P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-72 Olesen- 2057G GRBT050-Olesen-v6.cls August 5, 2005 20:27

Chapter 72

Hemodynamics and Muscle Metabolism of Tension-Type Headaches

Messoud Ashina and Michael Langemark

In spite of considerable progress in tension-type headache research in recent years (2), the origin of pain in this prevalent primary headache is unknown. Findings of increased myofascial tenderness (6,10,12,15) and muscle hardness (3,20) in patients with chronic tension-type headache suggest that tender pericranial muscles might be the sites of primary hyperalgesia. It has been hypothesized that disturbances in local muscle ischemia and metabolism in the tender areas may explain myofascial pain in tension-type headache and in other myofascial pain disorders such as trapezius myalgia (8). Various in vitro and in vivo methods, such as muscle biopsy, single-fiber laser Doppler, and magnetic resonance spectroscopy, have been used to explore the mechanisms responsible for myofascial pain. The results of these studies have been conflicting. Whereas open studies suggested abnormalities in microcirculation (13,14), controlled and blinded studies have failed to find firm evidence of peripheral abnormalities (21) in patients with chronic myofascial pain (25). In addition to myofascial factors in tension-type headache, it has also been suggested that nociceptive input from the cranial vasculature may contribute to a primary myofascial nociception in patients through mechanism of convergence of painful input from different compartments (16). In this chapter, we focus on various methods used to explore muscle blood flow and metabolism, as well as hemodynamics of cephalic nonmuscular compartments in patients with tension-type headache.

MUSCLE BLOOD FLOW AND METABOLISM

In an early study, blood flow in the splenius capitis muscle was measured by the sodium-24 clearance method in patients with muscle contraction headache (17). Mean muscle blood flow of patients during headache was found to be 33% higher than the mean blood flow in patients outside of headache. However, there were several methodologic shortcomings in this study, such as the tracer used not being freely diffusible, which introduces an important source of error. Furthermore, the electromyography level was not controlled.

Langemark et al. (11) studied temporal muscle blood flow by injecting ^{133}Xe into the muscle and recording the washout curve (Fig. 72-1). The resting temporal muscle blood flow in patients with chronic tension-type headache was not significantly different from that of controls. Resting blood flows on the two sides were highly correlated, and no right–left differences could be demonstrated. During isometric work, blood flow increased approximately fivefold in both patients and controls (Fig. 72-2). A brief reactive hyperperfusion after isometric work was found in eight patients and one control subject. The cause and importance of the phenomenon remains unexplained. No trend toward correlation was found between the reported severity of headache and the main flow parameters (resting flow and relative flow increase during exercise). The authors could not demonstrate any difference in relative hypoperfusion or hyperperfusion on the headache and nonheadache side. No correlation was found between mechanical pressure pain thresholds and muscle blood flow values in either rest or in response to isometric work.

Microdialysis is a unique technique for investigating and monitoring local muscle blood flow and metabolism in vivo within a tissue volume of less than 1 cm^3 (9). Using the microdialysis technique, Ashina et al. (4) estimated blood flow and interstitial lactate concentrations in the trapezius muscle at rest and in response to static exercise in patients with chronic tension-type headache. The major finding of that study was a decreased blood flow in response to static exercise in a tender point in patients. The increase in muscle blood flow from baseline to exercise

