1. Introduction

Shoulder pain is an important medical and socioeconomic problem in the western world, with between 7% and 26% of the population reporting shoulder problems at any one time [1]. The presence of pain and stiffness in the shoulder can lead to an inability to work and/or to carry out domestic and recreational activities, thus creating a high burden of disease for both the individual and society [2].

Pain and stiffness of the shoulder is commonly caused by rotator cuff disorders including tendonitis and bursitis, by adhesive capsulitis, and by osteoarthrosis of the glenohumeral joint [3]. The normal course of the disease consists of a gradual or sudden onset, accompanied by night pain and pain on moving the affected joint. The mobility of the shoulder joint then becomes progressively more limited, until in many cases a "frozen" or stiff shoulder is the result. The process, according to most of the literature, is generally "self-limiting", lasting for about 1–3 years. Nevertheless, a significant number of patients suffer from a residual, clinically detectable restriction of movement beyond 3 years [4]. The common treatments for shoulder pain are NSAIDs, physiotherapy, injections, and conservative "wait and see" [5]. Unfortunately, none of these treatments is clearly proven to be effective for chronic shoulder pain in the long run, calling for new treatment strategies to improve the situation of chronic shoulder pain sufferers [4,5].

Worldwide, chronic shoulder pain is considered one of the indications most amenable to treatment with acupuncture [6–10]. A small number of clinical and methodologically diverse trials have been published recently that show little evidence to support or refute the use of acupuncture for chronic shoulder pain [11]. However, whether the effect varies depending on the difference in the acupuncture technique has not clearly been demonstrated.

It is generally accepted that the acupuncture treatment administered in the studies conducted so far, have been based on clinical practice rather than empirical evidence. The method of point selection in published trials seems to be more simple and formulaic than that used in the standard acupuncture practice at our clinic. We believe that the response to acupuncture and therefore, the success of a trial, depend substantially on the choice of and the number of points treated.

The main aim of this study was to determine if acupuncture at trigger points is an effective treatment for chronic shoulder pain, when compared with sham (SH) treatment at trigger points.

2. Materials and methods

The design of this study was a blinded, SH-controlled, randomized clinical trial, in which one group received acupuncture treatment and the other SH acupuncture treatment. Patients aged ≥40 years, with a history of shoulder pain, were recruited from the Meiji University of Integrative Medicine Hospital specifically for the study. The patients were outpatients in whom chronic shoulder pain had been clinically diagnosed. Inclusion criteria were: (1) shoulder pain lasting for ≥6 months; (2) no neurological disorders causing shoulder pain; (3) an average pain score of 50 mm or on a 100-mm visual analogue scale (VAS) in the pre month; (4) age between 40 years and 70 years; (5) no referred pain from the cervical spine; (6) no osteoarthritis of the glenohumeral joint or systemic bone and joint disorder (e.g., rheumatoid arthritis); (7) no history of shoulder surgery; (8) no other current therapy involving analgesics; (9) had not received acupuncture in the last 6 months; and (10) insufficient response to the medications prescribed by their orthopedic specialist.

The patient could continue to use their medications as they had before enrolment. Exclusion criteria were major trauma or systemic disease, and other conflicting or ongoing treatments.

Patients who gave written informed consent were enrolled and randomly allocated using a computerized randomization program, to the trigger point acupuncture (TrP), or SH treatment groups. Each patient received a total of five treatments, one per week, each lasting 30 minutes, and was followed-up for 20 weeks from the first treatment.

Patients were blinded to their treatment. They were told before randomization that they would be allocated to one of two groups. The measurements were performed by an independent investigator, who was not informed about the treatment sequence or the treatment the patient received before each measurement. Patients were asked to cover their eyes with an eye mask to blindfold them, and to ensure that they avoided being aware of the SH procedure.

Ethical approval for this study was given by the ethics committee of the Meiji University of Integrative Medicine.

2.1. Trigger point acupuncture group

The trigger point acupuncture (TrP) group received acupuncture treatment at trigger points. The correct application of the technique requires experience in palpation and localization of taut muscle bands and myofascial trigger points. Precise needling of active myofascial trigger points provokes a brief contraction of muscle fibers. This local twitch response should be elicited for successful therapy, but it may be painful and posttreatment soreness is frequent [12,13]. In this study, the most important muscles of the neck and superior limb were examined for myofascial trigger points (Table 1).

