Complete Summary

GUIDELINE TITLE

Diagnosis and management of headache.

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Diagnosis and management of headache. Singapore: Singapore Ministry of Health; 2007 Sep. 104 p. [374 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Singapore Ministry of Health. Diagnosis and management of headache. Singapore: Singapore Ministry of Health; 2000 Nov. 25 p. [15 references]

The workgroup advises that these guidelines be scheduled for review 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released:

- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Headaches, including:

- Tension type headaches
- Migraine headaches
- Medication overuse headaches
- Secondary headaches

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Neurology
Obstetrics and Gynecology
Pediatrics
Preventive Medicine
Psychiatry
Psychology

INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

- To update the 2000 national guidelines on headache
- To raise awareness of the different forms of headaches and the importance of making a correct diagnosis
- To discuss the mainstay treatment for the various headaches as well as alternative treatments and to highlight the dangers of medication overuse headaches

TARGET POPULATION

Patients with various types of headaches, such as migraine, tension type headaches, and medication overuse headaches

*These guidelines are **not** intended for patients with intractable headaches.*

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis and Evaluation

1. Use of International Headache Society criteria for diagnosis and classification
2. Diagnosis of migraine using a validated 3-item questionnaire (ID-Migraine)
3. Assessment of disability using a standardized self-assessment questionnaires (The Migraine Disability Assessment [MIDAS] and the Headache Impact Test Questionnaire [HIT-6])
4. Evaluation of the psychiatric and psychological aspects of migraines and tension headaches
5. Neuroimaging

Note: Guideline developers considered but did not recommend skull x-rays and lumbar punctures for evaluation of headaches.

Management, Treatment, and/or Prevention

Pharmacological Treatment (see "Major Recommendations" for context)

1. Simple analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs)
2. Caffeine as analgesic adjuvant
3. Antiemetics
4. Nonselective 5-hydroytryptamine receptor agonists
5. Selective 5-hydroxytryptamine receptor agonists
6. Beta-blockers
7. Calcium channel blockers
8. Serotonin receptor antagonists
9. Antidepressants
10. Anticonvulsants
11. Angiotensin blockers
12. Other agents (feverfew, magnesium, riboflavin, coenzyme Q10, botulinum toxin A, butterbur)

Non-pharmacologic Measures

1. Avoidance of medication overuse
2. Patient education
3. Biofeedback, relaxation training, and physical therapy for migraine in pregnancy
4. Adjunctive psychological interventions, such as cognitive behavioral therapy or stress management therapy
5. Referral of patients with suspected secondary headaches

6. Acupuncture for prophylactic treatment of migraine and tension-type headache

MAJOR OUTCOMES CONSIDERED

- Effectiveness of measures used to prevent and/or treat headaches (headache frequency, severity, and duration; functioning, disability)
- Quality of life
- Scores on standardized questionnaires, such as the Migraine Disability Assessment Questionnaire (MIDAS) and the Headache Impact Test Questionnaire (HIT-6)
- Adverse effects, risks, safety, and benefits of medication

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level 1++: High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias.

Level 1+: Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.

Level 1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

Level 2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

Level 2+: Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

Level 2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

Level 3: Non-analytic studies, e.g., case reports, case series

Level 4: Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

These guidelines have been produced by a committee of neurologists, psychiatrists and family practitioners appointed by the Ministry of Health. This allows a multidisciplinary approach to this disorder. They were developed using the best available current evidence and expert opinion.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

Grade A: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or RCT rated as 1+ + and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1+ + or 1+

Grade C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2+ +

Grade D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Good Practice Points (GPP): Recommended best practice based on the clinical experience of the guideline development group.

COST ANALYSIS

In a European study, it was calculated that in 29% of headache patients who continued working over a 4 week study period, there was an average loss of labor productivity of 20.7%. 2.5% of these patients lost an average of 3.8 work days and the economic cost was US$8996 for migraine patients and US$4318 for tension headache patients. In all, the economic cost to the European Union is US$17 billion a year and US$ 28.7 billion annually for the United States. Another study looking at direct and indirect medical costs for migraine patients vs. non-migraineurs show that migraineurs had higher direct medical costs over the prior six months (US$522 versus US$415), primarily due to a greater frequency of physician and emergency department visits. The cost of lost productivity for the migraine group was also higher, by more than US$200. The combined total for direct and indirect costs was US$1,242 for migraineurs and US$929 for the comparison group. Additional analyses comparing those with moderate versus severe migraine demonstrated that more severe migraineurs had higher costs for lost productivity (US$1,021 versus US$251) and higher costs when direct and indirect costs were combined (US$1,656 versus US$685). 371 Co-morbid conditions, e.g., anxiety and depression, are also more prevalent in patients with tension and migraine headaches compared to matched controls, with a resultant increase in direct and indirect costs. In a recent study, migraineurs had a direct medical cost of US$5590 versus US$10,223 if associated with anxiety and US$10,582 if associated with depression. This, however, is still cheap compared to US$13,442 if these migraine patients had both anxiety and depression. In children outpatient costs were five times higher (US$5045 versus US$945). They were also more likely to be hospitalised.

