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METHODOLOGY

Open Access

# Revised French guidelines for the diagnosis and management of migraine in adults and children

Michel Lanteri-Minet<sup>1,2\*</sup>, Dominique Valade<sup>3</sup>, Gilles Geraud<sup>4</sup>, Christian Lucas<sup>5</sup> and Anne Donnet<sup>2,6</sup>

## Background

### Sponsor

These revised guidelines were prepared at the request of the *Société Française d'Etude des Migraines et des Céphalées* (SFEMC; French Society for the Study of Migraine Headache). They are a revision of the professional guidance on the "Diagnosis and therapeutic management of migraine in adults and children: clinical and economic aspects" published by the ANAES in 2002 and revised in 2012. Scope of the guidelines.

These guidelines concern the overall management of migraine, diagnostic and therapeutic strategies, economic aspects of the disease and its treatments, menstrual (catamenial) migraine, migraine in pregnancy, migraine and oral contraception, migraine and the menopause.

Headaches other than migraine will not be discussed except in the context of differential diagnosis. Other subjects not discussed in these guidelines include diseases associated with migraine apart from psychiatric problems, risk factors, migraine and smoking, chronic migraine rare forms and complications of migraine.

### Patients concerned by the guidelines

These guidelines concern adults and children.

### Professionals concerned by the guidelines

These guidelines are aimed at all professionals involved in the management of patients with migraine, including general practitioners (GPs), specialists and retail pharmacists.

### Grade of recommendations and study methodology

The recommendations proposed have been classed as grade A, B or C as follows:

- (i) a grade A recommendation is based on scientific proof established by studies with a high level of evidence such as adequately-powered comparative, randomised trials without major bias, or comparative, randomised meta-analyses or decision analyses based on well-conducted studies.
- (ii) a grade B recommendation is based on a scientific presumption provided by studies with an intermediate level of proof, such as randomised, comparative trials with low power, cohort studies, well-conducted non-randomised comparative studies or cohort studies.
- (iii) a grade C recommendation is based on studies with a lower level of proof such as case-control studies or case series.

In the absence of proof, the recommendations proposed are based on professional agreement between members of the working group. The absence of a level of proof does not signify that the recommendations are not pertinent and useful. The absence of proof should prompt complementary studies wherever possible.

Revision of these recommendations was carried out by the SFEMC, while respecting AGREE methodology. The working group was divided into four sub-committees, each attributed a particular set of themes, a coordinator and a number of participants:

- (i) diagnosis and complementary examinations:  
coordinator: Gilles Géraud (neurologist);  
participants: Pierrick Giraud (neurologist),  
Evelyne Guegan-Massardier (neurologist)
- (ii) handicap-epidemiology-socioeconomic cost:  
coordinator: Dominique Valade (neurologist);  
participants: Geneviève Demarquay (neurologist),  
André Pradalier (internal medicine)

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Full list of author information is available at the end of the article.

- (iii) acute treatment of migraine: coordinator: Christian Lucas (neurologist); participants: Gilles Baudesson (GP), Anne Ducros (neurologist), Serge Iglesias (neurologist), Claire Lejeune (internal medicine)
- (iv) prophylactic treatment: coordinator: Michel Lantéri-Minet (neurologist); participants: Henry Becker (neurologist), Anne Donnet (neurologist), Malou Navez (anaesthetist), Françoise Radat (psychiatrist).
- (v) Jean-Christophe Cuvellier (neuropaediatrician) was involved in all areas of migraine in children.

A reading group was set up comprised of members of the SFEMC and independent health professionals (notably community GPs and pharmacists), and members of the patients' association. Initially, the project was set up at the request of the *Haute Autorité de la Santé* (HAS), but the latter challenged the majority of members of the working group on the grounds of potential conflicts of interest. The SFEMC therefore decided to produce these recommendations in its own name.

## Migraine in adults

### Prevalence

In adults between 18- and 65-years, the prevalence of migraine is estimated to be between 17 and 21% depending on the diagnostic criteria used: strict migraine 8 – 11%, probable migraine 9 – 10%, with a female predominance of 3:1.

### Clinical diagnosis

It is recommended that the diagnostic criteria, established in 1988, revised in 2004 and confirmed in 2013 by the International Headache Society (IHS) on the basis of expert consensus, are used. Only the diagnosis of migraine without aura, typical migraine with aura and probable migraine without aura (satisfying all of the diagnostic criteria except one) are discussed in this document.

The diagnosis of migraine is based on the following clinical triad (professional agreement):

- (i) recurrent headache disorder manifesting in attacks
- (ii) typical characteristics;
- (iii) a normal clinical examination.

The IHS diagnostic criteria for migraine without and with aura are shown below in Tables 1 and 2. These criteria, which are easy to use, enable essential questions to be asked in a logical order and structure. It is recommended that they are used in a systematic way in daily practice (professional agreement).

