

# III

## Tension-type headache

## How is tension-type headache classified?

### Recommendation

Since 1962, various classifications for tension-type headache have been proposed. Currently, classification according to the International Classification of Headache Disorders 3rd Edition (beta version) (ICHD-3beta) published in 2013 is recommended.

Grade A

### Background and Objective

Diagnostic classification that forms the basis of guidelines is certainly important for formulating clinical care and treatment policies. The ICHD-3beta is not simply a document based on classification, it also addresses diagnosis and treatment scientifically and practically from all aspects.

### Comments and Evidence

The classification of tension-type headache (TTH) is provided by the International Classification of Headache Disorders 3rd edition beta version (ICHD-3beta).<sup>1,2)</sup>

The division of tension-type headache into episodic and chronic types adopted by the first edition of the International Classification of Headache Disorders (1988)<sup>3)</sup> is extremely useful. The International Classification of Headache Disorders 2nd edition (ICHD-II) further subdivides the episodic type according to frequency, and states that this is based on the difference in pathophysiology. The former *episodic tension-type headache* (ETTH) is further classified into 2.1 *infrequent episodic tension-type headache* (IETTH) with headache episodes less than once per month (<12 days/year), and 2.2 *frequent episodic tension-type headache* (FETTH) with higher frequency and longer duration (<15 days/month). The infrequent subtype has little impact on the individual, and to a certain extent, is understood to be within the range of physiological response to stress in daily life. However, frequent episodes may cause disability that sometimes requires expensive drugs and prophylactic medication. Headache classified as 2.3 *chronic tension-type headache* (CTTH) with 15 or more headache episodes per month ( $\geq 15$  days/month) significantly impacts quality of life (QOL) and causes severe disability in daily living, accompanied by high personal and socio-economic costs.

The classification of tension-type headache excerpted from the ICHD-3beta is shown below.

- 2. Tension-type headache
  - 2.1 Infrequent episodic tension-type headache
    - 2.1.1 Infrequent episodic tension-type headache associated with pericranial tenderness
    - 2.1.2 Infrequent episodic tension-type headache not associated with pericranial tenderness
  - 2.2 Frequent episodic tension-type headache
    - 2.2.1 Frequent episodic tension-type headache associated with pericranial tenderness
    - 2.2.2 Frequent episodic tension-type headache not associated with pericranial tenderness
  - 2.3 Chronic tension-type headache
    - 2.3.1 Chronic tension-type headache associated with pericranial tenderness
    - 2.3.2 Chronic tension-type headache not associated with pericranial tenderness
  - 2.4 Probable tension-type headache
    - 2.4.1 Probable infrequent episodic tension-type headache
    - 2.4.2 Probable frequent episodic tension-type headache
    - 2.4.3 Probable chronic tension-type headache

### References

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- 2) Headache Classification Committee of the International Headache Society (author), International Headache Classification Promotion Committee of Japanese Headache Society (translator): Japanese Edition of the International Classification of Headache Disorders 3rd edition (beta version). Igakushoin, 2014. (In Japanese)

- 3) Headache Classification Committee of the International Headache Society: Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. of headache. Headache Classification Committee of the International Headache Society. Cephalalgia 1988; 8(Suppl 7): 1-96.

- **Search terms and secondary sources**

- Search database: PubMed (2011/12/14)  
tension type headache 2458  
& classification 519  
& history 95  
(However, no useful references were identified)

## How is tension-type headache diagnosed?

### Recommendation

Tension-type headache is diagnosed according to the diagnostic criteria of the International Classification of Headache Disorders 3rd Edition (beta version) (ICHD-3beta).

Grade A

### Background and Objective

Diagnostic criteria should address diagnosis and treatment scientifically and practically from all aspects. As with other diseases, it is necessary to diagnose tension-type headache based on diagnostic criteria that fulfill the above requirements. Comments concerning the diagnosis of tension-type headache as well as the diagnostic criteria of the ICHD-3beta<sup>1)</sup> are given below.

### Comments and Evidence

The diagnostic criteria for tension-type headache are shown below.

Subtypes of tension-type headache are mainly diagnosed by their respective frequencies of headache (criterion A) as well as by fulfilling the following criteria (B to E).

B. Headache lasting from 30 minutes to 7 days

C. Headache has at least two of the following characteristics:

1. bilateral location
2. pressing or tightening (non-pulsating) quality
3. mild to 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

However, for chronic tension-type headache

1. no more than one of photophobia, phonophobia or mild nausea
2. neither moderate or severe nausea nor vomiting

E. Not better accounted for by another ICHD-3 diagnosis.

A.