Disposable stainless steel needles (0.2 mm × 50 mm, Seirin, Sizuoka, Japan) were inserted into the skin over the trigger point to a depth of 5–15 mm, appropriate to the muscle targeted, attempting to elicit a local muscle twitch response using the so called "sparrow pecking" technique. After the local twitch response was elicited, or a reasonable attempt made, the needle was retained for a further 10 minutes. The mean number of insertions was 4.1.

2.2. Sham acupuncture group

The sham (SH) group received SH treatment at trigger points. The methods of choosing trigger points were the same. For the SH group, similar stainless steel needles (0.2 mm × 50 mm) were used, but the tips had been cut off

Table 1 Muscles treated in the two trigger point acupuncture groups.

Muscle	Trigger point group	Sham group
Musculus trapezius	3	4
M. supraspinatus	4	6
M. infraspinatus	6	6
M. teres minor	4	3
M. teres major	2	2
M. subscapularis	5	6
M. latissimus dorsi	1	2
M. pectoralis major	2	2
M. pectoralis minor	2	1
M. biceps brachii	2	3
Other	2	3

to prevent the needle from penetrating the skin. The cut ends were smoothed with sandpaper manually under clean conditions [14]. The acupuncturist pretended to insert and manipulate the needle: place the needle with a guide tube over the designated point and tap the top of the needle handle and then remove the tube while holding the needle tip with the thumb and the forefinger of the left hand and thrust and withdraw the needle with the right hand, which holds the needle handle (sparrow pecking technique). A simulation of needle extraction was performed after 10 minutes, by touching the patient and noisily dropping needles into a metal case.

To facilitate blinding, we used an eye mask. The mean number of insertions was 4.4. The treatments were performed by two acupuncturists who had 4 years of acupuncture training and 3 or 10 years of clinical experience.

2.3. Evaluation

Primary outcome measures were pain intensity, quantified using a 100 mm VAS, and pain disability [15], measured using the Constant–Murley Score (CMS) [15,16]. The total CMS consists of nine questions (range 0–100 points, the worst condition being 100).

The VAS measures were assessed immediately before the first treatment and 1, 2, 3, 4, 5, 10, and 20 weeks after the first treatment. The CMS measures were assessed before the first treatment and 5, 10, and 20 weeks after the first treatment. The VAS and SMS measures were completed by participants immediately before each treatment (Fig. 1).

To examine the efficacy of the blinding technique of the study, the participants were asked to select an answer for the question "How did you feel when the acupuncture needle was inserted?" at the end of the first phases. The available answers were: (1) needles were inserted into muscle; (2) needles did not penetrate the skin; and (3) I could not discriminate the difference.

2.4. Statistical analysis

The data are reported as mean ± standard deviation (mean ± SD). Dunnett's multiple comparison test was applied to detect significant changes within each group. To compare the results of two groups, the area under the curve (AUC) of the pain VAS was calculated from the summation of the time–response curves for individual patients. The AUC data (arbitrary units) for each group were used for group comparison by a one-way analysis of variance (ANOVA) followed by *post hoc* multiple comparisons using the Bonferroni correction.

Assessment of the success of blinding was analyzed using a χ^2 test. SPSS software for Windows (version 11.0, SPSS Japan Inc., Shibuya, Tokyo, Japan) or Systat 11 (Systat Software, Washington, Chicago, USA) was used for the statistical analysis. A p value <0.050 was considered as statistically significant.

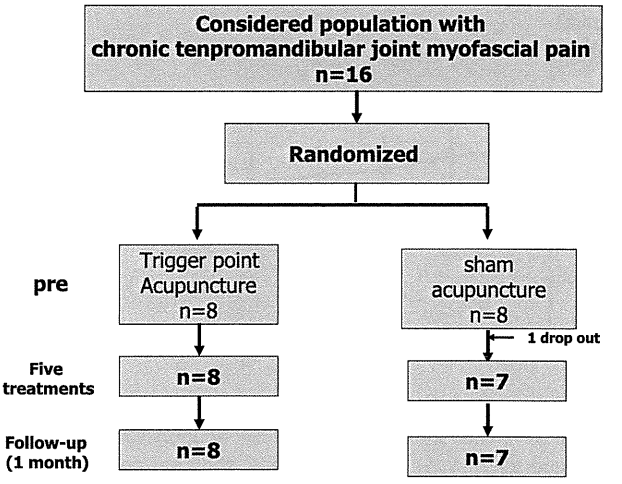

Figure 1 Participation flow in the study. One patient was excluded after she dropped out.