A critical analysis of these criteria shows acceptable inter-observer variability, good specificity, but poor sensitivity. These criteria are therefore restrictive and do

**Table 1 Diagnostic criteria for migraine without aura (ICHD-3 beta)**

A.	At least five attacks fulfilling to criteria B to D.
B.	Headache attacks lasting 4–72 hours (untreated or unsuccessfully treated).
C.	Headaches has at least two of the following 4 characteristics: 1- unilateral location 2- pulsating quality 3- moderate or severe pain intensity 4- aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs).
D.	During headache at least one of the following: 1- nausea and/or vomiting 2- photophobia and phonophobia.
E.	Not better accounted for by an order ICHD-3 diagnosis

not allow the diagnosis of all cases of migraine. In practice, to get around this inconvenience and not deprive some patients with migraine without aura of specific treatment, it is recommended to use the term « probable migraine without aura» for cases that fulfil all of the diagnostic criteria except one. If the five criteria, A, B, C, D and E are present, the diagnosis is migraine without aura in the strict sense of the term. If one of the criteria, A, B, C or D, is not satisfied completely, the diagnosis is probable migraine without aura.

There are three typical symptoms: visual, which are the most frequent (> 90%); sensitive; and aphasic..

A headache occurring after aura may sometimes be of non-migrainous semiology, or even absent (aura

**Table 2 Diagnostic criteria for migraine with aura (ICHD-3 beta)**

A.	At least two attacks responding to criteria B and C.
B.	One or more of the following fully reversible aura symptoms: 1- visual 2- sensory 3- speech and/or language 4- motor 5- brainstem 6- retinal
C.	At least two of the following four characteristics: 1- at least one aura symptom spreads gradually over $\geq 5$ minutes, and/or 2 or more symptoms occur in succession 2- each individual aura symptom last 5–60 minutes 3- at least one aura symptom is unilateral 4- the aura is accompanied, or followed within 60 minutes by headache
D.	Not better accounted for by an order ICHD-3 diagnosis, and transient ischemic attack has been excluded

without headache). Aura may sometimes occur during the headache. Migraine should be distinguished from a tension headache: more diffuse headache; non pulsatile; not aggravated by effort; less intense; without digestive signs; sometimes accompanied by phonophobia or photophobia but not both at the same time.<sup>1</sup> A loss of central vision or blurred central vision are possible. Migraine and tension headache may be associated or both occur in the same patient.

Faced with a migraine attack, two misdiagnoses are often allocated:

- « sinusitis » when the pain is frontal or sited around the cheekbone;
- « Arnold's neuralgia » when the pain starts in the occipital region and spreads forward as migraine.

### **Role of complementary examinations**

#### **Cerebral TDM and MRI**

It is recommended that all patients – migrainous or not – presenting with a headache of sudden onset, developing in less than 1 min (thunderclap headache), are sent to an emergency department for appropriate complementary examinations.

A CT scan or cerebral MRI is not indicated (professional agreement):

- In a patient with a migraine defined according to IHS criteria for migraine, with or without aura;
- To differentiate a migraine from other primary headaches, in particular a tension headache.

A CT scan or cerebral MRI is recommended (professional agreement):

- In a patient with migraine attacks appearing after the age of 50 years;
- In a patient with atypical aura: sudden onset; lasting for more than 1 h; always occurring on the same side; and/or without visual symptoms;
- An abnormal clinical examination.

In a known migrainous patient, it is recommended that a cerebral scan is performed without injection of a contrast agent in the case of an unusual headache, and if the scan is normal, a cerebral MRI with arterial and venous angioMRI can be performed subsequently, within a period to be determined depending on the context (professional agreement).

#### **EEG**

There is no indication to perform an EEG in a patient with migraine defined according to IHS criteria (professional agreement). EEG is not recommended to eliminate a

secondary headache, but cerebral imaging is indicated (professional agreement). Radiography of sinuses, radiography of the neck, ophthalmological examination, orthoptic examination, abdominal echography.

There is no indication to perform radiography of the sinuses, radiography of the neck, an ophthalmological examination, an orthoptic examination, or abdominal echography in the investigation of migraine (professional agreement).

### **How do we evaluate the handicap caused by migraine for optimal management?**

Migraine is a disabling disease, due to the frequency of attacks (two or more per month in 42 – 50% of patients), their duration (>24 h in 39% of patients), their intensity (severe or very severe in 48 – 74% of patients), the accompanying digestive signs and the alterations in professional, social and familial quality of life.

In order to optimise the management of patients with migraine, it is recommended (professional agreement) that the patient keep a diary of attacks outlining the number of days per month with a migraine headache, the duration and intensity of pain, any triggering factors and all medicines used at each migraine attack (on prescription or not). The diary should also include any headaches that occur in between and their treatments. This tool helps the physician to evaluate the severity of the migraine better, to take into account changes in quality of life, to determine treatment choice and the modalities of follow-up and to detect medication abuse.

The functional repercussions of migraine and changes in productivity can be evaluated using generic and specific scales, which have been validated in French. Among these, the HIT-6 and possibly the MIDAS scale are recommended (professional agreement).