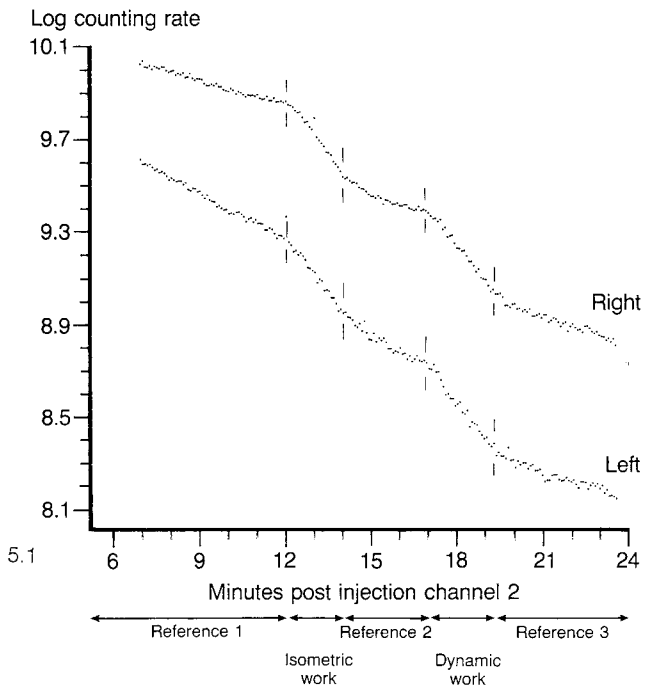

FIGURE 72-1. Logarithmically displayed xenon-133 clearance curves from right and left temporal muscles in a patient with chronic tension-type headache. Note the immediately increased steepness of the curves during isometric and dynamic work, which occurs in parallel on the two sides. (From Langemark M, Jensen K, Olesen J. Temporal muscle blood flow in chronic tension-type headache. *Arch Neurol.* 1990;47:654–658, with permission.)

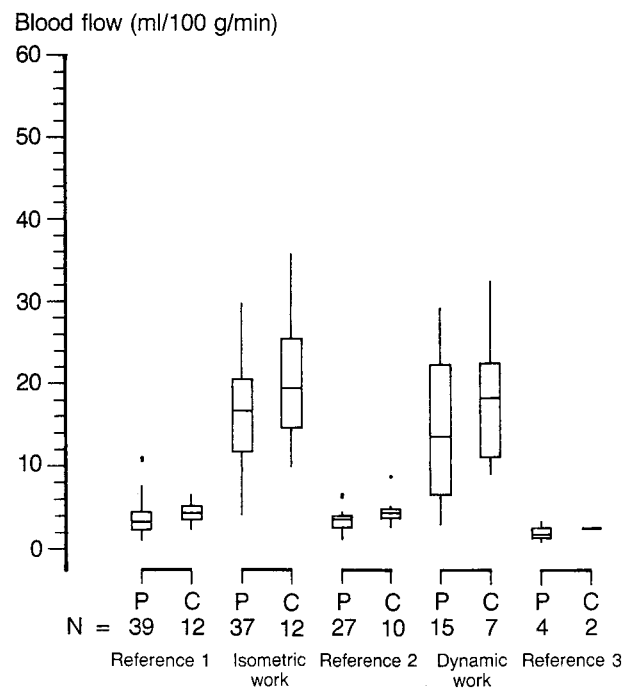

FIGURE 72-2. Temporal muscle blood flow in patients with chronic tension-type headache (*P*) and headache-free subjects (*C*). Note the lack of difference during rest as well as during isometric and dynamic work. (From Langemark M, Jensen K, Olesen J. Temporal muscle blood flow in chronic tension-type headache. *Arch Neurol.* 1990;47:654–658, with permission.)

and postexercise periods was lower in patients than controls (Fig. 72-3). There was no difference in resting blood flow between patients and controls. It could be suggested that patients develop a relative ischemia in the tender point during static exercise. If so, one would expect that the increase of interstitial lactate concentration would be higher in patients than controls. However, the authors observed no difference in local increase of interstitial lactate between patients and controls (Fig. 72-4). This seems to rule out the presence of ischemia in the tender point of patients with chronic tension-type headache during rest and static exercise.

To elucidate the possible role of inflammation or altered metabolism, Ashina et al. (5) investigated in vivo concentrations of various inflammatory mediators and other metabolites in tender muscle in response to static exercise in patients with chronic tension-type headache. The authors found no signs of ongoing inflammation in a tender trapezius muscle of patients in either resting muscle or in response to static exercise. Interstitial concentrations of prostaglandin E_2, adenosine 5′-triphosphate, glutamate, bradykinin, potassium, glucose, pyruvate, and urea did not differ between patients and controls (5).

The studies by Langemark et al. (11) and Ashina et al. (4,5) suggest normal muscle blood flow at rest in patients with chronic tension-type headache. The findings of diminished blood flow in the tender muscle during static work (4) is probably not associated with inflammation