3. Results

3.1. Patient characteristics

Eighteen patients (15 women, 3 men; aged 42–65 years) were randomized to two groups and administered treatment (Fig. 2). No differences were found the between the two groups in the variables measured at baseline, including age, disease, pain duration, VAS, and drug use (Table 2).

Patient progress through the trial is shown in Fig. 2. One patient in the SH group dropped out, as they had no response to treatment. The drop-out rate was not different among the groups ($p = 0.31$, Mann–Whitney U test). The analyses were performed on the 17 patients who completed the study.

3.2. VAS score

Pain intensity decreased at weeks 4–5 in the TrP group, when compared with pretreatment levels. These improvements persisted for 10 weeks after cessation of the treatment in the TrP group. The mean VAS score decreased significantly in the TrP group ($p < 0.001$ in the TrP by repeated measures ANOVA; Fig. 2).

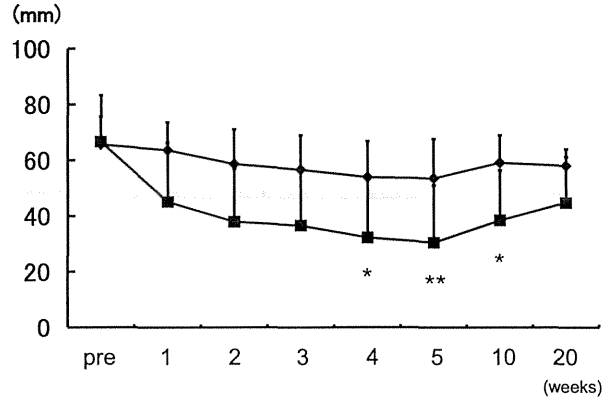

Figure 2 This shows the effect of acupuncture on visual analogue scale (VAS) score for chronic shoulder pain. The pain intensity was lower at weeks 4–5 in the trigger point acupuncture (TrP) group when compared to pretreatment scores. ■: TrP group ($n = 8$), ◆: sham acupuncture group ($n = 7$), $^{*}p < 0.05$, $^{**}p < 0.01$.

The AUCs for pain intensity (VAS score) are shown in Fig. 3. The score was significantly lower in the TrP group than in the SH group ($p = 0.024$).

3.3. Functional impairment

The reduction in the CMS score was higher at week 5 in the TrP group, when compared with that at pretreatment. These improvements persisted for 1 month after cessation of the treatment. The mean CMS score showed a significant reduction in the TrP group ($p < 0.001$ in the TrP; Fig. 4).

The AUCs for functional impairment (CMS score) are shown in Fig. 5. The score was not significantly higher in the TrP group than in the SH group ($p = 0.311$).

3.4. Assessment of the blinding technique

In the present procedure, 77.8% in the TrP group and 75.0% in the SH group stated that they received the needle insertion to the muscle, whereas 22.2% in the TrP group and 25.0% in the SH group stated they received no penetration of the needle. There was no significant difference between the two treatment types ($\chi^2 = 0.18$, $p = 0.89$).

Table 2 Characteristics and baseline values of patients in the two groups.

	Trigger point group	Sham group
Sample size	8	8
Age (y)	55.0 ± 12.6	59.3 ± 15.6
Pain duration (y)	2.1 ± 1.6	2.2 ± 1.6
Visual analogue scale (mm)	67.3 ± 18.2	66.9 ± 10.1
Constant–Murley Score	57.0 ± 9.9	57.6 ± 8.0
Drug user	0	0

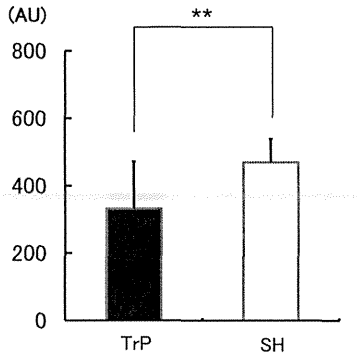

Figure 3 The columns indicate the area under the curve (AUC, arbitrary units) for changes in the pain visual analogue scale (VAS) score in the two groups. During the observation period, improvement was greater in the TrP group than the SH group ($p = 0.024$). $^{**}p < 0.01$.

4. Discussion

In the present study, there was a statistically significant difference between the TrP and SH acupuncture treatments, 5 weeks after the first treatment. These results suggest that TrP treatment is more effective than SH acupuncture treatment for chronic shoulder pain.

In many cases, chronic shoulder pain is correlated with deformation of the shoulder joint and muscle tension around the joint [17]. A wide range of treatments are used, including drugs, physical medicine methods, and manual treatments [4,5]. Acupuncture treatment has been used for pain relief for a long time. Several studies have examined the efficacy of acupuncture treatment for shoulder pain; however, the results have been mixed [11,17].