It is recommended that the patient be asked about the presence of mood or anxiety syndromes, because these increase disability and may require specific management. In practice, the HAD scale is proposed to evaluate the emotional component of migraine (professional agreement).

### **Pharmaceutical treatments**

Migraine is an under-diagnosed disease: in French studies, 40% of migrainous patients have never consulted a doctor about their migraine and 60% ignore their migrainous status and the available treatment options. This state leads to a high level of self-medication.

A study of the therapeutic behaviour of migrainous patients shows an overuse of non-specific analgesics, with several drugs often taken for the same attack and the absence of significant relief two hours after the dose in one case in two. Moreover, it reveals an

underuse of specific treatments which, when taken immediately, may be justified in patients having severe attacks or attacks that are not relieved by non-specific treatments.

### Acute treatment of migraine

#### *Efficacy of different drugs used for acute treatment*

Two types of treatment can be distinguished:

- Non-specific treatments (analgesics and non-steroidal anti-inflammatory drugs (NSAIDs);
- Specific treatments (triptans and ergot derivatives), which, by acting on 5 HT<sub>1B/D</sub> receptors, inhibit neurogenic inflammation and vasodilation supposed to be the origin of migraine headaches.

#### Non-specific treatments for migraine attacks

Proof of efficacy has been demonstrated for the following non-specific treatments:

- The following NSAIDs: naproxen, ibuprofen, ketoprofen and diclofenac (grade A methodology). Ketoprofen has marketing approval (MA) for the « treatment of migraine with or without aura » and ibuprofen has MA for the « treatment of mild to moderate migraine with or without aura »; the other NSAIDs do not have specific MA for the acute treatment of migraine;
- Acetylsalicylic acid (ASS; aspirin) as monotherapy (grade A methodology), or in association with metoclopramide (grade A methodology). Only the association ASS-metoclopramide has MA for the « symptomatic treatment of migraine and associated digestive problems »;
- Paracetamol as monotherapy (grade C methodology). Paracetamol does not have specific MA for the acute treatment of migraine.

The association of metoclopramide with ASS improves digestive symptoms, but does not increase the analgesic effect of ASS (professional agreement). There is no clinical proof that the association of caffeine with paracetamol and aspirin increases their efficacy and this combination cannot be recommended, particularly because caffeine may induce drug abuse (grade B methodology), or even addictive behaviour (professional agreement). It is recommended that opioids are avoided (codeine, opium, tramadol, morphine and other strong opioids), alone or in association, as they may induce drug abuse (grade A methodology), or even addictive behaviour (grade B methodology), and can also increase nausea (grade A methodology).

#### *Specific treatments for migraine attacks*

Proof of efficacy has been shown for the following specific treatments:

**Triptans (grade A methodology)** Triptans are effective against headaches, but also against the associated digestive symptoms as well as phonophobia and photophobia (grade A methodology). The following seven triptans have MA for « treatment of the headache phase of migraine »: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan.

There are minimal differences in efficacy and tolerance between the triptans (grade A methodology), but in practice there is great interindividual variability (professional agreement). A patient who is a non-responder to a triptan during the first attack may then be a responder (grade A methodology). Before concluding that a triptan is ineffective, it is recommended that it is tested over at least three attacks, except if there is poor tolerance (grade A methodology). A patient who is a non-responder to one triptan may respond to another (grade B methodology).

The association sumatriptan and naproxen sodium is more effective than either of the two drugs taken individually (grade A methodology). Taking a triptan early when the headache is mild is more effective than taking the triptan when the headache is moderate to severe in intensity (grade A methodology).

**Ergotamine tartrate (grade B methodology)** Ergotamine tartrate associated with caffeine has MA for the « acute treatment of migraine ».

**Dihydroergotamine (pernasal and injectable) (grade B methodology)** Dihydroergotamine via the pernasal route has MA for the « acute treatment of migraine ».

The acute treatments for migraine attacks with MA are shown in Table 3.

#### *Therapeutic strategy for migraine attacks*

The following strategy is recommended (professional agreement). During the first consultation, the patient should be asked about his/her usual treatment and the relief provided by this treatment. All acute treatments for attacks taken alone or in association should be evaluated by the response to the following four questions:

When you take your usual treatment:

- Do you have sufficient relief 1 to 2 h after taking this treatment?
- Do you use a single dose of this treatment in the day?
- Is this treatment effective over at least two attacks out of three?