A study looking at 592 neurologically normal patients complaining of headaches and having cranial computed tomography testing showed that the vast majority or 546 had a normal study compared to 46 which had an incidental finding of ischemic or atrophic changes not related to their headaches. None of these patients had gross intracranial pathology like space-occupying lesions or bleeding. Assuming a cost of US$117 per computed tomography (CT) scan, the cost of finding an important pathology would be US$23,400 per case.

Alternative treatments, e.g., acupuncture, are not used infrequently to treat headaches especially in eastern society where it is well accepted. A British study looked at the cost of acupuncture and its effect on quality adjusted life years (QALY) compared to traditional medical treatment. They found that acupuncture led to a mean health gain of 0.021 QALYs, equivalent to 8 quality adjusted days. This more than made up for the fact that health service costs were higher for these migraine patients.

Headache ought to be a public-health concern. Yet there is good evidence that very large numbers of people troubled by headache do not receive effective care. For example, in representative samples of the general populations of the United States only half of those identified with migraine had seen a doctor for headache-related reasons in the previous 12 months, and only about half had been correctly diagnosed. Most were solely reliant on over-the-counter medications.

Many governments, seeking to constrain health-care costs, do not acknowledge the substantial burden of headache on society. They might not recognize that the direct costs of treating headache are small in comparison with the huge indirect-cost savings that might be made (e.g., by reducing lost working days) if resources were allocated to treat headache disorders appropriately.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is rated based on the level of the evidence and the grades of recommendation. Definitions of the grades of the recommendations (A, B, C, D, Good Practice Points) and level of the evidence (Level 1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are presented at the end of the "Major Recommendations" field.

The following is a list of major changes or additions to the updated guidelines:

- Recommendations from the US Headache Consortium have been integrated into these guidelines.
- A section on migraine has been added detailing the various forms of migraine and its treatment modalities.
- Psychological aspects of headaches have also been added to provide a psychological viewpoint.
- The section on secondary headaches has been expanded.
- Investigations for headaches have been streamlined for clarity.
- A new section has been added on tension type headaches.
- The dangers of medication overuse headaches are deemed important enough to warrant a section on their own.
- Alternative headache treatments, specifically acupuncture, have been added.

Tension Type Headaches

Diagnosis and Classification

GPP - The clinical diagnosis of tension-type headaches should be guided by the International Headache Society criteria (Headache Classification Subcommittee of the International Headache Society, 2004). (**GPP**)

Treatment

A & B - Simple analgesics and nonsteroidal anti-inflammatory drugs are effective and may be used for acute treatment of tension type headaches at the following doses (von Graffenried & Nuesch, 1980; Diamond, 1983; Langemark & Olesen, 1987; Martínez-Martín et al., 2001; Nebe, Heier, & Diener, 1995; Peters, Fraim, & Masel, 1983; Ryan, 1977; Steiner, Lange, & Voelker, 2003; Dahlof & Jacobs, 1996; Mehlisch, Weaver, & Fladung, 1998; Migliardi et al., 1994; Packman et al., 2000; Prior et al., 2002; Schachtel et al., 1991; Schachtel, Furey, & Thoden, 1996; Steiner & Lange, 1998; Miller et al., 1987; Diener et al., 2005; Schachtel & Thoden, 1988; van Gerven et al.,1996; Kubitzek et al., 2003)

Drugs	**Dosage**	**Grade and Level**
Aspirin	500-1000 mg	**Grade A, Level 1+**
Paracetamol	1000 mg	**Grade A, Level 1+**
Ibuprofen	200-400 mg	**Grade A, Level 1+**
Ketoprofen	25-50 mg	**Grade A, Level 1+**
Naproxen	375-550 mg	**Grade B, Level 1+**
Diclofenac	25 mg	**Grade B, Level 1+**

A - Caffeine can be used as an analgesic adjuvant for acute treatment of tension-type headache (Migliardi et al., 1994; Schachtel et al., 1991; Diener et al., 2005; Diamond, Balm, & Freitag, 2000). (**Grade A, Level 1+**)

D - Medication overuse should be avoided as it increases the risk of developing chronic daily headache (Silberstein et al., 2005). (**Grade D, Level 4**)

D - Prophylactic treatment should be considered when headaches are frequent (Headache Classification Subcommittee of the International Headache Society, 2004). (**Grade D, Level 4**)

A - Amitriptyline 10-75 mg daily should be considered first for prophylactic treatment of tension-type headache (Schachtel & Thoden, 1988; Lance & Curran, 1964; Diamond & Baltes, 1971; Göbel et al., 1994; Cerbo et al., 1998; Bendtsen, Jensen, & Olesen, 1996). (**Grade A, Level 1++**)

B - Other locally available medications with less evidence of efficacy which may be used for prophylactic treatment of tension-type headache include:

Drugs	Dosage and Frequency	Grade and Level
Clomipramine	25-100 mg daily	**Grade B, Level 1+**
Maprotiline	25-75 mg daily	**Grade B, Level 1+**
Mirtazapine	15-30 mg daily	**Grade B, Level 1+**

GPP - Medications for prophylactic treatment of tension-type headache should be started at low doses and titrated up to therapeutic doses to minimize adverse effects. (**GPP**)

Migraine

Diagnosis

C - A validated 3-item questionnaire (ID-Migraine) covering disability, nausea, and sensitivity to light should be used by primary care physicians if screening for migraine is required (Rapoport & Bigal, 2004; Lipton et al., 2003; Sadovsky & Dodick, 2005). (**Grade C, Level 3**)

Assessment of Disability

B - Standardized self-assessed questionnaires, e.g., The Migraine Disability Assessment (MIDAS), Headache Impact Test Questionnaire (HIT-6) (see Appendix 1 and 2 in the original guideline document), to determine migraine disability should be administered where practicable. (**Grade B, Level 2++**)

Treatment Principles

B - Stratified care strategies (tailoring drugs to headache severity) should be used in preference to step-care strategies (using drugs in a progressive predetermined way) within or across attacks because the former provides significantly better clinical outcomes (Lipton, Stewart, & Sawyer, 2000). (**Grade B, Level 1+**)

C - Symptomatic medications should be administered early in an acute attack when pain is only mild to moderate (Gladstone & Dodick, 2003; Evers & Frese, 2005; Kaniecki, 2006; Foley et al., 2005). (**Grade C, Level 2+**)

D - Over-the-counter paracetamol-based medication should be tried as first-line acute treatment of migraine. (**Grade D, Level 2+**)

D - If paracetamol is ineffective in an individual patient, non-steroidal anti-inflammatory drugs should be tried. If non-steroidal anti-inflammatory drugs are ineffective or contraindicated, migraine-specific agents (triptans, ergotamine) should be tried. (**Grade D, Level 4**)

D - A non-oral route of administration should be chosen for patients who present with early nausea or vomiting. (**Grade D, Level 4**)

D - In some patients, concomitant treatment with an antiemetic and oral migraine medication may be appropriate. (**Grade D, Level 4**)

D - The danger of medication-overuse headache developing with excessive use of symptomatic migraine medication should be emphasized to the patient ("Classification and diagnostic criteria," 1988; Silberstein & Lipton, 1997). (**Grade D, Level 4**)

Pharmacological Treatment of Acute Attacks

A, B & C - Recommended dosage and frequency of various drugs used in the treatment of acute migraine episode:

Drugs	Dosage and Frequency	Grade and Level
Non-steroidal anti-inflammatory drugs		
Acetylsalicylic (Boureau et al., 1994; Tfelt-	600-800 mg 8 hrly/prn	**Grade B, Level 1+**

Drugs	Dosage and Frequency	Grade and Level
Hansen & Olesen, 1984)		
Ibuprofen (Havanka-Kanniainen, 1989; Kloster, Nestvold, & Vilming, 1992	400-800 mg 8 hrly/prn	**Grade A, Level 1++**
Naproxen sodium (Johnson, Ratcliffe, & Wilkinson, 1985; Sargent et al., 1988)	275-550 mg 6 hrly/prn	**Grade A, Level 1++**
Diclofenac (Del Bene et al., 1987)	I/M 30 mg 6 hrly, up to 2 doses/day	**Grade B, Level 1+**
Diclofenac-K (Dahlöf & Björkman, 1993)	50-100 mg stat	**Grade B, Level 1+**
Antiemetics		
Metoclopramide (Coppola, Yealy, & Leibold, 1995; Ellis et al., 1993; Tek et al., 1990; Tfelt-Hansen et al.,1980)	I/V 10 mg stat	**Grade B, Level 1+**
Prochlorperazine (Coppola, Yealy, & Leibold, 1995; Jones, Pack, & Chun, 1996)	I/M 10-12.5 mg stat	**Grade B, Level 1+**
*Domperidone (Amery & Waelkens, 1983; Waelkens, 1984)	20-40 mg	**Grade C, Level 2+**
Nonselective 5-hydroxytryptamine receptor agonists		
Ergotamine	1-2 mg 1 hrly	**Grade A,**