In evaluating the efficacy of acupuncture, three important parameters are the site, mode, and intensity of the stimulation. For assessing the 'stimulation site' parameter, one can define the number of stimulation sites and their location (traditional acupoint or tender/trigger point). In

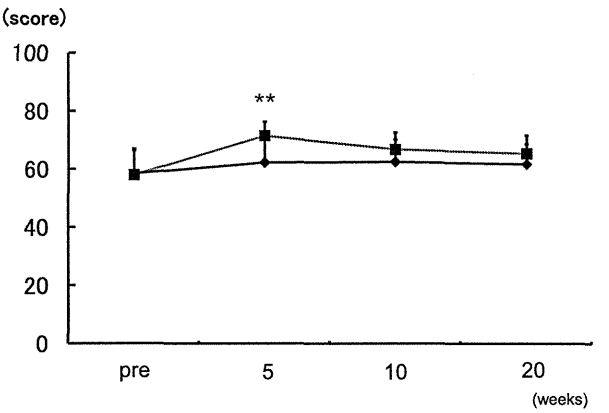

Figure 4 The effect of acupuncture on Constant–Murley Score (CMS) score indicating shoulder function. The CMS score was lower at weeks 5–10 in the trigger point acupuncture (TrP) group when compared to pretreatment scores. ■: TrP group (n = 9), ◆: sham acupuncture group ($n = 8$), $^{**}p < 0.05$.

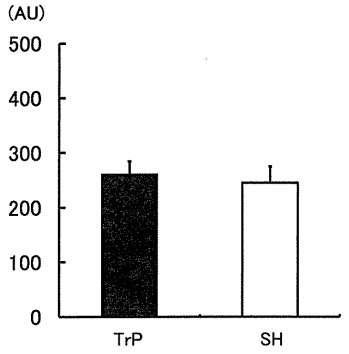

Figure 5 The columns indicate the area under the curve (AUC, arbitrary units) for changes in shoulder function in the two groups. The trigger point acupuncture (TrP) group, the score was higher than the sham (SH) group score, but the difference was not statistically significant ($p = 0.311$).

most previous studies, the stimulation sites were traditional acupuncture points [18—20]. However, our results suggest that the response to trigger points is greater than the response to treating traditional acupoints or non-trigger points [21,22]. These results suggest that the site of stimulation is important, and the acupuncture stimulation of myofascial trigger points might be most effective for chronic shoulder pain patients.

The importance of the sham-controlled, randomized clinical trials, to control for the strong placebo effects of acupuncture, has been debated [14,23,24]. Nabeta and Kawakita [14] found that there are many acupuncture randomized clinical trials in which various control groups have been employed, such as no-treatment controls [25], mere pricking (without penetration) [26], minimum acupuncture (shallow and weak needling) [27], and mock transcutaneous electrical nerve stimulation (without current pulse) [28,29]. However, in most previous studies, positive results were obtained in studies that used a non-acupuncture control group [25,30], and negative results tended to be reported in those that used SH acupuncture or mock transcutaneous electrical nerve stimulation [31,32]. Therefore, the choice of control might be very important. The SH acupuncture technique used in this study was very simple. We used a needle that had previously had its tip cut off so that it was blunt. The practitioner applied the same procedure as for the genuine acupuncture. Blinding in this study appears to have been successful. Although a few patients withdrew from the study, we considered the influence on the results to be minimal, because the number of withdrawals in each group did not differ much (1/7 in SH and 0/8 in TrP).

4.1. Effectiveness of the trigger point as a treatment site for acupuncture

The myofascial trigger points have often been used in the treatment of myofascial pain syndrome. The myofascial trigger point has been defined as a highly localized and hyperirritable spot in a palpable taut band of skeletal muscle fibers [13]. Important characteristics of myofascial trigger points include local pain or tenderness, referred pain or referred tenderness, and local twitch response [12,13]. Acupuncture or dry needling of a myofascial trigger point appears to provide immediate relief of pain related to that myofascial trigger point [21,33,34]. However, the effects of TrP on chronic shoulder pain remain unclear.

In this study, clinical results suggested that the analgesic effect of TrP is better than that of SH acupuncture. Myofascial active trigger points are supposed to be sites where nociceptors, such as polymodal-type receptors, have been sensitized by various factors [35,36]. In particular, sensitized nociceptors might be a cause of localized tenderness, referred pain, and local twitch response [37,38]. Moreover, the trigger point insertion of the needle (but not always acupuncture point insertion) affects sensitized nociceptors [38—40]. Thus, acupuncture stimulation of myofascial active trigger points may produce greater activation of sensitized polymodal-type receptors, resulting in greater pain relief.