**Table 3 Medicines with marketing approval (MA) for the acute treatment of migraine attacks**

Active component	Dose (per day)	Side-effects	Contraindications
<b>Symptomatic treatment for migraine attacks and for associated digestive problems</b>			
Lysine acetylsalicylate + metoclopramide	900 mg at the start of the attack	<p><i>Linked to metoclopramide</i></p> <p>Neuropsychiatric problems, late dyskinesia, extrapyramidal syndrome, endocrine problems</p> <p><i>Linked to salicylate</i></p> <p>Digestive problems, haemorrhagic syndrome, sensitivity reaction, Reyes syndrome</p>	<p><i>Linked to metoclopramide</i></p> <p>Pheochromocytoma, gastrointestinal haemorrhage, stenosis or perforation of the gut, previous history of late drug dyskinesia, contra-indicated in children</p> <p><i>Linked to salicylate</i></p> <p>Gastro-duodenal ulcer, hypersensitivity to salicylates, haemorrhagic risk</p>
<b>Specific treatments : ergot derivatives</b>			
Ergotamine tartrate	Adult/child >10 years Adult: 2 mg/day (up to 6 mg/day maximum and 10 mg/week maximum). Child >10 years: 1/2 dose	Ergotism, nausea, vomiting	Hypersensitivity to ergot derivatives, obstructive coronary artery disease, heart failure, shock, arterial hypertension, severe infection, severe liver failure
Dihydroergotamine	Adult >16 years and <65 years Endonasal solution One spray in each nostril at the start of the attack Injectable solution 1 renewable ampoule, 30 to 60 min later 2 mg maximum per day and 8 mg maximum per week	Ergotism, precordialgia with the injectable form, transient local reactions such as nasal obstruction and rhinorrhoea with the endonasal form	
<b>Specific treatments: selective 5HT1 receptor agonists (adults from 18 to 65 years)</b>			
Almotriptan	Tablet of 12.5 mg/maximum 25 mg/day	Vasomotor hot flushes, dizziness, feeling of weakness, asthenia, somnolence, nausea, vomiting, rare cases of heart flutter.	Hypersensitivity, previous history of: myocardial infarction, ischemic heart disease, coronary vasospasm (Prinzmetal angina), peripheral vascular disease, cerebrovascular accident or transitory ischemic accident
Eletriptan	Tablet of 40 mg/maximum 80 mg/day		
Frovatriptan	Tablet of 2.5 mg/maximum 5 mg/day		
Naratriptan	Tablet of 2.5 mg/maximum 5 mg/day		
Rizatriptan	Tablets of 5 and 10 mg, dry powder of 10 mg/maximum 20 mg/day		Patients with severe liver failure
Sumatriptan	Tablet of 50 mg/maximum 300 mg/day SC injection ampoule 6 mg/maximum 12 mg/day. Nasal spray of 10 and 20 mg/maximum 40 mg/day	Moderate or severe hypertension, of pins and needles, sensation of heat, of pressure or of suffocation	Moderate or severe hypertension and in patients with uncontrolled mild hypertension
Zolmitriptan	Tablet of 2.5 mg, orodispersible at 2 mg/maximum 10 mg/day		Association with monoamine oxidase inhibitors (MAOI)

- Is this treatment well-tolerated?

If the patient answers yes to the four questions, it is recommended that acute treatment is not modified. If the patient answers no to at least one of the four questions, it is recommended that a NSAID and a triptan are prescribed on the same prescription.

The patient will first take the NSAID and will keep the triptan as rescue therapy if the migraine is not relieved 1 to 2 h after taking the NSAID. This therapeutic sequence should be assessed after three attacks. If the NSAID is effective over at least two out of three attacks and if it is well-tolerated, this therapeutic sequence

should be repeated. If the NSAID is ineffective over at least two out of three attacks, the triptan should be taken as first-line to treat following attacks and the treatment should be reevaluated after three new attacks.

If the triptan used straightaway is ineffective over at least two out of three attacks and is well-tolerated, it is important to first check that the dose of triptan has been taken early (in the hour following the onset of the attack) and if this is not the case, recommend to the patient to re-try the triptan by taking it early over three consecutive attacks. If the early dose is ineffective or if it is poorly tolerated, the triptan should be changed and reevaluated by taking it early over three consecutive attacks. Finally, if

this strategy is ineffective, the patient should be told to use a NSAID and a triptan taken simultaneously.

Treatment should be adapted to the severity of the digestive signs. Antiemetics are recommended in patients with disabling nausea or vomiting.

For all patients, it is recommended to record the number of days per month when the patient is taking acute treatment, in order to spot overuse, which is frequent in migraine sufferers and may lead to chronic daily headaches. It is recommended that a patient consults as soon as they use a treatment regularly two days or more per week for more than 3 months in view of the possible prescription of prophylactic treatment (professional agreement).

No treatment has proof of efficacy to reduce the duration of aura and the triptans are not effective to prevent headaches when taken at the time of aura (grade B methodology). In the case of a migraine with aura, it is recommended that a NSAID is taken immediately at the start of aura to prevent or limit the subsequent headache (professional agreement) and to wait until the start of the headache before taking a triptan (professional agreement).