Drugs	Dosage and Frequency	Grade and Level
(Kangasniemi & Kaaja, 1992; Ostfeld, 1961; Waters, 1970; Friedman, DiSerio, & Hwang, 1989; Ryan, 1970; Sargent et al., 1988)	(up to total of 3 doses) + Caffeine	**Level 1++**
Selective 5-hydroxytryptamine receptor agonists		
Sumatriptan (Akpunonu et al., 1995; Bates et al., 1994; Bousser, d'Allens, & Richard, 1993; Cady et al., 1993; Cady et al., 1991; Facchinetti et al., 1995; Cady et al., 1998; Gross et al., 1994; Henry & d'Allens, 1993; Jensen et al., 1995; Mathew et al., 1992; Russell et al., 1994; "Treatment of migraine," 1991; "Self-treatment," 1991)	S/C 6 mg stat Oral 50-100 mg 2 hrly (up to 2 doses/day) (Cutler et al., 1995; Jackson, 1996; Myllylä et al., 1998; Nappi et al., 1994; "Sumatriptan," 1991; "Evaluation," 1991; Pfaffenrath et al., 1998; Pini et al., 1995; Sargent et al., 1995; Tfelt-Hansen et al., 1995; Cutler et al., 1996)	**Grade A, Level 1++**
Zolmitriptan (Rapoport et al., 1997; Solomon et al., 1997; Visser et al., 1996)	2.5 mg 2 hrly (up to 2 doses/day)	**Grade A, Level 1++**
Naratriptan (Klassen et al., 1997; Mathew et al., 1997)	2.5 mg 4 hrly (up to 2 doses/day)	**Grade A, Level 1++**

Drugs	Dosage and Frequency	Grade and Level
Eletriptan (Diener, 2005; Takiya, Piccininni, & Kamath, 2006; Stark et al., 2002; Diener et al., 2002)	40-80 mg 2 hrly (up to 2 doses/day)	**Grade A, Level 1++**

* Domperidone can be used as an adjunct to oral treatment when nausea is prominent.

Abbreviations: hrly = hourly; prn = as needed; stat = immediately; I/M = intramuscular; I/V = intravenous; S/C = subcutaneous

Prophylaxis

D - The following principles will enhance the success of prophylactic treatment

1. *Medication use*:
    A. Therapy may need to be started with the lowest effective dose, with a gradual upward titration of the dose until clinical benefits are achieved in the absence of adverse events or until limited by adverse events.
    B. Give each treatment an adequate trial of at least 1 month to establish benefit or lack thereof.
    C. Use of a long-acting formulation may improve compliance.

2. *Patient education*:
    A. Maximize compliance. Discuss with the patient the rationale for a particular treatment, when and how to use it, and what adverse events are likely.
    B. Address patient expectations. Discuss with the patient the expected benefits of therapy and how long it will take to achieve them.
    C. Create a formal management plan

3. *Evaluation*:
    A. Patients with difficult headaches should be monitored with headache diaries. Diaries should be user-friendly and should measure attack frequency, severity, duration, disability, response to type of treatment, and adverse effects of medication.

(**Grade D, Level 4**)

D - Daily migraine prophylactic treatment should be considered if 2 or more attacks a month occur (Tfelt-Hansen & Welch, 1993). (**Grade D, Level 4**)

D - The decision to start or withhold pharmacological prophylaxis should be individualized to the patient with migraine. Apart from the frequency of attacks, attack severity, failure or intolerance of acute treatments, concurrent medical

conditions and prolonged aura may be relevant considerations (Silberstein & Lipton, 1997). (**Grade D, Level 4**)

GPP - If benefit is seen with the migraine prophylactic treatment, a course of medication ideally lasting at least 6 months should be given. (**GPP**)

A & B - Recommended dosage and frequency of various drugs used in the prevention of recurrent migraine episodes:

Drugs	Dosage and Frequency	Grade and Level
Beta blockers		
Atenolol (Forssman, Lindblad, & Zbornikova, 1983; Johannsson et al., 1987)	50-100 mg om	**Grade A, Level 1++**
Propranolol (Ahuja & Verma, 1985; Børgesen, Nielsen, & Møller, 1974; Dahlöf, 1987; Forssman et al., 1976; Johnson, Hornabrook, & Lambie, 1986; Mikkelsen, Pedersen, & Christiansen, 1986; Pita et al., 1977; Pradalier et al.,1989; Sargent et al.,1985; Stensrud & Sjaastad, 1976; Tfelt-Hansen et al., 1984; Widerøe & Vigander, 1974)	40-240 mg/day	**Grade A, Level 1++**
Metoprolol (Andersson et al., 1983; Kangasniemi et al., 1987; Steiner et al., 1988; Gerber et al., 1991;	50-300 mg/day	**Grade A, Level 1++**

Drugs	Dosage and Frequency	Grade and Level
Kangasniemi & Hedman. 1984; Olsson et al., 1984)		
Bisoprolol (van de Ven, Franke, & Koehler, 1997)	5 mg/day	**Grade B, Level 1+**
Calcium channel blockers		
Flunarizine (al Deeb et al., 1992; Diamond & Freitag, 1993; Louis, 1981; Mendenopoulos et al., 1985; Pini et al., 1985; Sørensen, Hansen, & Olesen, 1986; Thomas, Behari, & Ahuja, 1991; Frenken & Nuijten, 1984)	5-10 mg on	**Grade A, Level 1++**
Verapamil (Solomon, 1986; Markley, Cheronis, & Piepho, 1984; Solomon, Steel, & Spaccavento, 1983)	240 mg om	**Grade A, Level 1++**
Serotonin receptor antagonists		
Pizotifen (Bellavance & Meloche, 1990; Ryan, 1968; Arthur & Hornabrook, 1971; Carroll & Maclay, 1975; Hughes & Foster, 1971; Krakowski & Engisch, 1973; Lance & Anthony,	0.5-2 mg tds	**Grade A, Level 1++**