TrP, compared with standard acupuncture, provides significantly more relief of chronic low back pain and neck pain [21,22], but not of chronic knee pain [41]. These findings suggest that the myofascial pain near joints in contrast to other types of chronic pain, may depend on different factors, such as inflammation and joint pain. Therefore, the effects of standard acupuncture on chronic shoulder pain may be as effective as TrP. However, the limited sample size and poor quality of these studies highlights and supports the need for large scale, good quality placebo controlled trials in this area [42].

Disclosure statement

The author affirms there are no conflicts of interest and the author has no financial interest related to the material of this manuscript.

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各種薬剤の選び方と上手な使い方

片　頭　痛　治　療　薬

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特集／外来で汎用される薬剤の上手な使い方

各種薬剤の選び方と上手な使い方

片頭痛治療薬

伊藤康男　荒木信夫

はじめに

このたび，日本頭痛学会と日本神経学会が中心となり，日本神経治療学会，日本脳神経外科学会の協力のもと，「慢性頭痛の診療ガイドライン2013」[1]が2013年5月に完成した。本ガイドラインでは，片頭痛治療に関した各種薬物療法が急性期治療，予防療法に分けてエビデンスとともに示されている。本稿では，片頭痛の急性期治療，予防療法について「慢性頭痛の診療ガイドライン2013」のクリニカルクエスチョンと推奨を抜粋し，実際の片頭痛治療薬処方のポイントを概説したいと思う。

Ⅰ．片頭痛の基本的知識

片頭痛の診断は国際頭痛分類第2版（ICHD-2)[2][3]を用いる。

片頭痛の診断で重要なのは，①「頭痛が発作性であるか」，②「体動による増悪があるか」，③「頭痛時に吐き気を伴うのか」，④「光過敏・音過敏の症状を持っているか」である。これらの症状がそろっていれば片頭痛の可能性が高い。「前兆のある片頭痛」では，眼前がきらきらした光・点・線が見える，あるいは視覚消失を訴える閃輝暗点，感覚症状（チクチク感または感覚鈍麻)，失語性言語障害の3症状が典型的前兆である。片頭痛の発症機序は従来，片頭痛の前兆期に血管が収縮し，その後，血管が拡張して頭痛が生じるという「血管説」が広く信じられてきた。しかし，近年，片頭痛の病態は大脳皮質の神経細胞の過剰興奮による「神経説」や三叉神経と頭蓋内血管との関係に注目した「三叉神経血管説」が提唱されている。

埼玉医科大学神経内科

Ⅱ．片頭痛の急性期治療

1．片頭痛の急性期治療には，どのような方法があり，どのように使用するか[1]

片頭痛急性期の治療は，薬物療法が中心である。治療薬として①アセトアミノフェン，②非ステロイド系抗炎症薬（NSAIDs)，③エルゴタミン製剤，④トリプタン，⑤制吐薬があり，片頭痛の重症度に応じた層別治療が推奨される。軽度～中等度の頭痛にはアスピリン，ナプロキセンなどのNSAIDsを使用する。次に中等度～重度の頭痛，または軽度～中等度の頭痛でも過去にNSAIDsの効果がなかった場合にはトリプタンが推奨される。また片頭痛薬剤使用方法（タイミング，使用量，使用頻度)，妊娠中や授乳中の薬剤の対応，急性期発作中の患者指導と注意点についての説明が必要である[1]。

片頭痛急性期治療薬には，一般的に①アセトアミノフェン，②非ステロイド系抗炎症薬(NSAIDs)，③エルゴタミン製剤，④トリプタン，⑤制吐薬がある。片頭痛発作重積や治療抵抗性片頭痛発作などの重症片頭痛に対しては⑥鎮静麻酔薬，⑦副腎皮質ステロイド（デキサメサゾン）などが使用されている（表1，2)[1]。

2．妊娠中，授乳中の片頭痛治療（急性期・予防）はどうするか[1]

発作が重度で，治療が必要な場合には発作頓挫薬としてはアセトアミノフェンが勧められる。妊娠期間中のトリプタン使用の安全性は確立されていないが，妊娠初期の使用での胎児奇形発生率の増加は報告されていない。多くの片頭痛患者は妊娠中には片頭痛発作の頻度が減少するため，予防薬が必要となる患者は少ない。また予防薬は投与しないことが望ましいが，必要な場合にはβ遮断薬があげられる。授乳婦がトリ