## Prophylactic treatment

### *Efficacy of different drugs used as prophylactic treatment*

Most drugs proposed as prophylactic treatment for migraine are old molecules which have not been evaluated in controlled therapeutic studies with adequate methodological quality. Taking into account the often weak methodology, the different drugs have been classed in three categories: efficacy demonstrated, probable or doubtful (Table 4):

- Efficacy demonstrated (grade A methodology): valproate and sodium divalproate, metoprolol (MA), propranolol (MA), topiramate (MA);
- Efficacy probable (grade B or C methodology): amitriptyline, atenolol, candesartan, flunarizine (MA), methysergide (MA/recently reevaluated by the Commission de Transparence with an unfavourable benefit/risk ratio), nadolol, naproxen sodium, nebivolol, oxetorone (MA), pizotifen (MA), timolol, venlafaxine;
- Efficacy doubtful (grade B or C methodology): dihydroergotamine (MA), indoramin (MA), gabapentin

The age of these drugs explains the absence of correlation between level of proof and MA. Thus, the following have MA as prophylactic treatment for migraine: dihydroergotamine, flunarizine, indoramin, metoprolol, methysergide, oxetorone, pizotifen, propranolol, topiramate. In addition to the level of proof and MA, the strategy in terms of prophylaxis is also determined by the benefit/risk ratio

(professional agreement). No drug has been shown to have superior efficacy compared to the others (grade B methodology).

### *Therapeutic strategy for prophylactic treatment (professional agreement)*

This strategy depends on a number of questions which the prescriber faces.

**When should prophylactic treatment be started?** It is recommended that prophylactic treatment is started:

- As a function of the frequency and intensity of attacks, but also the familial, social and professional handicap caused by the attacks;
- As soon as the patient uses treatment(s) for attacks more than 2 days each week, for 3 months, even in the case of efficacy, in order to avoid drug abuse.

The initiation of prophylactic treatment should be associated with an educational strategy in which it should be explained to the patient that prophylactic treatment will not prevent attacks but will reduce their frequency and intensity. Keeping a diary of attacks will allow a better appreciation of the efficacy of prophylactic treatment.

**Which drugs should be used as prophylactic treatment?** Considering the level of proof of efficacy, the benefit/risk ratio and the existence of MA, the preferred drugs to be used as prophylaxis are propranolol and metoprolol, in the absence of a contraindication to the use of betablockers. In the case of a contraindication, intolerance or inefficacy of these betablockers, the choice of drug depends on the context, including comorbidities and migraine severity, whilst also considering the benefit/risk ratio (weight gain, sedation, asthenia and teratogenic risk) and the existence of MA.

**How should prophylactic treatment be started?** It is recommended that prophylactic treatment is started as monotherapy and at a low dose, and that the dose is increased progressively to achieve the optimal dose, taking into account possible side-effects.

**How should prophylactic treatment be evaluated?** Prophylactic treatment is considered to be effective when it reduces the frequency of attacks by at least 50%. It is important to also take into account the decrease in consumption of acute treatments, and the intensity and duration of attacks. Effectiveness should be evaluated

**Table 4 Dosage, side-effects and contraindications for prophylactic treatment**

Active component	Dosage (per day)	Side-effects	Contraindications
Propranolol	40-240 mg	Frequent: asthenia, poor tolerance to effort	Asthma, heart failure, atrio-ventricular block, bradycardia
Metoprolol	100-200 mg		
Timolol (without MA)	10-20 mg		
Atenolol (without MA)	100 mg	Rare: insomnia, nightmares, impotence, depression	NB: possibility of aggravation of migraines with aura
Nadolol (without MA)	80-240 mg		
Nebivolol (without MA)	5 mg		
Oxetorone	60-180 mg (1-3 tablets) as one dose in the evening	Frequent: somnolence Rare: diarrhoea necessitating discontinuation of treatment	
Amitriptyline	10-50 mg in the evening	Dry mouth, somnolence Weight gain	Glaucoma, prostatic adenoma
Pizotifen	3 tablets per day at progressive doses	Sedation Weight gain Rare: digestive problems, dizziness, muscular pain, asthenia	Glaucoma, uredo-prostatic problems
Topiramate	50-100 mg	Paresthesia Weight loss Cognitive effects (word-finding difficulties) Rare: renal calculi, acute myopia associated with secondary angle closure glaucoma	Hypersensitivity to topiramate Pregnancy
Sodium valproate (without MA)	500-1000 mg	Nausea, weight gain, somnolence, trembling, alopecia, liver attack	Liver diseases Pregnancy
Methysergide	2-6 mg (1-3 tablets) Necessary to stop treatment for 1 month every 6 months	Frequent: nausea, dizziness, insomnia Rare: retroperitoneal fibrosis	Hypertension, heart failure, arteriopathologies, gastric ulcer, liver and kidney failure, association with triptans
Flunarizine	10 mg (1 tablet in the evening). Not for more than 6 consecutive months	Frequent: somnolence, weight gain Rare: depression, extrapyramidal syndrome	Depressive syndrome, extra-pyramidal syndrome
Gabapentin (without MA)	1200-2400 mg	Nausea, vomiting, convulsions, somnolence, ataxia, dizziness	Hypersensitivity to gabapentin
Dihydroergotamine	10 mg	Nausea	Association with triptans
Indoramin	50 mg	Somnolence, nasal congestion, dry mouth, ejaculation problems	Hypersensitivity to one of the components of the drug product, Parkinson's disease, severe heart, liver and kidney failure
Candesartan (without MA)	8-16 mg	Arterial hypotension, dizziness	Hypersensitivity, severe liver and kidney failure 2nd and 3rd trimester of pregnancy
Venlafaxin (without MA)	75-150 mg	Nausea, dizziness, hypersudation, somnolence, nervousness, dry mouth	Hypersensitivity to venlafaxine, association with non-selective MAOI, congenital galactosaemia, breast feeding



after three months. In the case of failure, there are two possibilities:

- The dose can be increased, in the absence of side-effects;
- Another treatment may be proposed.