Drugs	Dosage and Frequency	Grade and Level
1968; Lawrence, Hossain, & Littlestone, 1977; Osterman, 1977; Ryan, 1971; Sjaastad & Stensrud, 1969; Symon & Russell, 1995)		
Antidepressants		
Amitriptyline (Couch & Hassanein, 1976; Couch & Hassanein, 1979; Gomersall & Stuart, 1973; Ziegler et al., 1987)	10-150 mg on	**Grade A, Level 1++**
Fluoxetine (Adly, Straumanis, & Chesson, 1992; Steiner et al., 1998)	10-40 mg om	**Grade B, Level 1+**
Venlafaxine (Ozyalcin et al., 2005; Adelman et al., 2000)	75-150 mg/day	**Grade B, Level 1+**
Anticonvulsants		
Sodium Valproate/Valproic acid (Klapper, 1997; Mathew et al., 1995; Hering & Kuritzky, 1992; Jensen, Brinck, & Olesen, 1994)	500-1500 mg/day	**Grade A, Level 1++**
Topiramate (Bussone et al., 2005; D'Amico et	50-200 mg/day	**Grade A, Level 1++**

Drugs	Dosage and Frequency	Grade and Level
al., 2005; Mei et al., 2004; Diener et al 2004; Silberstein et al., 2004; Brandes et al., 2004; Storey et al., 2001)		
Gabapentin (Mathew et al., 2001; Di Trapani et al., 2000)	1200 mg/day	**Grade B, Level 1+**
Non-steroidal anti-inflammatory		
Naproxen sodium (Bellavance & Meloche, 1990; Lindegaard, Övrelid, & Sjaastad, 1980; Sances et al., 1990; Szekely et al., 1989; Welch, Ellis, & Keenan, 1985; Ziegler & Ellis, 1985)	550 mg bd	**Grade A, Level 1++**
Angiotensin blockers		
Candesartan (Tronvik et al., 2003)	16 mg/day	**Grade B, Level 1+**
Lisinopril (Schrader et al., 2001)	10-20 mg/day	**Grade B, Level 1+**
Others		
Feverfew (Palevitch, Earon, & Carasso, 1997; De Weerdt, Bootsma, & Hendriks, 1996; Pfaffenrath et al., 2002; Murphy, Heptinstall, &	50-82 mg/day	**Grade B, Level 1+**

Drugs	Dosage and Frequency	Grade and Level
Mitchell, 1988)		
Magnesium (Peikert, Wilimzig, & Köhne-Volland, 1996; Pfaffenrath et al., 1996; Facchinetti et al., 1991)	400-600 mg/day	**Grade B, Level 1+**
Riboflavin (Schoenen, Jacquy, & Lenaerts, 1998; Schoenen, Lenaerts, & Bastings, 1994; Maizels, Blumenfeld, & Burchette, 2004)	200 mg bd	**Grade B, Level 1+**
Coenzyme Q10 (Sandor et al., 2005)	300 mg/day	**Grade B, Level 1+**
Botulinum toxin A (Chilson & Brown, 2005; Gobel, 2004; Silberstein et al., 2000; Evers et al., 2002)	Botox 25U	**Grade A, Level 1+**
Butterbur (Petadolex) (Diener, Rahlfs, & Danesch, 2004; Grossmann &, Schmidramsl, 2000; Lipton et al., 2004)	50 mg-150/day	**Grade B, Level 1+**

Abbreviations: bd = twice a day; om = every morning; on = every night; tds = three times a day

A - Homeopathic treatment should not be used for migraine prophylaxis (Whitmarsh, Coleston-Shields, & Steiner, 1997; Straumsheim et al., 2000). (**Grade A, Level 1+**)

Migraine in Pregnancy and Lactation

D - Non-pharmacological management of migraine is preferred in pregnancy (Silberstein, 2000). (**Grade D, Level 2**)

D - Biofeedback, relaxation training, and physical therapy may be tried in the treatment of migraine in pregnancy (Hickling, Silverman, & Loos, 1990; Marcus, Scharff, & Turk, 1995). (**Grade D, Level 3**)

The U.S. Food and Drug Administration classify drugs according to the foetal risk associated with their use.