2.1 For *infrequent episodic tension-type headache*, headache occurring on <1 day per month (<12 days per year)

2.2 For *frequent episodic tension-type headache*, headache occurring on 1 to 14 days per month (≥12 days and <180 days per year)

2.3 For *chronic episodic tension-type headache*, headache occurring on ≥15 days per month (≥180 days per year)

2.4 In *probable tension-type headache*, fulfilling one of the diagnostic criteria for tension-type headache, but not meeting criteria for migraine.

According to the opinions of general clinicians, migraine and tension-type headache often cannot be differentiated by severity and the presence or absence of nausea, vomiting, photophobia and phonophobia. Furthermore, the existence of transitional form or intermediate form of tension-type headache and migraine is also a problem.<sup>2)3)</sup> In addition, the diagnosis of chronic headache is associated with the issue of medication overuse, and hence differentiation is often difficult. These problems have not been completely solved (see CQ III-5, page 158).

On the other hand, it was criticized that the diagnostic criteria for tension-type headache in the first edition of the International Classification of Headache Disorders (1988)<sup>4)</sup> adopted many negative features, which might be picked up by other headache disorders. To address the shortcoming of the first edition, the International Classification of Headache Disorders 2nd Edition (ICHD-II)<sup>5)</sup> has incorporated items of “*probable chronic migraine*” and “*probable tension-type headache*”, which have almost solved the issues. The essential feature of the diagnostic criteria may be considered a reverse of the diagnosis of migraine. Furthermore, in ICHD-II,<sup>5)</sup> episodic tension-type headache is subdivided into an infrequent subtype with headache episodes less than once per month and a frequent subtype. The infrequent subtype has relatively little

impact on the individual and does not draw much attention from the medical profession. However, frequent occurring tension-type headache may be associated with disability that sometimes necessitates treatment with expensive drugs or prophylactic medications. Moreover, headache classified as the chronic subtype is a serious disease, having great impact on quality of life (QOL) and causing severe disability.

The ICDH-3beta<sup>1</sup>) is not simply a document based on classification, but involves careful scrutiny of almost all the available articles with high level of evidence. Its use for diagnosis is highly recommended.

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## • Search terms and secondary sources

- Search database: PubMed (2011/12/14)  
tension type headache 2458  
& classification 519  
& history 95  
(However, no useful references were identified)

## How big is the population of tension-type headache patients?

## What are the risk factors, triggers, and prognosis?

## What is the real prevalence of tension-type headache?

### Recommendation

Tension-type headache is the most common headache among the primary headaches, and the prevalence varies widely among surveys. To find the precise prevalence, it is necessary to establish suitable survey methods and correct the problems of diagnosis. The risk factors and triggers of tension-type headache have not been defined. The prognosis of episodic tension-type headache is good in majority of the cases, but there exist some cases of poor outcome with progression to chronic tension-type headache.

**Grade B**

### Background and Objective

Tension-type headache is the most common primary headache, but is also the least studied. Identifying the risk factors and triggers and knowing the prognosis are important in the treatment of tension-type headache.

### Comments and Evidence

Headache societies including the International Headache Society (IHS) in collaboration with the World Health Organization (WHO) started the initiative 'Lifting The Burden: The Global Campaign to Reduce the Burden of Headache Worldwide'. As a part of the initiative, Stovner et al.<sup>1)</sup> calculated the global prevalence of headache by reviewing the results of headache epidemiological surveys conducted worldwide. According to their study, the percentage of the global population with tension-type headache was 38%, and 46% when adult population was calculated. However, only 12 epidemiological studies on adults with tension-type headache were used in their estimation, and the number was extremely small compared to migraine. Moreover, the prevalence reported in different studies varied greatly: ranging from 21.7% to 86.5% in 1-year prevalence, and 12.9% to 78% in life-time prevalence. In Japan, the epidemiological study conducted by Takeshima et al.<sup>2)</sup> in Daisen reported 1-year prevalence of 21.7%. This figure was also used in the above-mentioned estimation of global prevalence. Following the report of Stovner et al., several epidemiological studies have been conducted, also showing great variation in prevalence. However, most of the studies do share two common findings: tension-type headache has the highest prevalence among the primary headaches, and the prevalence is higher in women than in men. Although some studies reported significant differences in prevalence depending on factors such as educational level and place of domicile (urban or rural), the results were not consistent among studies. Because the prevalence is high in Europe and low in Africa, a report emphasized the correlation between latitude and prevalence.<sup>3)</sup> The discrepancy in prevalence has been attributed to survey methodology (personal interview, telephone interview, questionnaire, others).<sup>1)</sup> To obtain the correct prevalence, apart from establishing appropriate survey methods, it is necessary to address the diagnostic issues such as dual diagnosis of chronic migraine and chronic tension-type headache as well as the differentiation between transformed migraine and chronic tension-type headache.<sup>4)</sup>

There are few studies on risk factors and triggers of tension-type headache, and these factors have not been established. Obesity, insufficient exercise and smoking have been reported to be independent risk factors.<sup>5)</sup> On the other hand, there is also report that while obesity is a risk factor for chronification of episodic migraine, it is not a risk factor for tension-type headache.<sup>6)</sup>

The prevalence of tension-type headache decreases with age, but the decrease is not as marked as for migraine. Although rare, first onset after age 50 has been reported, and the prevalence remains high even among the elderly.<sup>7)</sup> Although the prognosis is generally favorable for episodic tension-type headache, transition to chronic tension-type headache is found in some cases. Lyngberg et al.<sup>8)</sup> reported that factors associated with poor outcome for tension-type headache include chronic headache at baseline, coexisting migraine, being single, and sleeping problems.