The association of two prophylactic treatments at a lower dose may be envisaged with the aim of reducing the side-effects of each drug, after having tested them separately. In the case of repeated failures, compliance or drug abuse should be investigated.

**When should prophylactic treatment be stopped?** In the case of success, prophylactic treatment at the effective dose should be continued for six months to one year, adapted as closely as possible to the spontaneous evolution of migraine and then decreased very slowly before being stopped. The same treatment may be restarted if the frequency of attacks increases again.

### Other treatments

Relaxation, retrocontrol (biofeedback) and cognitive and behavioural therapies for the management of stress have proof of efficacy (grade A methodology) and may be recommended. Data in the literature are inconclusive about the efficacy of acupuncture (grade A methodology), but do not recommend homeopathy (grade A methodology) or spinal manipulation (professional agreement) for the prevention of migraine.

### Characteristics of migraine in children

#### Prevalence

The prevalence is estimated to be between 3 and 10%.

#### Positive diagnosis

Migraine in children can be distinguished from adult migraine by:

- Shorter attacks (1–48 h in children <15-years according to the IHS);
- A more frequent bilateral localisation;
- Digestive problems are often more important;
- Frequent initial pallor.

As in adults, it is recommended to use the diagnosis of «probable migraine without aura» when all diagnostic criteria are fulfilled except one, so as not to deprive some children of specific management. In this context, the IHS criteria for the diagnosis of migraine without aura have a lower sensitivity in children than in adults.

### Place of complementary examinations

The place of complementary examinations is the same in children as in adults. However, the indications for neuroimaging should be extended due to the difficulties in the aetiological diagnosis of headaches in children.

### Evaluation of handicap

No quality of life scale has been validated in French for migraine in children. It is recommended to keep a diary of attacks in order to help the child and his/her family identify triggering factors, to evaluate the efficacy of treatments and to allow the doctor to appreciate the severity of the migraine (frequency, intensity of attacks, associated digestive signs) and its repercussions on daily life (absenteeism from school).

### Acute treatment of migraine attacks

The following drugs are recommended in children and adolescents as first-line:

- Ibuprofen in children >6 months (grade A methodology);
- Then (professional agreement): diclofenac in children >16 kg, naproxen in children >6 years or >25 kg, aspirin as monotherapy, paracetamol as monotherapy.

In the treatment of moderate to severe migraine attacks, sumatriptan nasal spray (10–20 mg) is effective (grade A methodology) and has specific MA in adolescents from 12 to 17 years. It is recommended (professional agreement):

- To take treatment as early as possible;
- To use the rectal route in the case of nausea and vomiting;
- To use the nasal route from 12-years of age or in children >35 kg;
- To use sumatriptan nasal spray in the case of failure with paracetamol, aspirin and NSAIDs;
- For the triptans and ergot derivatives, to wait for the onset of the headache to treat an attack with aura.

### Prophylactic treatment

#### Non-pharmaceutical treatments

Relaxation, retrocontrol (biofeedback) and cognitive and behavioural therapies for the management of stress can be recommended (grade B methodology). These treatments are more effective than betablockers (grade B methodology).

#### Pharmaceutical treatments

It is recommended that prophylactic drug treatment is used after failure of non-pharmacological treatments

(professional agreement), although none of these treatments has MA in this paediatric indication. In the absence of established scientific proof, the following drugs may be proposed, in no preferential order (professional agreement):

- Amitriptyline, 3–10 mg/day;
- Flunarizine in children >10 years, 5 mg/day;
- Metoprolol, 25–50 mg/day;
- Oxetorone, 15–30 mg/day;
- Pizotifen in children >12 years, 1 mg/day;
- Propranolol, 2–4 mg/kg/day;
- Topiramate, 50–100 mg/day.

It is recommended to use these drugs at low doses, in order to limit the side-effects, particularly their sedative effects.