Category A - safety established using human studies

Category B - presumed safety based on animal studies

Category C - adverse effects in animal studies, human effects unknown

Category D - known foetal risks

Category X - high foetal risks

GPP - Drugs with a Category A or Category B rating should be used to manage migraine in pregnancy. Category C drugs should be considered after careful consideration of potential risks and benefits. Category D or Category X drugs should be avoided. (**GPP**)

GPP - Therapy for migraine in women who are pregnant or lactating should be approached cautiously and initiated only with the consent of the patient after informed evaluation of the risks. (**GPP**)

D - Paracetamol (Category B) is the drug of choice for treatment of acute migraine in pregnancy. Codeine which is category B drug becomes category D in 3rd trimester. Therefore, codeine is not recommended in the 3rd trimester (Aube, 1999). (**Grade D, Level 4**)

B - Naproxen, ibuprofen, and aspirin which are category B drugs become category D after 32 weeks of gestation. Hence, their use should be avoided after 32 weeks of gestation because of the risk of maternal or foetal bleeding and premature closure of the foetal ductus arteriosis. (**Grade B, Level 2+**)

D - Intravenous magnesium sulphate 1g over one to three minutes up to a maximum of three IV injections given a week apart may be given to patients who experience frequent disabling headaches during pregnancy (Demirkaya, et al., 2001). (**Grade D, Level 3**)

D - Intravenous prochlorperazine may be considered if extreme nausea and vomiting are present during migraine in pregnancy (Rozen, 2003). (**Grade D, Level 3**)

D - Fluoxetine, metoprolol and magnesium (category B) can be used as prophylactic treatment of migraine (Bousser & Massiou, 1993; Pfaffenrath & Rehm. 1998; Gendolla & Evers, 2004). (**Grade D, Level 4**)

B - Valproic acid and its derivatives can be teratogenic and should be avoided. Lisinopril and candesartan should not be used during pregnancy (Silberstein, 2004; Marcus, 2003). (**Grade B, Level 2+**)

D - Acetaminophen, narcotics, diclofenac, ibuprofen, prochlorperazine, beta-blockers, and moderate caffeine may be considered for treating migraine in lactating women (American Academy of Pediatrics Committee on Drugs, 1994). (**Grade D, Level 4**)

Menstrual Migraine

A & B - Recommended dosage and frequency of various drugs used in the prophylaxis of menstrual migraine (where 90% of the headaches occur within the 48 hours prior to menses).

Drugs	Dosage and Frequency	Grade and Level
Oestrogen patches/gel* (Macgregor & Hackshaw, 2002; Dennerstein et al., 1988; de Lignières et al.,1986)	50 micrograms - 1.5 mg/day	**Grade A, Level 1++**
Naproxen (Sances et al., 1990)	275-550 mg bd	**Grade B, Level 1+**
Naratriptan (Newman et al., 2001)	2.5 mg bd	**Grade B, Level 1+**
Magnesium (Facchinetti et al., 1991)	360 mg of magnesium pyrrolidone carboxylic acid	**Grade B, Level 1+**

* Migraine without aura is not an established contraindication to contraceptive use.

D - Estrogen-containing oral contraceptives should be avoided in women with migraine with focal neurologic signs (Benson & Rebar, 1986). (**Grade D, Level 4**)

Migraine in Children Less than 18 Years Old

A - Acute migraine attacks in a child should be treated with paracetamol or ibuprofen. Oral triptans are not superior to placebo in paediatric migraine (Damen et al., 2005; Lewis, Scott, & Rendin, 2002; Lewis et al., 2005). (**Grade A, Level 1++**)

A - Propranolol (60-120 mg/day) or flunarizine (5-10 mg/day) should be considered if migraine prophylaxis is required in a child (Victor & Ryan, 2003; Lewis et al., 2004). (**Grade A, Level 1+**)

B - Amitriptyline or cyproheptadine may also be used for childhood migraine prophylaxis (Victor & Ryan, 2003; Lewis et al., 2004). **(Grade B, Level 2++**)

D - Valproate, topiramate, and levetiracetam may also be considered for childhood migraine prophylaxis on the basis of limited data (Pakalnis et al., 2001; Serdaroglu et al., 2002; Hershey et al., 2002; Campistol et al., 2005; Miller, 2004). (**Grade D, Level 3**)

Headaches - Psychiatric and Psychological Aspects

Psychological Management

D - Patients with migraines and tension headaches should be evaluated for psychiatric co-morbidities such as anxiety or depression (Rowan & Andrasik, 1996). (**Grade D, Level 4**)

D - If hyperventilation accompanies tension headache and migraines, specific explanation and advice regarding anxiety disorder should be provided (Silberstein & Rosenberg, 2000). (**Grade D, Level 3**)

Biofeedback

C - Adjunctive psychological interventions should be considered in patients with headaches that are difficult to manage. (**Grade C, Level 2+**)

Secondary Headaches

Referral of Patients with Suspected Secondary Headaches

GPP - All patients with suspected secondary headaches should be referred to a specialist.