## • References

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## • Search terms and secondary sources

- Search database: PubMed (2011/3/10)
  - tension type headache 2347
  - & prevalence 652
  - & risk factor 205
  - & prognosis 311

## What is the proposed pathophysiology for tension-type headache?

### Recommendation

The pathophysiology and the pathogenetic mechanism of tension-type headache remain unknown. Evidence is accumulating supporting the possibility that peripheral pain mechanism plays a role in infrequent episodic tension-type headache and frequent episodic tension-type headache, while central pain mechanism plays a more important role in chronic tension-type headache.

**Grade B**

### Background and Objective

Tension-type headache is the most common headache among the primary headaches. However, the precise pathogenetic mechanism is still unclear, and tension-type headache is also one of the least studied primary headaches regarding the pathophysiology.

In the past, tension-type headache was considered to be primarily psychogenic. After publication of the first edition of the International Classification of Headache Disorders (1988), many studies were published strongly suggesting a neurobiological basis, at least for the severe subtypes of tension-type headache. This section reviews the evidence for the pathophysiology of tension-type headache.

### Comments and Evidence

#### 1. Peripheral elements

A high prevalence of pericranial muscle tenderness in tension-type headache patients than in healthy persons has been proven. Moreover, the degree of tenderness is known to correlate with the frequency and intensity of tension-type headache.<sup>1)</sup> This tendency has been reported to be strong in women.<sup>2)</sup> On the other hand, muscle tenderness in pericranial and neck-shoulder regions has been reported to be normal in children with tension-type headache.<sup>3)</sup> However, evaluation of severity of tenderness varies among investigators, and objective assessment is difficult to achieve. For the evaluation of tenderness in tension-type headache, the usefulness of total tenderness score (TTS) and objective assessment using muscle hardness meter has been proven.<sup>4)-6)</sup> Electromyography also has been used to measure muscle tone in tension-type headache.<sup>4)</sup>

In a study that examined the effect of administration of botulinum toxin on chronic tension-type headache, although electromyographic improvement in the temporal muscle was observed, headache did not improve.<sup>7)</sup> Other studies also reported no difference in interstitial lactate concentration in the trapezius muscle at rest and during exercise in patients with chronic tension-type headache compared to healthy controls,<sup>8)</sup> and also no increase in inflammatory mediators at tender points of the trapezius muscle.<sup>9)</sup> These findings thus suggest that the pathophysiology of chronic tension-type headache is not associated with hyperactivity, inflammation or metabolic disturbance of pericranial muscles.<sup>10)</sup>

#### 2. Central elements

Because exercise-induced increase in trapezius muscle blood flow is blunted in patients with chronic tension-type headache, involvement of sympathetic vasoconstriction due to over-excitation of the central nervous system is possible.<sup>11)</sup> Moreover, increased pain perception was observed in both single and repetitive 2-Hz electrical stimulations, suggesting abnormality in pain control mechanism in the central nervous system.<sup>12)</sup>

Administration of nitroglycerin that generates nitric oxide in the body is known to induce typical tension-type headache after several hours,<sup>13)</sup> suggesting that central hypersensitivity to nitric oxide may also be involved in chronic tension-type headache, as in migraine.<sup>10)</sup> In addition, administration of L-N(G)-methylarginine hydrochloride that inhibits nitric oxide has been shown to reduce muscle tenderness and attenuate headache clinically.<sup>14)15)</sup> These findings may provide evidence supporting the hypothesis that sensitization of the trigeminal nerve may also be a central element involved in tension-type headache.<sup>13)</sup>

In normal persons, when the trigeminal nerve is stimulated as an afferent pathway, a muscle contraction inhibitory mechanism mediated by interneurons in the lateral pontine tegmentum connecting with the spinal trigeminal nucleus is known to exist. In some types of tension-type headache, this central muscle contraction inhibitory mechanism has been



reported to be deficient.<sup>15,16</sup> In chronic tension-type headache, the possibility of secondary involvement of nociceptors in the trigeminal system has been suggested.<sup>17</sup>

On the other hand, in episodic tension-type headache, peripheral sensitization of myofascial afferent sensory nerves has been suggested to be a cause of hypersensibility.<sup>18</sup>

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## • Search terms and secondary sources

- Search database: PubMed (2011/12/21)  
tension type headache & pathophysiology 745

## What is the relationship between transformed migraine and tension-type headache?

### Recommendation

When headache episodes are diagnosed individually, differentiation between transformed migraine and chronic tension-type headache is difficult. The two can be discriminated by a comprehensive approach to diagnosis considering the treatment, headache response and clinical course. *Chronic migraine* in the International Classification of Headache Disorders 3<sup>rd</sup> Edition (beta version) includes the concept of transformed migraine.

