Calcitonin gene-related peptide (CGRP) has a well-established relationship with nociception. It is known that activation of the trigeminovascular system stimulates release of powerful vasoactive peptides (neurokinin A, substance P, CGRP). In animal experiments, these substances appear to stimulate vasodilation and dural plasma extravasation. In particular, CGRP is released from primary sensory afferents around vessels and the central terminals in the dorsal horn of the spinal cord. Therefore, the possible changes of CGRP concentration in the periphery and in the central nervous system may be reflected in the blood.

The interest in CGRP in primary headache has grown. The first studies were conducted in migraine patients and showed increased CGRP levels during the migraine attack compared with healthy subjects. Recently, it was shown that CGRP levels are also increased interictally in migraine patients compared with healthy subjects. In addition, CGRP levels have been shown to increase in patients with cluster headache during the headache attacks.

The theory of headache disorders as a continuum, with chronic tension-type headache (CTTH) and migraine distinguished by their numbers of attacks, has been debated. The relationship of CGRP in migraine is well established, so the aim of this study was to examine the plasma levels of CGRP in patients with CTTH. The CGRP plasma levels in the peripheral and cranial circulation were evaluated during periods with and without headache.

Thirty CTTH patients (based on International Headache Society [IHS] criteria) and 34 healthy subjects with no previous history of migraine or other type of primary headache were recruited from the outpatient headache clinic at Glostrup University Hospital in Denmark. All participants were examined (physically and neurologically), and blood was drawn from the antecubital vein for analysis. In the first 15 patients and the first 20 healthy subjects, blood samples were also drawn from the external jugular vein. The 15 patients were examined on 2 days: one day with a typical episode of tension-type headache (TTH) and one day without headache. Measurements of CGRP levels were done by radioimmunoassay and were performed blindly with respect to patients and subjects.

The results showed that CGRP levels in the peripheral circulation were the same in patients and subjects during periods without headache. Moreover, peripheral CGRP levels in patients during periods without headache did not differ from levels that were measured during periods with headache. Similar results were observed for cranial CGRP levels in patients, and no differences in either peripheral or cranial CGRP levels were observed between patients and subjects. These data are markedly different from the results seen in migraine patients and suggest that nociception in CTTH does not cause a release of CGRP.

**PROCEEDINGS**

CALCITONIN GENE-RELATED PEPTIDE (CGRP) IN CHRONIC TENSION-TYPE HEADACHE

Based on a presentation by Mesioud Ashina, MD, PhD; with Lars Bendtsen, MD, PhD; Rigmor Jensen, MD, PhD; Søren Schifter, MD, PhD; Inger Jansen-Olesen, PhD; and Jes Olesen, MD, PhD

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Because it had previously been shown that migraine patients have increased interictal CGRP levels, the possibility of a correlation between headache quality and CGRP levels was investigated. In 8 of the study patients, the usual headache quality was pulsating, as is often seen with migraine. However, they had no accompanying migraine symptoms such as nausea, photophobia, or phonophobia, so they fulfilled IHS criteria for TTH. Interestingly, these patients showed significantly increased interictal CGRP levels in peripheral and cranial plasma compared with healthy subjects.7

The authors suggest that CGRP levels are normal in patients with CTTH, do not vary during periods with or without headaches, and are similar in the cranial and peripheral circulation. Because of the increased interictal CGRP levels in patients with pulsating headache, the authors suggest that the headaches experienced by these patients may be pathophysiologically related to migraine. The interesting, unanswered question is why these patients, as well as migraine patients, have increased CGRP levels on days without headache.5 Future studies with larger numbers of patients with CTTH and migraine should also examine a relationship between plasma CGRP levels and headache quality.

REFERENCES