TTH and chronic TTH, 45% experienced remission, 39% had unchanged frequent episodic TTH, and 16% had unchanged or newly developed chronic TTH at follow-up. Outcome was worse in those with baseline chronic TTH, coexisting migraine, and sleep difficulties and in unmarried individuals [9].

Pathophysiology

TTH originally was thought to be related to stress and tension. The pathophysiology was considered to be related to muscle contraction and ischemia of the head and neck muscles that could be activated by stress/tension [8••]. This theory later was refuted when electromyogram studies failed to show consistent changes in muscle tone in patients with TTH, and muscle lactate levels were found to be normal in patients with TTH performing static exercises [10, 11]. Myofascial factors likely play a role in the pathophysiology of TTH. In patients with TTH, pericranial myofascial tissues are tender compared to healthy patients, and the increased tenderness is

correlated with the intensity and frequency of headache [8••]. This implies a peripheral mechanism in the pathophysiology of TTH, with peripheral sensitization of myofascial nociceptors. Recurrent episodes of TTH may lead to central sensitization and excitation of second-order neurons at the level of the spinal dorsal horn and trigeminal nucleus, or impaired descending inhibition of supraspinal neurons, also leading to increase sensitization [12]. This may be triggered by prolonged activation of primary sensory afferents in tender myofascial tissue [12]. Increased central sensitization may decrease antinociceptive activity from supraspinal structures, lowering the threshold for further TTH episodes [8••]. Over time, this can lead to chronic TTH [2].

There seems to be a link between TTH and migraine, though where this link exists is unclear. Many patients with migraine, when asked about their headache history, will describe their first headaches as moderate in severity with no associated features (tension-type in nature). In time, with age or change in life situations, most describe an evolution of their headaches to being more severe in pain, with an onset of associated symptoms. Still, out of the number of patients who ever have had a TTH, only a small portion develops migraine headaches. For these patients, it still is unclear why their TTHs transformed to migraines; is it because their TTHs were a milder form of migraine, or is having TTH a risk factor for developing migraines? It could be that with an increase in frequency of TTH, central mechanisms begin to play a role in the pathophysiology of headache, leading to more migrainous-type symptoms.

Sex Hormones and Tension-Type Headache

The role of sex hormones in TTH may be the link between TTH and migraine. In women, sex hormones are influenced by the menstrual cycle. The menstrual cycle is a normal series of physiologic changes that occur in fertile women. There are four phases of the menstrual cycle: menses, follicular phase, ovulation, and luteal phase, in that order [13]. The average length of the cycle is 28 days. The menstrual cycle is under the control of various sex hormones, such as follicular-stimulating hormone (FSH) and luteinizing hormone (LH), produced in the pituitary gland, and estrogen and progesterone, produced by the ovaries. The interplay of these hormones is what moves the menstrual cycle from one phase to the next (Fig. 1). During menses, all hormone production is low. FSH is stimulated at the end of menses. The rise of FSH stimulates ovarian follicles during the follicular phase. As they mature, follicles stimulate estradiol, a form of estrogen. Estradiol suppresses the production of LH at the end of the follicular phase. When the follicle is near maturity, estradiol levels reach a certain threshold and begin to stimulate LH

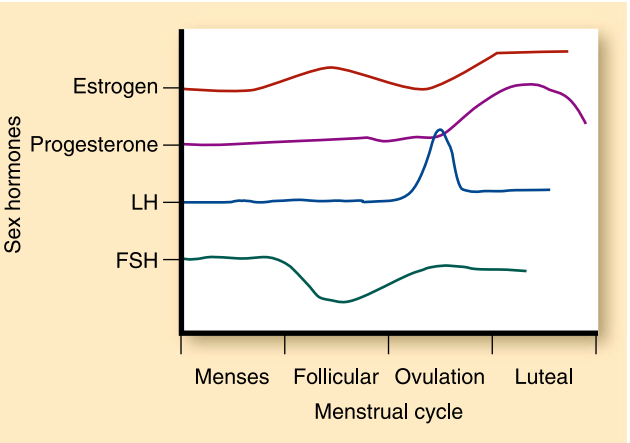

Fig. 1 Graphic representation of the fluctuations of different hormones during the phases of the menstrual cycle. Of note, LH, FSH, progesterone, and estrogen levels all are very low during menopause. FSH—follicle-stimulating hormone; LH—luteinizing hormone

production. LH production surges before ovulation, triggering a rise in progesterone. Once progesterone levels increase, this causes a small rise in estrogen. The combined increase in estrogen and progesterone reduces the production of FSH and LH during the luteal phase. If the egg is not fertilized, progesterone levels and then estrogen levels fall, signaling the start of the next menstrual cycle [13].