A referral is indicated if the following features are present:

1. Systemic symptoms such as fever or change in mental state
2. Neurological deficits
3. Sudden onset or maximum severity at onset
4. The first severe or worst headache in an individual's life
5. New persistent or progressively worsening headaches
6. Changed character in the normal established headache pattern
7. A new headache in middle age or later
8. Headache precipitated by coughing, sneezing, standing, bending forwards or recumbency

(GPP)

Headache Attributed to Chronic Subdural Haematoma

D - Chronic subdural haematoma should always be considered in an elderly patient with a progressive headache, particularly if there is some cognitive impairment or focal signs. (**Grade D, Level 3**)

Investigations for Headaches

Neuroimaging

C - Neuroimaging should be considered in patients with nonacute headache and an unexplained abnormal finding on neurological examination. (**Grade C, Level 2+**)

C - Neuroimaging is not warranted for patients diagnosed with migraines and having a normal neurological examination (Igarashi et al., 1991; Cuetter & Aita, 1983; Cull, 1995; De Benedittis et al., 1995; Hungerford, du Boulay, & Zilkha, 1976; Kuhn & Shekar, 1990; Osborn, Alder, & Mitchell, 1991; Robbins & Friedman, 1992; Sargent et al, 1979). (**Grade C, Level 2+**)

Skull X-rays

D - Skull X-rays are not recommended in the evaluation of headaches. (**Grade D, Level 3**)

Lumbar Punctures

D - Lumbar punctures are not recommended in the routine evaluation of headaches. (**Grade D, Level 3**)

GPP - Neuroimaging is mandatory before lumbar puncture if a neurological deficit is present or increased intracranial pressure is suspected. (**GPP**)

Medication Overuse Headaches

Management

C - For ergotamine-induced medication overuse headache, naproxen 500 mg twice daily may be used for pain reduction during the withdrawal period (Matthew, 1987). (**Grade C, Level 2+**)

GPP - During withdrawal, prophylactic treatment of the primary headache should be started concurrently. (**GPP**)

GPP - Strictly limited doses of anti-emetic medication and analgesics may be used to treat break-through attacks. (**GPP**)

C - Prednisolone 60 mg/day for 2 days, 40 mg/day for next 2 days and 20 mg/day for last 2 days and ranitidine 200 mg/day during the 6 days should be taken to alleviate headache intensity (Diener & Dahlöf, 1999). (**Grade C, Level 2+**)

D - Highly motivated patients who are not using barbiturates and tranquilizers (benzodiazepines) may be treated as outpatients. Patients who overuse drugs containing codeine, barbiturates, or tranquilizers, those who are depressed or who have failed previously to withdraw as outpatients, would be candidates for hospitalized management (Fritsche & Diener, 2002). (**Grade D, Level 4**)

Prevention

GPP - The best strategy to reduce the prevalence of medication overuse headache is to prevent the development of medication overuse headache in the first place. Doctors should set maximal monthly dosages for headache abortive drugs. Maximum doses and frequencies of types of medications that cause medication overuse headache:

Medication	Maximum Dose
Simple analgesics (aspirin and paracetamol)	Intake <10 days per month
Combination analgesics (caffeine or barbiturate-containing drugs)	$\leq$3 tablets/day
Opioids	$\leq$1 tablet /day
Ergotamine (oral)	Max 4 mg/attack and $\leq$20 mg/month
Serotonin 5-$HT_{1B/1D}$ receptor agonists ("triptans")	<2 doses/attack and <6 doses per month

(GPP)

D - Patients should be educated on the risk of medication overuse headache (Fritsche & Diener, 2002). (**Grade D, Level 4**)

D - A headache diary is a useful tool for patients and their doctors to monitor the frequency of headaches and medication usage (Fritsche & Diener, 2002). (**Grade D, Level 4**)

Use of Acupuncture in the Management of Migraine and Tension Headache

Evidence for Efficacy

A - Acupuncture may be considered for headache prophylactic treatment (Melchart et al., 2001). (**Grade A, Level 1++**)

Cautions

GPP - Caution should be exercised in using acupuncture in the following conditions:

- Patients with severe bleeding disorders or on anti-coagulant treatment – a contraindication for needle acupuncture
- Pregnancy
- Presence of a cardiac pacemaker – a contraindication for electrical stimulation
- Indwelling needles should not be used in patients at risk from bacteremia, such as asplenic patients or those who may become neutropenic

(GPP)

Definitions:

Grades of Recommendation

Grade A: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or RCT rated as 1+ + and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

Grade B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1+ + or 1+

Grade C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2+ +

Grade D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Good Practice Points (GPP): Recommended best practice based on the clinical experience of the guideline development group.

Levels of Evidence

Level 1++: High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias.

Level 1+: Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.

Level 1-: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

Level 2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

Level 2+: Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

Level 2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

Level 3: Non-analytic studies, e.g., case reports, case series

Level 4: Expert opinion

CLINICAL ALGORITHM(S)

None available

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate diagnosis and management of headaches, which do often affect the patient's quality of life and may occasionally signal the presence of a more sinister disorder.
- These guidelines were developed to raise awareness of the different forms of headaches and the importance of making a correct diagnosis. A correct diagnosis will lead to appropriate management and speedy control of the patients' headaches which will in turn reduce disability caused by headaches.
- Acute treatment aims at aborting the headache symptoms while prophylactic treatment aims to decrease the frequency and intensity of headaches.