## **Migraine and the hormonal cycle in women**

### **Migraine and pregnancy**

#### ***Management of migraine in a woman desiring a pregnancy***

Confronted with a female migraine sufferer who wishes to become pregnant, the following recommendations can be made regarding the planning of migraine treatment:

- Reassure her that, as far as it is known, migraine is not associated with a poor evolution of pregnancy (grade A methodology);
- Reassure her by indicating that for the great majority of women with migraine, pregnancy is associated with a partial or even complete remission of migraine attacks (grade A methodology);
- Do not start prophylactic treatment (professional agreement);
- According to recommendations suggest acute treatment favouring paracetamol, but not limiting the use of aspirin, NSAIDs and triptans (ideally favouring triptans in the first 2 weeks of the cycle and aspirin or NSAIDs during the rest of the cycle) (professional agreement);
- Inform her about the antimigraine drugs that are contraindicated during pregnancy (ergot derivatives, valproate and sodium divalproate; aspirin and NSAIDs from the end of the fifth month of pregnancy) (professional agreement);
- Remind her of the risk of some drugs (notably ibuprofen) and phytotherapeutics available in the pharmacy or parapharmacy without prescription (professional agreement);
- Inform her that migraine can be treated during her pregnancy, if necessary, and that breast feeding (which is advised) will be possible (professional agreement).

#### ***Steps to take in a female migraine sufferer who has used antimigraine drugs unaware that she was pregnant***

A woman with migraine may seek advice because she has just become pregnant and has used antimigraine drugs when she did not know that she was pregnant.

#### ***Taking antimigraine drugs prophylactically when she did not know that she was pregnant***

For most of the prophylactic antimigraine drugs, it is sufficient to reassure the patient and inform them that no surveillance of the pregnancy is necessary (except if the patient has taken prophylaxis with ergot derivatives [DHE or methysergide] or valproate or sodium divalproate) (professional agreement). In the case of prophylactic treatment with a drug belonging to the class of betablockers (propranolol and metoprolol) or with tricyclic antidepressants (amitriptyline), this drug should be stopped immediately bearing in mind that if it is justified by the migraine, this treatment could be continued at the minimal effective dose (professional agreement).

In the case of prophylactic treatment with a drug that is neither a betablocker nor a tricyclic, the drug should be stopped. If prophylactic treatment is justified however, the drug should be replaced by a betablocker (propranolol or metoprolol) or possibly by a tricyclic (amitriptyline) (professional agreement).

#### ***Taking acute antimigraine treatment when the patient does not know that she is pregnant***

For most antimigraine drugs used as acute treatment for attacks, it is advisable to reassure the patient and inform them that no surveillance of the pregnancy is necessary (except if the patient has used large quantities of DHE or ergotamine tartrate) (professional agreement).

Concerning the continuation of a drug during pregnancy, the advice will depend on the drug concerned (professional agreement):

- Paracetamol: its use as first-line is possible;
- Aspirin and NSAIDs: paracetamol is preferred as first-line, but these drugs can be used as rescue therapy during the second and third trimesters, while they are contraindicated from the end of the fifth month;
- DHE and ergotamine tartrate: their use is positively contraindicated;
- Triptans: although pharmacovigilance data are reassuring, their use is contraindicated.

In all cases, exposure of the patient to drugs should be declared to pharmacovigilance (pharmacovigilance unit of the hospital, pharmacovigilance department of the company producing the drug concerned, reference centre for teratogenic agents [<http://www.lecrat.org>]).

### **Recommendations for the management of migraine in pregnancy when treatment is necessary**

A number of recommendations allow treatment in a pregnant migraine sufferer to be optimised if necessary. These recommendations are as follows:

- Plan monthly follow-up visits when remission from attacks is not observed (professional agreement);
- Propose acute treatment with paracetamol as first-line and a NSAID as rescue therapy (only during the first and second trimesters because after this time aspirin and NSAIDs are contraindicated) (professional agreement);
- If prophylactic treatment is necessary, favour a betablocker (propranolol or metoprolol) or as second-line a tricyclic antidepressant (amitriptyline) (reminding the patient that it is necessary to stop these drugs before delivery) (professional agreement);
- Remind the patient about the risks of these drugs (ibuprofen in particular) and of the phytotherapeutic preparations available from the pharmacy or parapharmacy without a prescription (professional agreement).

In all cases where a drug is prescribed, it is necessary to remember that exposure of the patient to the drug should be declared to pharmacovigilance (pharmacovigilance unit of the hospital, pharmacovigilance department of the company producing the drug concerned, reference centre for teratogenic agents: <http://www.lecrat.org>).

### **Catamenial (menstrual) migraine**

According to the international classification of headaches by the IHS (ICHD-III beta), the diagnosis of menstrual migraine depends on the appearance, during at least two out of three consecutive menstrual cycles, of an attack without aura starting between the second day before and the third day following the menstrual period, whether this menstrual period corresponds to natural menstruation or withdrawal bleeding following the discontinuation of oral oestrogenic contraceptive. The diagnosis of catamenial migraine (or purely menstrual migraine) is made in migraine sufferers who do not cite any other attack outside the menstrual period.

Although nearly half of migraine sufferers report menstrual attacks, less than 10% report a catamenial migraine (grade B methodology).

Monthly attacks are secondary to the fall in oestrogens occurring during the luteal phase of the natural menstrual cycle or during the discontinuation of oral oestrogenic contraceptive (grade B methodology). Catamenial migraine indicates a particular sensitivity to these hormonal variations in women who suffer from them.