The fall in estrogen levels before menstruation is thought to trigger migraine in 60% of women who have migraines [14]. Headaches in relation to menses are experienced by 14% of women with migraine. Menses is a trigger for headache for 38% to 45% of women with TTH, implying some link between TTH and sex hormones [7, 14, 15].

If an egg is fertilized after ovulation, the embryo produces human chorionic gonadotropin. Similar to LH, this keeps progesterone levels elevated, therefore keeping estrogen levels stable. Postpartum estrogen and progesterone levels begin to drop and reach prepregnancy levels by 5 days after birth [13]. During pregnancy, when estrogen levels are elevated, headaches have a tendency to diminish [15]. This is seen in both migraine and nonmigraine headache, though some studies suggest this finding is more prominent with migraine headaches compared to TTH [15, 16•].

As women age, the ovarian production of estrogen and progesterone reduces, causing infrequent menstrual cycles. When menstruation ceases for 1 year, women are considered to be in menopause and estrogen and progesterone levels are very low. The transition time between normal menstrual cycles and menopause is called perimenopause. During this time, estrogen and progesterone levels fluctuate significantly, sometimes worsening headache. Like migraine, TTH more commonly develops in the second decade of life and can peak again between the ages of 50 and 59 years [7, 17]. This correlates to menarche and menopause in women, two time periods where sex hormones fluctuate [18].

Migraine and TTH are known to share a number of triggers: stress, altered dietary schedule, fatigue, and lack of sleep being the most common (Table 2) [15]. Migraine is known to have some unique triggers of its own, such as weather changes and certain foods [7]. Menses traditionally has been considered a trigger for migraine, with menstrual migraine and menstrually related migraine appearing in the International Headache Society classification system [1]. Though literature review shows the presence of non-migraine or TTH being triggered by menses, there only has been one study that has formally evaluated the existence of pure menstrual TTH [19•]. In the population studied, 12.7% of women had menstrual TTH or menstrually related TTH (findings were statistically significant). About 3% of this group also had migraines, or were using oral contraceptives. Larger population studies need to be done to further evaluate patients who only have TTH to see what portion of these patients have headache triggered by menses.

The theories on the pathophysiology of TTH do not lend themselves to having hormonal fluctuations as a trigger. During menses, fluctuations in estrogen cause prostaglandin levels to rise, which can decrease pain threshold by affecting descending norepinephrine pain control systems in the brain [17]. In addition to this, falls in estrogen levels produce dopamine receptor hypersensitivity, which lead to elevated prolactin levels that in turn cause opioid dysregulation to occur. Hormone fluctuation causing alteration in central pain pathways triggering migraine is understandable, because the pathophysiology of migraine is thought to be a central process. However, if TTH is primarily a peripheral phenomenon, why would fluctuations in estrogen cause headache? Does hormonal flux triggering TTH give evidence for TTH and migraine sharing common pathophysiological features? It is possible that the pathophysiology of episodic TTH may involve a connection between the central and peripheral nervous system, with triggers activating the trigeminal nucleus, which then somehow causes peripheral sensitization of myofascial nociceptors. It may be that the central process in TTH only is activated once a certain threshold is reached; TTH may begin to look more like migraine beyond this threshold, responding to changes in sex hormones for a small population. This may be where the link between episodic TTH and migraine exists.

Currently, the diagnostic criteria for hormone-related headaches only exist for migraines (Table 1). Even these are listed separately, in the appendix section of the second edition of the International Classification of Headache Disorders (ICHD-II) [1]. Menstrual migraine is defined as a migraine without aura that occurs on day +1/–2 of menstruation in at least two out of three menstrual cycles. Menstrually related migraine is defined as a migraine without aura that occurs on day +1/–2 of menstruation in at least two out of three menstrual cycles, in addition to other times in the cycle. Some consider that hormonal changes are a trigger for headache, but menstrual migraine or menstrual TTH do not warrant their own classifications as separate disorders. This may be true for a large portion of women who have headache both related and not related to menses, but there is a smaller subgroup of women who experience headache only related to menses. More studies need to be done in this subgroup to identify how common migraine features are compared to TTH features during menstrual-related headaches, and if patients actually fluctuate between migraine and TTH during different cycles. This may help show the clinical link between migraine and TTH. During the current revision of the ICHD- II, a revision to the appendix to include "hormonal-related headaches" that can include both menstrual migraine and menstrual nonmigraine, as well as headache related to perimenopause, should be considered.