表 1　急性期治療エビデンスサマリ

薬剤	エビデンスの質	科学的根拠	臨床的な印象	副作用	推奨グレード	薬物のgroup	推奨用量
トリプタン							
スマトリプタン	Ⅰ	＋＋＋	＋＋＋	時々	A	1	50mg/回・200mg/日
スマトリプタン点鼻	Ⅰ	＋＋＋	＋＋＋	時々～頻繁	A	1	20mg/回・40mg/日
スマトリプタン注射アンプル	Ⅰ	＋＋＋	＋＋＋	頻繁	A	1	3 mg/回・6 mg/日
スマトリプタン自己注射	Ⅰ	＋＋＋	＋＋＋	頻繁	A	1	3 mg/回・6 mg/日
sumatriptan (suppositories)	Ⅰ	＋＋＋	－	－	A*	1	－
sumatriptan (subcutaneous)	Ⅱ	＋＋	－	－	A*	1	－
ゾルミトリプタン	Ⅰ	＋＋＋	＋＋＋	時々	A	1	2.5mg/回・10mg/日
zolmitriptan (nasal spray)	Ⅰ	＋＋＋	－	－	A*	1	－
エレトリプタン	Ⅰ	＋＋＋	＋＋＋	時々	A	1	20mg/回・40mg/日
リザトリプタン	Ⅰ	＋＋＋	＋＋＋	時々	A	1	10mg回・20mg/日
ナラトリプタン	Ⅰ	＋＋＋	＋＋＋	時々	A	1	2.5mg/回・5 mg/日
naratriptan (injection)	Ⅰ	＋＋＋	－	－	A*	1	－
almotriptan	Ⅰ	＋＋＋	－	－	A*	1	－
frovatriptan	Ⅰ	＋＋＋	－	－	A*	1	－
制吐薬，精神安定薬，麻酔準備薬							
メトクロプラミド	Ⅰ	＋＋＋	＋＋	時々	A*	2	5 mg/回・30mg/日
メトクロプラミド筋注・静注	Ⅰ	＋＋＋	＋＋	時々	A*	2	10mg/回・20mg/日
ドンペリドン	Ⅱ	＋＋	＋＋	時々	A*	2	5 mg/回・30mg/日
ドンペリドン坐薬	Ⅱ	＋＋	－	時々	B*	4	60mg/回
プロクロルペラジン	Ⅰ	＋＋＋	－	時々～頻繁	B*	4	5 mg/回
プロクロルペラジン筋注	Ⅰ	＋＋＋	－	時々～頻繁	B*	4	5 mg/回
クロルプロマジン	Ⅰ	＋＋＋	－	時々～頻繁	B*	4	30mg/回
クロルプロマジン筋注	Ⅰ	＋＋＋	－	時々～頻繁	B*	4	10mg/回
ドロペリドール筋注	Ⅱ	＋＋	－	時々～頻繁	C*	4	－
プロポフォール筋注	Ⅲ	＋	－	頻繁	C*	4	－
ジアゼパム筋注・静注	Ⅲ	＋	－	頻繁	C*	4	－
アセトアミノフェン・非ステロイド系消炎鎮痛薬							
アセトアミノフェン	Ⅰ	＋＋＋	＋＋	時々	A	2	0.5(～1.0) g/回・1.5(～4) g/日**
アスピリン	Ⅰ	＋＋＋	＋＋	時々	A	2	330mg/回・990mg/日
イブプロフェン	Ⅰ	＋＋＋	＋＋	時々	A*	2	100～200mg/回・600mg/日
ジクロフェナク	Ⅰ	＋＋＋	＋＋	時々	A*	2	25～50mg/回・75～100mg/日
ナプロキセン	Ⅰ	＋＋＋	＋＋	時々	A*	2	100～300mg/回・300～600mg/日
エトドラク	Ⅱ	＋＋	＋＋	時々	A*	2	100～200mg/回・400mg/日
セレコキシブ	Ⅱ	＋＋	＋＋	まれ～時々	A*	2	100～200mg/回・400mg/日
メフェナム酸	Ⅱ	＋＋	＋＋	時々	A	2	250～500mg/回・1,500mg/日
ザルトプロフェン	Ⅲ	＋	＋＋	時々	A*	2	80～160mg/回・240mg/日
プラノプロフェン	Ⅲ	＋	＋＋	時々	A*	2	75～150mg/回・225mg/日
ロキソプロフェン	Ⅲ	＋	＋＋	時々	A*	2	60～120mg/回・240mg/日
ロルノキシカム	Ⅲ	＋	＋＋	時々	A*	2	4～8 mg/回・24mg/日