Compared to attacks occurring outside the menstrual period, menstrual attacks are characterised by a greater severity, a longer duration and a poorer response to acute treatment (grade A methodology). These attacks may have serious repercussions as some patients may suffer anxious anticipation, the time in the menstrual cycle drives them to «anticipate» the appearance of monthly menstrual attack (professional agreement).

Menstrual migraine attacks should be treated in the same way as migraine attacks occurring outside the menstrual period (professional agreement).

In patients suffering from catamenial migraine and if acute treatment is not effective, sequential prophylactic treatment may be considered, that is to say, limited to the menstrual period. Several options can be considered knowing that none have specific MA in this indication. It is possible to use cutaneous oestradiol at a dose of 1.5 mg/day for 7 days starting on the second day before the menstrual period or withdrawal bleeding (grade B methodology). More recently, some triptans have been shown to be effective as prophylactic sequential therapy: frovatriptan at a daily dose of 2.5 mg two times/day (grade A methodology), naratriptan at a dose of 1 mg two times/day (grade B methodology) and zolmitriptan at a dose of 2.5 mg two times/day (grade B methodology). In patients taking oral contraception, menstrual migraine can be prevented by using a continuous oestrogenic or a pure progestative (professional agreement).

### **Migraine and oral contraception**

The use of oral contraception in a migraine sufferer should be considered carefully bearing two questions in mind:

- Is there a risk that the contraception will aggravate the migraine?
- Will the contraception expose the patient to a particular vascular risk?

The association between the prevalence of migraine and past or present use of oral contraception is linked to the presence of ethinyl-oestradiol (independent of the dose) but not to that of the progestative (grade A methodology). In spite of this association, the influence of contraception on migraine is subject to great inter-individual variability; thus, oral contraception is not in principle contraindicated in women with migraine (professional agreement).

Young patients (<35 years) suffering from migraine with aura have an increased neurovascular risk (grade A methodology). This neurovascular risk is increased in the presence of cofactors, particularly smoking and the use of oestrogenic oral contraception (grade A methodology). In young migraine sufferers with aura, particularly when they smoke, oestrogenic oral

contraception is contraindicated and oral contraception which is purely progestative or another means of contraception should be preferred (professional agreement).

#### **Migraine and hormonal treatment of the menopause (HRT)**

The use of hormone replacement therapy (HRT) in a woman with migraine should be considered bearing two questions in mind:

- Is there a risk that HRT will have an influence on the migraine?
- Is there a risk of cerebral ischaemia from HRT in the migrainous patient?

#### ***Influence of HRT on the course of migraine***

Transversal studies (grade B methodology) have demonstrated a significant association between HRT use and persistence of migraine attacks. Longitudinal studies (grade B methodology) have shown that transdermal oestradiol induces fewer migraines than oral conjugated oestrogens and that HRT taken continuously induces fewer migraine attacks than discontinuous treatment.

#### ***HRT, migraine and the risk of cerebral infarction***

HRT is an independent risk factor for cerebral infarction with a low but significant relative risk (RR = 1.29; 95%CI: 1.06 – 1.56) as shown in a meta-analysis (grade A methodology). No data are available on the risk associated with both migraine and HRT combined.

Overall, migraine is not a contraindication for HRT, but if aggravation of migraine is observed, notably with aura on HRT, alternatives should be discussed with the patient, including a change to a transdermal form, a reduction of the oestradiol dose, or stopping HRT completely.

#### **Future developments**

Taking into account the current clinical developments (such as CGRP receptor antagonists and other non-vasoconstrictive treatments), the recommendations of the working group should be amended when necessary during the next five years. Future actions should also be adapted to the recommendations for patients.

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#### Competing interests

MLM declares conflicts of interest with: Allergan, Almirall SAS, AstraZeneca Pharmaceuticals, GlaxoSmithKline Inc, Grunenthal, Eli Lilly & Company, Johnson & Johnson, Medtronic, Menarini, Merck, Pierre Fabre, Pfizer Inc, Sanofi-Aventis, UCB, Zambon.

DV declares conflicts of interest with: Allergan, Almirall, BMS, MSD, GSK, Janssen Cilag, Menarini, MSD, Pfizer, Sanofi-Aventis, UCB, Astra-Zeneca, Zambon.

GG declares conflicts of interest with: Allergan, AstraZeneca Pharmaceuticals, Menarini, Merck, Pfizer Inc., Zambon.

CL declares conflicts of interest with: Allergan, Almirall, AstraZeneca Pharmaceuticals, Boehringer, GlaxoSmithKline Inc, Grunenthal, Lilly, Menarini, Merck, SanofiAventis, Pfizer Inc., UCB-Schwarz-Pharma, Zambon.

AD declares conflicts of interest with: Allergan, Almirall SAS, AstraZeneca Pharmaceuticals, GlaxoSmithKline Inc, Grunenthal, Merck, Menarini, Orkyn, Pfizer Inc, Zambon.

#### Authors' contributions

MLM, DV, GG, CL and AD drafted the manuscript. All authors read and approved the final manuscript.

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