**Grade B**

### Background and Objective

Although transformed migraine is not described in the International Classification of Headache Disorders 2nd Edition (ICHD-II), it is an important headache disorder encountered in the routine clinical setting. While differentiation between transformed migraine and chronic tension-type headache may be difficult, discrimination of the two is important in the treatment of chronic headaches.

### Comments and Evidence

“Transformed migraine” as proposed by Mathew<sup>1)</sup> is not included in the International Classification of Headache Disorders 2nd Edition (ICHD-II), but this headache disorder is widely accepted in routine clinical practice. A large number of patients present with a pattern consisting of infrequent but severe migraine attacks at younger ages, evolving to more frequent but less severe headaches as age advances, with a gradual loss of migraine characteristics. Transformed migraine is generally diagnosed according to the Silberstein-Lipton diagnostic criteria.<sup>2,3)</sup> These diagnostic criteria include the item of “a history of migraine”, while the current headache diagnostic criteria only specify the frequency and duration of headache attacks. With the Silberstein-Lipton diagnostic criteria, if the headache fulfilled the criteria for migraine in the past, then transformed migraine can be diagnosed even though the present headache has lost all the elements of migraine. In other words, transformed migraine is not diagnosed as a point at one headache episode, but as a line including the past history of headache.

The ICHD-II<sup>4)</sup> basically diagnoses headache episodes individually, and diagnosis criteria including also the past history are not compatible with ICHD-II. This constitutes the difference in concept between *chronic migraine* in ICHD-II published in 2004 and *transformed migraine*.<sup>2)</sup> The 2004 diagnostic criteria for chronic migraine require that individual headache episodes fulfill the characteristics of migraine. Therefore, for patients who satisfy the Silberstein-Lipton criteria for transformed migraine, if their present headaches have lost all the features of migraine, they are most probably not diagnosed with chronic migraine but with chronic tension-type headache if there is no medication overuse. However, to address the criticism that very few patients fit into the 2004 diagnostic criteria for chronic migraine, the International Headache Society published revised diagnostic criteria for chronic migraine in 2006, to be included in the appendix of ICHD-II.<sup>5)</sup> According to these criteria, a headache can be diagnosed as chronic migraine if headaches fulfilling the diagnostic criteria for migraine occur on more than 8 days per month, even in the presence of other headaches. Furthermore, in the case that the present headache has no characteristics of migraine but progression to migraine attack is suggested, the criterion “treated and relieved by triptans or ergot before the expected development of migraine symptoms” was added to allow a diagnosis of chronic migraine. Using these criteria, a considerable number of cases of transformed migraine without medication overuse would be diagnosed as chronic migraine. However, if triptan or ergotamine is not effective, then the headache will not be classified as chronic migraine. Eventually, transformed migraine and chronic migraine are not the same entity. In the International Classification of Headache Disorders 3<sup>rd</sup> Edition (beta version) published in 2013,<sup>6)</sup> *chronic migraine* includes the concept of transformed migraine.

In conclusion, when headache episodes are diagnosed individually, differentiation between chronic tension-type headache and transformed migraine is difficult, but the two can be discriminated if past history is considered.<sup>7)</sup> The general treatment strategy for chronic tension-type headache that has evolved from episodic tension-type headache may differ from that for transformed migraine that has lost the migraine features and resembles chronic tension-type headache. When making a

diagnosis of chronic tension-type headache, the possibility of transformed migraine has to be borne in mind and a careful clinical interview including past history of headache has to be conducted.

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## • Search terms and secondary sources

- Search database: PubMed (2011/3/10)  
tension type headache 2347  
& transformed migraine 84

## How is tension-type headache treated?

### Recommendation

Various types of tension-type headache exist, and the types that cause disability in daily living should be treated. Among them, frequent episodic tension-type headache and chronic tension-type headache require treatment. Therapies can be divided into acute treatment and prophylactic treatment, each of which can be pharmacotherapy and non-pharmacotherapy. For acute treatment, attention has to be paid to medication-overuse headache. For prophylactic therapy, occurrence of adverse effects should be monitored.