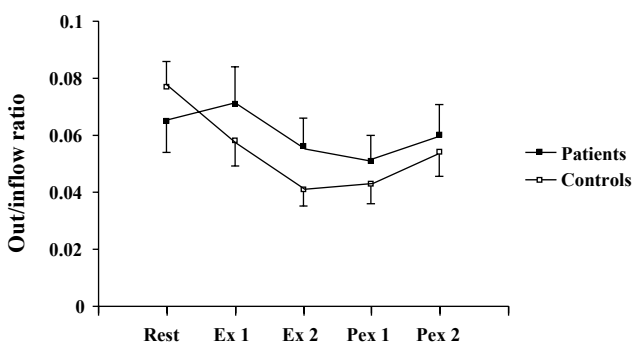

FIGURE 72-3. Mean nutritive muscle blood flow in 16 patients with chronic tension-type headache and in 17 healthy control subjects. The figure shows that the increase in muscle blood flow from baseline (*Rest*) to exercise (*Ex 1* and *Ex 2*) and postexercise periods (*Pex 1* and *Pex 2*) was significantly lower in patients than in controls ($P = 0.03$). The plots represent mean ± standard error of mean scores. (Reproduced from Ashina et al. [4], by permission of Oxford University Press.)

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-72 Olesen- 2057G GRBT050-Olesen-v6.cls August 5, 2005 20:27

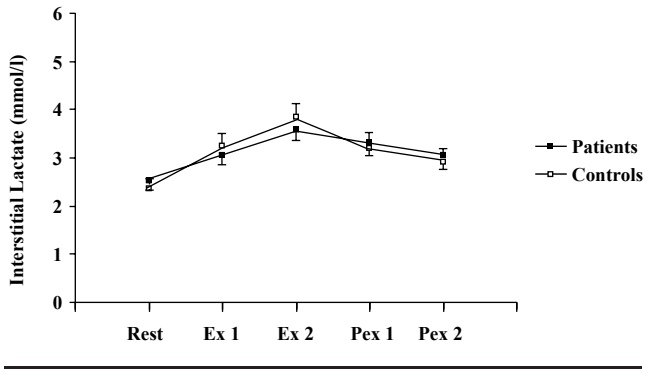

FIGURE 72-4. Mean interstitial concentration of lactate in 16 patients with chronic tension-type headache and in 17 healthy control subjects. There was no difference in change in interstitial concentration of lactate from baseline (*Rest*) to exercise (*Ex 1* and *Ex 2*) and postexercise (*Pex 1* and *Pex 2*) periods between patients and controls ($P = 0.38$). (Reproduced from Ashina et al. [4], by permission of Oxford University Press.)

or altered muscle metabolism (5). The lack of difference in local increase of interstitial lactate between patients and controls seems to rule out the presence of ischemia in the tender point of patients with chronic tension-type headache during static exercise. It is possible that because of increased excitability of neurons in the central nervous system, the central interpretation and response to normal sensory input are altered in patients with chronic tension-type headache. This may lead to enhanced sympathetically mediated vasoconstriction and thereby a decreased blood flow in response to static exercise (2).

CEREBRAL HEMODYNAMICS AND NONMUSCULAR EXTRACEREBRAL BLOOD FLOW

In several studies, patients with tension-type headache have been used as controls for comparison with patients suffering from migraine and other neurologic diseases. Only one study has focused specifically on regional cerebral blood flow (rCBF) in patients with tension-type headache (1). In this short communication, Andersen et al. (1) reported normal rCBF in patients with chronic tension-type headache.

In a pilot study, ultrasonically determined blood flow velocities were reported to be increased in episodic tension-type headache (23), but in a subsequent study of chronic tension-type headache, no disturbance was found (24).

Vasoconstriction of conjunctival vessels in tension-type headache has been reported in uncontrolled studies (18,19), but these observations have never been reproduced in a controlled study. The thermographic pattern of patients with muscle contraction headache in uncontrolled studies is similar to that of controls (7,22).

CONCLUSIONS

Despite many efforts, firm evidence for peripheral muscle pathology as a cause of chronic headache is still lacking. It is not clear which tender muscles are most relevant for study. Furthermore, the pericranial muscles are relatively small and not readily accessible for invasive procedures. The available data suggest that any muscle pathology will be much more subtle than that of other diseases which cause painful muscles, for example, polymyalgia. Studies of tissue blood flow are hampered by the fact that pain itself is accompanied by secondary stress phenomena, such as increased heart rate and blood pressure as well as redistribution of blood flow to vital organs. Available data show no signs of altered cerebral hemodynamics or nonmuscular extracerebral blood flow, and there is little theoretical basis to support further pursuit of nonmuscular hemodynamic studies with present-day techniques. More sensitive techniques are needed to answer the question of whether tension-type headache and other myofascial pain disorders are associated with peripheral pathology in tender muscles.