表 1　(つ　づ　き)

薬　剤	エビデンスの質	科学的根拠	臨床的な印象	副作用	推奨グレード	薬物のgroup	推　奨　用　量
エルゴタミン							
エルゴタミン・カフェイン配合薬	Ⅱ	＋＋	＋＋	頻繁	B	4	日本での発売中止
エルゴタミン・カフェイン・ピリン系配合薬	Ⅱ	＋＋	＋＋	頻繁	B	4	1錠/回・3錠/日・週10錠までトリプタンとの併用禁忌
ジヒドロエルゴタミン	Ⅱ	＋＋	＋＋	頻繁	B	4	1 mg/回・3 mg/日 トリプタンとの併用禁忌
ステロイド							
デキサメタゾン静注	Ⅲ	＋	＋＋	時々	C	3	2～8 mg/回
ヒドロコルチゾン	Ⅲ	＋	＋＋	時々	C	3	200～500mg/回
その他							
トラマドール	Ⅲ	＋	－	時々～頻繁	C*	4	100mg/回・300mg/日
トラマドール・アセトアミノフェン配合薬	Ⅲ	＋	－	時々～頻繁	C*	4	1錠/回・4錠/日
トラマドール筋注	Ⅲ	＋	－	時々～頻繁	C*	4	－
マグネシウム製剤	Ⅲ	＋	－	まれ	C*	2	－

エビデンスの質
Ⅰ．システマティック・レビュー/メタ・アナリシスあるいは1つ以上のランダム化比較試験による。
Ⅱ．非ランダム化比較試験による/あるいは分析疫学的研究（コホート研究や症例対照研究）による。
Ⅲ．記述研究（症例報告やケースシリーズ）による。
Ⅳ．患者データに基づかない，専門委員会や専門家個人の意見。

臨床的な印象
－　　使用経験が少なく，現時点で評価困難。
＋　　何らかの効果あり：少数の患者で臨床的に有意な改善。
＋＋　有効：ある程度の患者で臨床的に有意な改善。
＋＋＋　著効：大部分の患者で臨床的に有意な改善。

推奨グレード：ガイドライン本文に記載の基準によった，わが国で保険適用が承認されている薬剤と，エビデンスの質が高い薬剤について記載した。
推奨用量：わが国におけるエビデンスとコンセンサスによる，すべて成人量である。
推奨使用量について「－」と表記した部分は評価，用量について現時点で評価困難なことを示す。
*保険適用外である。**(　) 内用量は海外推奨量を示す。
本邦未発売は英語表記

表 2　急　性　期　治　療　薬　効　群

Group 1（有効）	Group 2（ある程度有効）	Group 3（経験的に有効）	Group 4（有効，副作用に注意）	Group 5（無効）
トリプタン	**制吐薬**	**ステロイド点滴静注**	**精神安定薬．麻酔準備薬**	
スマトリプタン	メトクロプラミド	デキサメタゾン	ドンペリドン坐薬	
スマトリプタン点鼻	メトクロプラミド筋注	ヒドロコルチゾン	プロクロルペラジン	
スマトリプタン注射アンプル	メトクロプラミド静注		プロクロルペラジン筋注	
スマトリプタン自己注射	ドンペリドン		クロルプロマジン	
sumatriptan (suppositories)	**アセトアミノフェン**		クロルプロマジン筋注	
sumatriptan (subcutaneous)	**非ステロイド系消炎鎮痛薬**		ドロペリドール筋注	
ゾルミトリプタン	アセトアミノフェン		プロポフォール静注	
zolmitriptan (nasal spray)	アスピリン		ジアゼパム筋注・静注	
エレトリプタン	イブプロフェン		**エルゴタミン**	
リザトリプタン	ジクロフェナク		エルゴタミン・カフェイン配合薬	
ナラトリプタン	ナプロキセン		エルゴタミン・カフェイン・ピリン系配合薬	
naratriptan (injection)	エトドラク		ジヒドロエルゴタミン	
almotriptan	セレコキシブ		**その他**	
frovatriptan	メフェナム酸		トラマドール	
	ザルトプロフェン		トラマドール・アセトアミノフェン配合薬	
	プラノプロフェン		トラマドール筋注	
	ロキソプロフェン			
	ロルノキシカム			
	その他			
	マグネシウム製剤			