**Grade A, C**

### Background and Objective

Tension-type headache is the most common headache among the primary headaches. Among the various types, frequent tension-type headache and chronic tension-type headache cause severe disability in daily living, and are conventionally treated with acute and prophylactic therapies. Comments on the evidence for the necessity and options of these treatments are given in this section.

### Comments and Evidence

The International Classification of Headache Disorders 3rd Edition (beta version) (ICHD-3beta)<sup>1)</sup> subdivides episodic tension-type headache into an infrequent subtype with headache episodes less than once per month and a frequent subtype. Tension-type headaches that occur infrequently and improve with over-the-counter (OTC) drugs usually do not require consultation of medical facility, except for the patient's own reassurance. On the other hand, when headache restricts daily life or when headache frequency and intensity increase, then treatment is required. Furthermore, patients who are taking OTC drugs more than necessary may develop medication-overuse headache or rebound headache, and these patients also require appropriate treatment<sup>2)3)</sup> (grade A recommendation).

In general, patients who need treatment are those who have frequent episodic tension-type headache or chronic tension-type headache. While central pain mechanisms (including stress, depressed mood, central pain processing abnormality, and central sensitization) play more important roles in chronic tension-type headache, peripheral pain mechanisms (including muscle strain, myofascial factor, and peripheral sensitization) are most likely involved in infrequent episodic tension-type headache. Treatments for central mechanisms such as tricyclic antidepressants, stress management, relaxation training, and acupuncture; and therapies for peripheral mechanisms such as relaxation training and physical therapy have been investigated<sup>4)</sup> (grade C recommendation).

Therapies for tension-type headache are divided into acute (abortive) treatment and prophylactic treatment. Each consists of pharmacotherapy and non-pharmacotherapy<sup>4)5)</sup> (grade A recommendation).

For acute treatment by pharmacotherapy, medication-overuse headache that results in treatment failure should always be borne in mind, and use for more than 2 to 3 days per week should be avoided<sup>1)3)</sup> (grade A recommendation).

Prophylactic therapy should be considered for patients with frequent episodic tension-type headache and patients who do not respond adequately to acute treatment. Especially, for patients who have headaches two or more times per month, prompt initiation of prophylactic therapy should be considered because headache may subsequently increase exponentially<sup>6)</sup> and the effectiveness of prophylactic therapy may be reduced by frequent use of acute medications.<sup>2)</sup> However, whether treatment can prevent or delay the progression of infrequent tension-type headache to chronic tension-type headache remains unclear.<sup>2)</sup> Furthermore, a review reported no prophylactic effect of antidepressants.<sup>7)</sup> For this reason and considering also adverse effects, if there is no response, a decision has to be made on whether to continue medication for three months (6 months the longest) or discontinue treatment<sup>4)5)</sup> (grade A recommendation).

On the other hand, stress and mental strain are risk factors of tension-type headache,<sup>8)9)</sup> while depressive and anxiety disorders are risk factors of progression to chronic headache.<sup>10)</sup> Moreover, compared to headache-free subjects, patients with migraine and chronic tension-type headache are 2 to 5 times more likely to have depressive and anxiety disorders as comorbidities.<sup>11)-14)</sup> These psychiatric disorders also require treatment (grade C recommendation).

Regarding treatment for oromandibular dysfunction, since headache-free subjects may also have oromandibular

dysfunction, this aspect has not been analyzed adequately. However, since oromandibular dysfunction is a risk factor of tension-type headache, treatment should be considered<sup>15-17)</sup> (grade C recommendation).

Other factors that may induce tension-type headache include inadequate exercise and prone posture, and basic treatment should be considered (grade C recommendation).

When encountering cases in which diagnosis of headache type is difficult or treatment effect is inadequate, referral to an expert is recommended.<sup>2)</sup>

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## • Search terms and secondary sources

- Search database: PubMed (2011/12/21)  
tension headache & treatment 646  
tension (type) headache & treatment 1215

## What kinds of acute treatment (during headache) are available for tension-type headache? How effective are they? How should these drugs be used differentially?

### Recommendation

Pharmacotherapy is the mainstay of acute treatment for tension-type headache. Medications are primarily analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), and their efficacy has been proven. There is little evidence on differential use of these drugs. It is important to always pay attention to medication-overuse headache that results in treatment failure. Specifically, use for more than 2 to 3 times per week should be avoided.

Grade A-C

### Background and Objective

Tension-type headache is the most commonly encountered headache in routine clinical care, and occupies the largest fraction of functional headache. Various pharmacotherapies are the mainstay of acute treatment for tension-type headache. However, acute pharmacotherapy should be used with caution so as not to induce medication-overuse headache.