REFERENCES

1. Andersen AR, Langemark M, Olesen J. Regional cerebral blood flow in chronic tension-type headache. In: Olesen J, ed. *Migraine and other headaches: the vascular mechanisms*. New York: Raven; 1991:319–321.
2. Ashina M. Neurobiology of chronic tension-type headache. *Cephalalgia*. 2004;24:161–172.
3. Ashina M, Bendtsen L, Jensen R, et al. Muscle hardness in patients with chronic tension-type headache: relation to actual headache state. *Pain*. 1999;79:201–205.
4. 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.
5. Ashina M, Stallknecht B, Bendtsen L, et al. Tender points are not sites of ongoing inflammation—in vivo evidence in patients with chronic tension-type headache. *Cephalalgia*. 2003;23:109–116.
6. Bendtsen L, Jensen R, Jensen NK, et al. Pressure-controlled palpation: a new technique which increases the reliability of manual palpation. *Cephalalgia*. 1995;15:205–210.
7. Drummond PD, Lance JW. Facial temperature in migraine, tension-vascular and tension headache. *Cephalalgia*. 1984;4:149–158.
8. Henriksson KG, Lindman R. Morphologic, physiologic, and biochemical changes in tender and painful muscle. In: Olesen J, Schoenen J, eds. *Tension-type headache: classification, mechanisms and treatment*, vol. 3. New York: Raven; 1993:97–107.
9. Hickner RC, Bone D, Ungerstedt U, et al. Muscle blood flow during intermittent exercise: comparison of the microdialysis ethanol technique and 133Xe clearance. *Clin Sci (Colch)*. 1994;86:15–25.
10. Jensen R, Bendtsen L, Olesen J. Muscular factors are of importance in tension-type headache. *Headache*. 1998;38:10–17.
11. Langemark M, Jensen K, Olesen J. Temporal muscle blood flow in chronic tension-type headache. *Arch Neurol*. 1990;47:654–658.
12. Langemark M, Olesen J. Pericranial tenderness in tension headache. A blind, controlled study. *Cephalalgia*. 1987;7:249–255.
13. Larsson SE, Bodegard L, Henriksson KG, et al. Chronic trapezius myalgia. Morphology and blood flow studied in 17 patients. *Acta Orthop Scand*. 1990;61:394–398.
14. Larsson R, Oberg PA, Larsson SE. Changes of trapezius muscle blood flow and electromyography in chronic neck pain due to trapezius myalgia. *Pain*. 1999;79:45–50.

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-72 Olesen- 2057G GRBT050-Olesen-v6.cls August 5, 2005 20:27

15. Lipchick GL, Holroyd KA, Talbot F, et al. Pericranial muscle tenderness and exteroceptive suppression of temporalis muscle activity: a blind study of chronic tension-type headache. *Headache*. 1997;37:368–376.
16. Olesen J. Clinical and pathophysiological observations in migraine and tension-type headache explained by integration of vascular, supraspinal and myofascial inputs. *Pain*. 1991;46:125–132.
17. Onel Y, Friedman AP, Grossman J. Muscle blood flow studies in muscle-contraction headache. *Neurology*. 1961;11:935–939.
18. Ostfeld AM, Reis DJ, Wolff HG. Studies in headache; bulbar conjunctival ischemia and muscle contraction headache. *AMA Arch Neurol Psychiatry*. 1957;77:113–119.
19. Ostfeld AM, Wolff HG. Studies on headache: observations on the behavior of the conjunctival vessels in vascular headache. *Trans Am Neurol Assoc*. 1955;216–217.
20. Sakai F, Ebihara S, Akiyama M, et al. Pericranial muscle hardness in tension-type headache. A non-invasive measurement method and its clinical application. *Brain*. 1995;118:523–531.
21. Simms RW. Fibromyalgia is not a muscle disorder. *Am J Med Sci*. 1998;315:346–350.
22. Swerdlow B, Dieter JN. The validity of the vascular "cold patch" in the diagnosis of chronic headache. *Headache*. 1986;26:22–26.
23. Wallasch TM. Transcranial Doppler ultrasonic features in episodic tension-type headache. *Cephalalgia*. 1992;12:293–296.
24. Wallasch TM. Transcranial Doppler ultrasonic features in chronic tension-type headache. *Cephalalgia*. 1992;12:385–386.
25. Yunus MB, Kalyan-Raman UP, Masi AT, et al. Electron microscopic studies of muscle biopsy in primary fibromyalgia syndrome: a controlled and blinded study. *J Rheumatol*. 1989;16:97–101.