プタンを使用した場合には，スマトリプタンは使用後12時間，その他のトリプタンは24時間経過した後に授乳させる事が望ましい[1]。

Ⅲ．片頭痛の予防療法

1．どのような患者に予防療法が必要か？[1]

片頭痛発作が月に2回以上あるいは6日以上ある患者では予防療法の実施について検討してみることが勧められる。急性期治療のみでは片頭痛発作による日常生活の支障がある場合，急性期治療薬が使用できない場合，永続的な神経障害をきたすおそれのある特殊な片頭痛には予防療法を行うよう勧められる[1]。

また，急性期治療薬の乱用は薬物乱用頭痛（MOH；Medication overuse headache）を誘発する[4]ので，急性期治療薬の過剰な使用がある場合も予防療法が必要となる。

2．予防療法にはどのような薬剤があるか[1]

片頭痛の予防療法に使用される薬剤には表3[1]のような薬剤がある。また，予防療法における有効性のエビデンスの強さと効果，有害事象のリスクなどから片頭痛予防薬は表4[1]のようにグループ分けすることができる。

3．抗てんかん薬（バルプロ酸）は片頭痛の予防に有効か[1]

月に2回以上の頭痛発作がある片頭痛患者にバルプロ酸を経口投与すると，1ヵ月あたりの発作回数を減少させることが期待できる。成人の場合，バルプロ酸ナトリウム400～600mg/日の内服が勧められる。妊娠可能年齢の女性へ投与する場合には副作用・催奇形性について説明の上，徐放剤を選択し，他の抗てんかん薬を併用しない。妊娠中，および妊娠の可能性のある女性には原則禁忌とする[1]。

4．ボツリヌス毒素（botulinum neurotoxin：BoNT）は片頭痛の予防に有効か[1]

A型ボツリヌス毒素は，慢性片頭痛に対する症状軽減効果が複数のプラセボを用いたランダム化無作為試験で証明されている。また，慢性片頭痛に対する症状軽減効果は，トピラマートと同等であることが複数の試験によって証明されている。一方，発作性片頭痛に対する効果は明確でない。したがって，慢性片頭痛に対して他の治療が無効の場合には使用することを考慮してもよいと考えられる。ただし本邦では保険適用はない[1]。

Ⅳ．片頭痛治療薬の処方例[5]

1．発作時の治療

STEP1　片頭痛発作が軽度の場合

1）バファリン®（330mg）1回1錠　頓用
2）ナウゼリン®（10mg）1回1錠　頓用（片頭痛に対しての保険適応はないが，悪心・嘔吐の保険適応あり）

片頭痛発作が軽度の場合はアスピリンなどの鎮痛薬が第1選択となる。早期服用が有効であり，必要に応じて制吐薬を併用するとよい。これらの処方で1～2時間しても軽快しない場合はSTEP2のトリプタン系薬剤に切り替える[5]。

STEP2　片頭痛発作が中等度から重度の場合

1）イミグラン®（50mg）1回1錠　頓用
2）ゾーミック®（2.5mg）1回1錠　頓用
3）レルパックス®（20mg）1回1錠　頓用
4）マクサルト®（10mg）1回1錠　頓用
5）アマージ®（2.5mg）1回1錠　頓用
6）イミグラン点鼻液®（20mg）1回1本　点鼻
7）イミグラン注®（3mg）1回3mg　皮下注

トリプタン系薬剤で治療する場合，1）～7）のいずれかを用いる。1）～4）は効果不十分の場合に2時間後に1錠追加投与可能である。5）は4時間後に追加投与可能。痛みが強く嘔吐している場合には7）が第1選択薬となる[5]。

トリプタンは頭痛発現後早期に服用するよう指導する。前兆期には使用しない。血管収縮作用があり，虚血性脳血管障害，冠動脈疾患を有する患者では禁忌である。片頭痛発作回数が多い（月に2回以上），発作が重度である，頓挫療法が無効の場合にはSTEP3の予防療法を検討する[5]。

2．予防的治療

STEP3　片頭痛発作回数が多い（月に2回以上），発作が重度である，頓挫療法が無効の場合

1）ミグシス®またはテラナス®（5mg）2～4錠　分2（片頭痛に対して保険適応あり）
2）デパケンR®（200mg）2～3錠　分2～3
　または　セレニカR（400mg）1錠　分1
　（2010年より片頭痛に対して保険適応あり）
3）インデラル®（10mg）2～4錠　分2～3