### Comments and Evidence

Pharmacotherapy using analgesics and NSAIDs is the main acute treatment for tension-type headache.<sup>1)-7)</sup> The representative analgesic is acetaminophen, and the representative NSAIDs aspirin, mefenamic acid, and ibuprofen are recommended (grade A recommendation). However, since adverse effects such as gastrointestinal disturbance and hematopoietic disturbance may occur, caution has to be exercised during administration. For pregnant women with onset of tension-type headache, acetaminophen is selected also from the safety viewpoint.

Combination therapy with caffeine, which is known to be an effective acute medication, is fast-acting but can cause dependence, with a risk of inducing medication-overuse headache.<sup>8)</sup> A recent report has indicated the effectiveness of selective cyclooxygenase (COX)-2 inhibitor for the treatment of episodic tension-type headache.<sup>9)</sup>

Representative drugs and the recommendation grades are listed below.

#### 1. Analgesics and NSAIDs (grade A recommendation)

- (1) acetaminophen 500 mg
- (2) aspirin 500 to 1,000 mg
- (3) ibuprofen 200 to 800 mg
- (4) ketoprofen 25 mg
- (5) naproxen 200 to 600 mg
- (6) diclofenac 12.5 to 50 mg
- (7) loxoprofen 60 mg

All taken as needed

#### 2. Caffeine 65 to 200 mg taken as needed (useful when used in combination) (grade B recommendation)

#### 3. Selective COX-2 inhibitors (grade C recommendation)

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## • Search terms and secondary sources

- Search database: PubMed (2011/12/21)
  - tension headache & treatment 654
  - tension (type) headache & treatment 1208

## How should prophylactic therapy for tension-type headache be conducted?

### Recommendation

Prophylactic therapy for tension-type headache can be broadly divided into pharmacotherapy and non-pharmacotherapy. Pharmacotherapy using mainly antidepressants, and non-pharmacotherapies using electromyographic biofeedback therapy, physical therapy, acupuncture, exercise therapy (exercise to relax neck and occipital muscles), psychotherapy, and cognitive behavioral therapy (such as lifestyle guidance) are being conducted. Regarding the treatment duration for pharmacotherapy using mainly antidepressants, assess the outcome after around 3 months (the longest 6 months) and decide whether to continue or discontinue medication. On the other hand, evidence for the treatment duration for non-pharmacotherapies have not been established.

**Grade A-C**

### Background and Objective

Prophylactic therapies for tension-type headache comprise pharmacotherapy and non-pharmacotherapy. Pharmacotherapy is conducted mainly using antidepressants. In contrast, non-pharmacotherapy attempts to reduce headache utilizing combinations of various modalities such as electromyographic biofeedback therapy, physical therapy, acupuncture, exercise therapy (exercise to relax neck and occipital muscles), psychotherapy, and lifestyle guidance.

### Comments and Evidence

Among the different types of tension-type headache, prophylactic therapy is used for episodic tension-type headache (especially the frequent subtype) and chronic tension-type headache. In episodic tension-type headache, since not only increased craniocervical muscle tension induces pain but central pain mechanisms are also involved,<sup>1)2)</sup> pain processing dysfunction caused by psychological stress or emotional disturbance is presumed to be the fundamental problem. From this point of view, treatment with oral antidepressants is most frequently used as a treatment with high level of evidence.<sup>3)-8)</sup> Especially, prophylactic therapy using tricyclic antidepressants such as amitriptyline is recommended (grade B recommendation). Tetracyclic antidepressants are also sometimes selected because they can be used in combination with muscle relaxants such as tizanidine and eperison, with also the merit of few adverse effects.

For chronic tension-type headache also, first a history should be taken on whether there is medication overuse; and in the case of overuse, in principle medication is discontinued or tapered. Pharmacotherapy for chronic tension-type headache also mainly uses muscle relaxants and antidepressants. Since chronic tension-type headache is often evolved from episodic tension-type headache, the tricyclic antidepressant amitriptyline is especially effective as a prophylactic medication. For treatment, start from a low dose of 5 to 10 mg/day, and titrate up to around 30 mg/day, but pay attention to adverse effects such as thirst and constipation. In chronic tension-type headache, headache per se is a stressor, and tends to cause secondary depression or anxiety. And, these psychological factors may further exacerbate headache, leading to refractory headache. For patients who have developed refractory headache, explain to the patients about the relationship between psychological stress and headache. At the same time, in addition to tricyclic or tetracyclic antidepressants for the treatment of depression as for episodic tension-type headache, selection and use of appropriate serotonin-noradrenaline reuptake inhibitor (SNRI) or noradrenergic and specific serotonergic antidepressant (NaSSA) is recommended. For patients who complain of strong anxiety, use of anxiolytic in treatment provides prompt relief. The effectiveness of anxiolytic was investigated in a randomized controlled trial (RCT) of etizolam and mefenamic acid combination therapy in 144 patients with frequent or infrequent tension-type headache. While no overall significant difference for etizolam was detected, headache and shoulder pain were improved significantly in female and young patients treated with etizolam and mefenamic acid combination compared to mefenamic acid alone.<sup>9)</sup>