POTENTIAL HARMS

- Risks and side effects of medications
- Rare infections or trauma associated with acupuncture

CONTRAINDICATIONS

CONTRAINDICATIONS

Medications

- Valproic acid and its derivatives can be teratogenic and should be avoided during pregnancy. Lisinopril and candesartan should not be used during pregnancy
- Codeine is not recommended in the 3rd trimester.
- Naproxen, ibuprofen, and aspirin which are category B drugs become category D after 32 weeks of gestation. Hence, their use should be avoided after 32 weeks of gestation because of the risk of maternal or foetal bleeding and premature closure of the foetal ductus arteriosis.
- Estrogen-containing oral contraceptives should be avoided in women with migraine with focal neurologic signs.

Acupuncture

Caution should be exercised when using acupuncture in the following conditions:

- Patients with severe bleeding disorders or on anticoagulant treatment – a contraindication for needle acupuncture
- Pregnancy
- Presence of a cardiac pacemaker – a contraindication for electrical stimulation
- Indwelling needles should not be used in patients at risk from bacteremia, such as asplenic patients or those who may become neutropenic

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The guideline is not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.
- The contents of the guideline document are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
- Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supercede recommendations in these guidelines.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Clinical Quality Improvement

The following clinical quality improvement parameters, based on recommendations in these guidelines, are proposed:

1. Proportion of patients with tension headaches diagnosed using The International Classification of Headache Disorders criteria.
2. Proportion of patients with tension headaches treated with aspirin, paracetamol and non-steroidal anti-inflammatory drugs (NSAIDS) alone or in combination.
3. Proportion of patients with tension-type headaches given amitriptyline, mirtazapine, or venlafaxine as prophylactic treatment.
4. Proportion of migraine patients (in primary care setting), who had their diagnosis made using the validated 3-item questionnaire (ID-Migraine) covering disability, nausea and sensitivity to light.
5. Proportion of migraine patients with migraine receiving instructions from their doctor regarding the following:
    a. The rationale for a particular treatment
    b. When to take the medication
    c. How to take the medication
    d. Advice on the likely types of adverse events
    e. Expected benefits of therapy
    f. How long will the process of therapy be in order to achieve these benefits
    g. What course of actions to take if the headache is not improved
6. Proportion of patients who had 2 or more attacks of migraine a month receiving daily migraine prophylactic treatment.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Chart Documentation/Checklists/Forms
Personal Digital Assistant (PDA) Downloads
Quick Reference Guides/Physician Guides
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Diagnosis and management of headache. Singapore: Singapore Ministry of Health; 2007 Sep. 104 p. [374 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Nov (revised 2007 Sep)

GUIDELINE DEVELOPER(S)

National Committee on Neuroscience (Singapore) - National Government Agency [Non-U.S.]
National Medical Research Council (Singapore Ministry of Health) - National Government Agency [Non-U.S.]
Singapore Ministry of Health - National Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

These guidelines on the diagnosis and management of headache were prepared by the Singapore National Committee on Neuroscience through its Subcommittee on Headache.

SOURCE(S) OF FUNDING

Singapore Ministry of Health

GUIDELINE COMMITTEE

Workgroup on the Diagnosis and Management of Headache

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Workgroup Members: Dr Siow Hua Chiang, Charles, Consultant Neurologist, Siow Neurology, Headache and Pain Centre, Mount Alvernia Hospital, Mount Elizabeth Hospital (*Chairperson*); Dr Ho King Hee, Consultant Neurologist, K H Ho Neurology & Medical Clinic; Gleneagles Medical Centre; Dr Lim Shih Hui, Senior Consultant, Dept of Neurology, NNI (SGH Campus); Dr Lee Sze Haur, Senior Consultant, Dept of Neurology, NNI (TTSH Campus); Dr Chan Yee Cheun, Consultant, Division of Neurology, NUH; Dr Ng Beng Yeong, Consultant, Dept of

Behavioural Medicine, SGH; Dr Tan Ngiap Chuan, Director, SingHealth Polyclinics-Pasir Ris

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Singapore Ministry of Health. Diagnosis and management of headache. Singapore: Singapore Ministry of Health; 2000 Nov. 25 p. [15 references]

The workgroup advises that these guidelines be scheduled for review 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Singapore Ministry of Health Web site.

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

AVAILABILITY OF COMPANION DOCUMENTS

Audit indicators and a continuing medical education (CME) self-assessment are available in the original guideline document.

The full text guideline and summary card are available for PDA download in ISilo and MSReader formats from the Singapore Ministry of Health Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on October 25, 2001. The information was verified by the guideline developer on November 16, 2001. This summary was updated by ECRI on January 12, 2005 following the release of a public health advisory from the U.S. Food and Drug Administration regarding the use of some non-steroidal anti-inflammatory drug products. This summary was updated on April 15, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug

Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on October 3, 2005, following the U.S. Food and Drug Administration advisory on Paxil (paroxetine). This summary was updated by ECRI on December 12, 2005, following the U.S. Food and Drug Administration advisory on Paroxetine HCL - Paxil and generic paroxetine. This NGC summary was updated by ECRI Institute on February 13, 2008.

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