Conclusions

TTH is the most common form of headache, experienced by most people at some point in life. TTH, especially in its

Table 2 Features of tension-type headache versus migraine

Headache subtype	Average age of onset, *y*	Prevalence, *m:f*	Triggers	Hormonal link and headache frequency
TTH	11–20	3:4	Stress, starvation, fatigue, lack of sleep	Menses: increase; pregnancy: decrease; menopause: likely decrease, no clear evidence
Migraine	20–30	1:2	Same triggers as TTH and, in addition, change in weather, change in temperature, food, smells, light, smoke	Menses: increase; pregnancy: decrease; menopause: decrease

m:f male-to-female ratio, *TTH* tension-type headache

chronic form, is more disabling than migraine, and can have a poor long-term prognosis. In women, TTH can be triggered by menses, may improve during pregnancy, and possibly can improve after menopause. It is unclear if fluctuations in sex hormones imply a central process in the pathophysiology of episodic TTH, or if TTH being triggered by changes in estrogen imply that TTH is on the same spectrum as migraine. Studies focusing specifically on the role of menses, pregnancy, and menopause and episodic TTH would be helpful in clarifying how large a role sex hormone fluctuations play in the frequency of TTH.

Disclosures No potential conflicts of interest related to this article were reported.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Headache Classification Subcommittee of the International Headache Society: The International Classification of Headache Disorders: 2nd edition. Cephalalgia 2004, 24(Suppl 1):9–160.
2. Solomon GD: Chronic tension-type headache: advice for the viselike-headache patient. Cleve Clin J Med 2002, 69:167–172.
3. Rasmussen BK, Jensen R, Schroll M, Olesen J: Epidemiology of headache in a general population: a prevalence study. J Clin Epidemiol 1991, 44:1147–1157.
4. •• Stovner LJ, Hagen K, Jensen R, et al.: The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia 2007, 27:193–210. *This article is a good overview of headache burden*.
5. Rasmussen BK, Jensen R, Olesen J: Epidemiology of tension-type headache in a general population. In Tension-type Headache: Classification, Mechanisms, and Treatment. Edited by Olesen J, Schoenen J. New York: Raven Press; 1993:9–13.
6. Lyngberg AC, Rasmussen BK, Jørgensen T, Jensen R: Has the prevalence of migraine and tension-type headache changed over a 12 year period? A Danish population survey. Eur J Epidemiol 2005, 20:243–249.
7. Zivadinov R, Willheim K, Sepic-Grahovac D, et al.: Migraine and tension-type headache in Croatia: a population-based survey of precipitating factors. Cephalalgia 2003, 23:336–343.
8. •• Bendtsen L, Jensen R: Tension-type headaches. Neurol Clin 2009, 27:525–535. *This article is an outstanding overview of tension-type headache*.
9. Andlin-Sobocki P, Jönsson B, Wittchen HU, Olesen J: Cost of disorders of the brain in Europe. Eur J Neurol 2005, 12:1–27.
10. Jensen R: Pathophysiological mechanisms of tension-type headache: a review of epidemiological and experimental studies. Cephalalgia 1999, 19:602–621.
11. Ashina M, Stallknecht B, Bendtsen L, et al.: In vivo evidence of altered skeletal muscle blood flow in chronic tension-type headache. Brain 2002, 125:320–326.
12. Mørk H, Ashina M, Bendtsen L, et al.: Possible mechanisms of pain perception in patients with episodic tension-type headache. A new experimental model of myofascial pain. Cephalalgia 2004, 24:466–475.
13. Silberstein SD: Endocrinology of the female life cycle. In Sex Hormones and Headaches. Edited by Silberstein SD. Philadelphia: Current Medicine Group; 2008:45–59.
14. Silberstein SD: The role of sex hormones in headache. Neurology 1992, 42(3 Suppl 2):37–42.
15. Spierings EL, Ranke AH, Honkoop PC: Precipitating and aggrevating factors of migraine versus tension-type headache. Headache 2001, 41:554–558.
16. • Aegidius K, Zwart JA, Hagen K, Stovner L: The effect of pregnancy and parity on headache prevalence: the Head-HUNT study. Headache 2009, 49:851–859. *This is one of the few articles examining the effect of pregnancy on headache*.
17. Silberstein SD: Sex hormones and headache. Rev Neurol (Paris) 2000, 156(Suppl 4):4 S30–4 S41.
18. Marcus DA: Sex hormones and chronic headache in women. Expert Opin Pharmacother 2001, 2:1839–1848.
19. • Arjona A, Rubi-Callejoin J, Guardado-Santervas P, et al.: Menstrual tension-type headache: evidence for its existence. Headache 2007, 47:100–103. *This is one of the few articles discussing menstrual cycle and tension headaches*.