Studies in recent years have found that among patients with chronic tension-type headache, some manifest headache as a somatic symptom of psychiatric disorder,<sup>10)</sup> and the prevalence of such cases is high. The majority are somatoform disorders such as somatization disorder and pain disorder, emotional disorders such as major depression and dysthymia, and anxiety



disorders such as panic disorder and generalized anxiety disorder. These are secondary headaches [International Classification of Headache Disorders, 3rd edition (beta version); A12. *Headache attributed to psychiatric disorder*], and treatment in corroboration with psychosomatic specialist or psychiatrist is recommended.

No evidence can be found for the therapeutic effect of greater occipital nerve block that has long been used for the treatment of chronic tension-type headache. Several studies investigating the effectiveness of botulinum toxin<sup>11)-14)</sup> reported no therapeutic effect for episodic tension-type headache, and therapeutic effect for chronic tension-type headache only when relatively large doses were injected at specific sites. It should be noted that when botulinum toxin is chosen to treat tension-type headache, fast-acting effect should not be expected. Other non-pharmacotherapies<sup>7)</sup>, used for prophylactic therapy<sup>15)-17)</sup> include electromyographic biofeedback therapy (grade A recommendation) and exercise for headache relief (grade B recommendation), as well as cognitive behavioral therapy, neck acupuncture, acupuncture, Tiger Balm, percutaneous electrical nerve stimulation (PENS), and hypnotherapy, all of which are grade C recommendation.

Representative drugs used in prophylactic therapy are shown below.

1. Antidepressants/antiepileptic drugs
  - 1) Tricyclic antidepressants
    - (1) amitriptyline 5 to 75 mg/day (grade A recommendation)
    - (2) clomipramine 75 to 150 mg/day (grade B recommendation)
  - 2) Tetracyclic antidepressants (grade B recommendation)
    - (1) maprotiline 75 mg/day
    - (2) mianserin 30 to 60 mg/day
  - 3) NaSSA
    - mirtazapine 30 mg/day (grade B recommendation)
  - 4) Antiepileptic drug
    - topiramate (grade C recommendation)
2. Anxiolytics
  - (1) alprazolam 0.4 to 1.2 mg/day (grade B recommendation)
  - (2) etizolam 0.5 to 1 mg/day (grade B-C recommendation for combination therapy)  
(for both, avoid continuous use)
3. Muscle relaxants
  - (1) tizanidine 3 to 6 mg/day (grade B recommendation)
  - (2) eperison 150 mg/day (grade C recommendation)

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- **Search terms and secondary sources**

- Search database: PubMed (2011/12/21)
  - tension headache & treatment654
  - tension (type) headache & treatment1208

## Apart from pharmacotherapy, what other therapies are used for tension-type headache?

### Recommendation

Non-pharmacotherapies for tension-type headache include psycho-behavioral therapy, physical therapy, acupuncture, and Tiger Balm<sup>®</sup>, and those with proven usefulness warrant recommendation as treatment method. Among them, combined use of electromyographic biofeedback (psycho-behavioral therapy) and relaxation training is recommended.

**Grade A**

### Background and Objective

Non-pharmacotherapies for tension-type headache include psycho-behavioral therapy, physical therapy, acupuncture, and Tiger Balm<sup>®</sup>, and only those that are proven useful would warrant recommendation. The evidence for the effectiveness of non-pharmacotherapy for tension-type headache is reviewed and commented.

### Comments and Evidence

Non-pharmacotherapies comprise the following:

- A. Psycho-behavioral therapy (grade A or C recommendation)
  - (1) electromyographic biofeedback (grade A recommendation)
  - (2) cognitive behavioral therapy (grade C recommendation)
  - (3) relaxation training (grade C recommendation)
  - (4) hypnotherapy (grade C recommendation)
- B. Physical therapy (grade C recommendation)
  - (1) exercise program
    - \*Exercise for relief of headache (grade B recommendation)
  - (2) massage, neck acupressure
  - (3) ultrasound and electrical stimulation
  - (4) improvement of posture
  - (5) oromandibular treatment
  - (6) hot and cold packs
- C. Acupuncture (grade C recommendation)
- D. Tiger Balm<sup>®</sup> (grade C recommendation)

Psycho-behavioral therapies consist of electromyographic (EMG) biofeedback, cognitive behavioral therapy, relaxation training and hypnotherapy.

In EMG biofeedback, an electromyograph is used to present the action potential of muscles to the patient, so that the patient becomes aware of the muscle tension and try to control it. This method is considered effective. Active use of EMG biofeedback combined with relaxation training achieves long-term efficacy more easily.<sup>1)</sup> However, it is not clear whether the effect differs depending on the subtype of tension-type headache.

Cognitive behavioral therapy is an approach to enable patient to recognize the relationship between stress and headache. Various exercises are used. The method is considered effective, but clear evidence is lacking at present.<sup>2)3)</sup>

Relaxation training includes breathing exercise and meditation. Evidence for effectiveness is inconclusive.<sup>2)</sup>

The effectiveness of hypnotherapy is unknown.<sup>2)4)</sup>

Many of the physical therapies are difficult to evaluate precisely, but study has suggested the effectiveness of exercise program, and this approach is recommended also because of low cost.<sup>5)</sup> Exercise for relief of headache has level 4 evidence, based on expert opinion and experience. However, because of few adverse effects and low cost, exercise for relief of headache is given grade B recommendation. In addition, combined use with massage, relaxation and exercise program is effective.<sup>6)7)</sup> Other treatments are also widely used, but there are no report clearly showing effectiveness. Spinal manipulation has been

used, but no effectiveness is demonstrated and this method is not recommended.

Acupuncture is effective for short-term outcome (up to three months), and is speculated to be more effective in the long term.<sup>8)9)</sup> However, further study is needed.

Topical application of Tiger Balm<sup>®</sup> or peppermint oil on the forehead is reported to be superior to placebo.<sup>10)</sup>

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## • Search terms and secondary sources

- Search database: PubMed (2011/12/21)  
tension headache & treatment 646  
tension (type) headache & treatment 1215

## Is botulinum toxin effective for tension-type headache?

### Recommendation

At the present time, the effectiveness of botulinum toxin (BTX) for tension-type headache has not been established. Most of the adverse effects of BTX are due to excessive pharmacological action, and no serious effects have been reported. Therefore, BTX may be used to reduce symptoms of chronic tension-type headache when other treatments have failed. However, BTX is not fast-acting and is currently not covered by health insurance in Japan.

Grade C

### Background and Objective

The pathogenetic mechanisms of tension-type headache remain unclear. Several hypotheses have been proposed. (1) Hypersensitivity to pain in craniocervical tissues (especially increased muscle tone) has been proposed as the peripheral factor. (2) Changes in central pain sensitivity (especially lowering of pain threshold and amplification of normal central nociceptive input) due to continuous excessive nociceptive input from the periphery have been proposed as the central factor. The latter is considered to occur more commonly in chronic tension-type headache.

In tension-type headache, the major action of BTX, which is reducing muscle tone, is expected to improve the peripheral factor. In addition, inhibition of input from muscle spindle may also improve the central factor. Since these effects persist for several months (usually 3-4 months), BTX can be expected to be useful as a prophylactic therapy, but not as a fast-acting agent.

In this section, the effectiveness of BTX in tension-type headache is evaluated.

### Comments and Evidence

Since Zwart et al.<sup>1)</sup> first reported the effect of BTX on tension-type headache in 1994, a large number of reports have appeared. The earlier reports were mostly open-label studies. Recently, randomized placebo-controlled double-blind studies have been conducted.<sup>2)-7)</sup> Among them, two reports corresponding to level I evidence have been published.<sup>2)3)</sup>

A study of BTX treatment in 112 patients with chronic tension-type headache comparing headache at 6 weeks before treatment and 12 weeks after treatment found no significant difference between BTX (500 mouse unit) and placebo.<sup>2)</sup> A study in 300 patients with chronic tension-type headache reported no difference in headache improvement at day 60 after treatment between all BTX doses and placebo, but less decrease in days with headache with 150 U BTX compared to placebo.<sup>3)</sup> However, this study reported 50% reduction in headaches at day 90 in the other dose groups.

Other studies suggested a tendency of symptom improvement up to 12 weeks but no significant difference,<sup>4)5)</sup> and a reduction in headache after a prolonged observation period of 240 days.<sup>6)</sup>

Based on the above reports, the conclusion in American and European countries is that BTX is not effective for chronic tension-type headache, at least by short-term treatment.<sup>8)</sup>

However, there are issues regarding the evaluation of effectiveness of BTX therapy; differences in total dose and site of injection among studies. On one hand, increasing the dose does not achieve effectiveness. On the other hand, two methods of administration are used: injection at a specified site (fixed method), and injection at the site of pain (follow the pain method). In the future, comparative studies including control subjects and using a fixed injection method should be conducted to examine the usefulness of BTX for tension-type headache.

Adverse effects were reported in 2.5 to 25% of subjects treated with BTX, mainly as transient or mild muscular weakness. Safety is rated as tolerable.<sup>8)</sup>

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- **Search terms and secondary sources**

- Search database: PubMed (2011/12/21)  
Headache & botulinum 379  
{tension type headache} & botulinum 114