Guideline- Management of Migraine and Cluster Headache

1. BACKGROUND

Headache is a common neurological condition which accounts for 4.4% of primary care consultations and 30% of neurology appointments. Primary headache disorders include migraine, tension-type and cluster headache. Twice as many women as men are affected by headache disorder. This is thought to be due to changes in hormone levels during the menstrual cycle, which can be more pronounced at puberty and menopause.

Recommendations within this guideline are based on best evidence and national/international guidelines. They are followed by consultants and specialist nurses working within the neurology department. Some recommendations may be for medicines prescribed outside their product license i.e. off label. It is noted in the guideline when the medicine is off label and relevant guidelines should be followed when prescribing medicines off label.

The colours on the drug names in this guidance refer to the classification in the joint formulary i.e.
- Red – specialist prescriber only
- Amber – prescribed in accordance with approved shared care framework
- Blue - Guideline Led prescribed on advice of specialist or in line with national / local guideline
- Green – other items listed on formulary suitable for initiation and prescribing by any prescriber

If printed in black and white please refer to joint formulary for classification of medicines.

Migraine

Migraine is often underdiagnosed, misdiagnosed and undertreated. It is estimated in UK that around £3 billion/annum is lost in direct and indirect costs due to migraine.

Acute treatment

Offer combination therapy for acute treatment of attacks e.g. triptan plus NSAID. Acute treatment is used either to abort an attack of migraine or to significantly reduce the severity of the headache and other symptoms. Acute treatment should be taken as soon as the patient knows they are developing a migraine headache.

**NSAID**

Use ibuprofen 400mg or naproxen 500mg as a first line treatment option. Both ibuprofen and naproxen are effective for 2 hours pain relief as well as relieving migraine associated symptoms of nausea and photophobia. Ibuprofen is licensed for acute migraine treatment and the dose can be increased to 600mg if ineffective. Naproxen is not licensed for acute treatment of migraine.

Ibuprofen can be used in pregnancy until 28 weeks and is the NSAID of choice in pregnancy. Repeated use should be avoided after 28 weeks gestation.
Aspirin
Aspirin 900mg is effective for 2 hour pain relief and is recommended as a first line treatment option. High dose aspirin is a potential gastric irritant, however single doses usually only have mild transient adverse effects. It is contraindicated in under 16s due to risk of Reyes syndrome and in the third trimester of pregnancy.

Triptans
Sumatriptan 50mg-100mg is the first line triptan. In patients with severe acute migraine or early vomiting non-oral triptans may be considered. Eletriptan is superior for pain free at 2 hours and associated with a reduced need for rescue medicines. It may be recommended by specialist in patients with insufficient response to sumatriptan. For menstrual migraine frovatriptan is the triptan of choice. If early vomiting is an issue nasal or subcutaneous triptans may be recommended by specialist.

Antiemetics
If a prokinetic effect required either metoclopramide or domperidone are recommended. If nausea/vomiting are an issue buccal prochlorperazine should be considered.

Paracetamol
Paracetamol should only be used for migraine when other treatments unsuitable.

Opiates
Opiate based medicines for the acute treatment of migraine and are not recommended.

Prevention of Migraine
Migraine can have considerable impact on quality of life and daily function. The decision about when to start migraine prophylaxis is best guided by the impact of migraine on each patient (rather than focusing on the absolute number of migraines per month). Overusing acute medicines can limit the effectiveness of prophylaxis medicines and medication overuse should be assessed and addressed.

Prophylactic treatment should be used for at least 3 months at maximum tolerated dose prior to deciding if it is effective or not. In many patients it is possible to phase out their prophylactic medicine after 6-12 months. There are very few trials comparing different prophylactic drugs for migraine and those that are available are not powered sufficiently to assess effectiveness between treatments; hence the first line treatments listed below should be offered dependent on patient preference and concomitant medicines and medical conditions.

Beta blockers
Beta blockers are a first line treatment for prophylaxis of episodic and chronic migraine as per NICE guidelines. The beta blocker of choice is propranolol. It should be titrated up to a dose of 80-160mg per day (MR preparation preferred). Atenolol can also be used at a dose of 50-100mg/day if sleep disturbances are an issue. Beta blockers should not be used in asthmatic patients.

Candesartan
There is evidence suggesting that candesartan is effective at reducing number of headache days in migraine. This is an unlicensed use of candesartan. Candesartan is well tolerated and has a good side effect profile. Candesartan can be prescribed at a dose of 16mg daily for episodic or chronic migraine. It does not usually affect blood pressure in normotensive patients. [SIGN 2018]
**Tricyclic antidepressants (TCAs)**
TCAs are a first line treatment for migraine. Amitriptyline can be used at a dose of 25-150mg at night – this can be started at 10mg and titrated up according to response and tolerance. TCAs are unlicensed for treatment of migraine. The main side effects from TCA therapy are drowsiness and dry mouth. If drowsiness is an issue with amitriptyline a less sedating TCA can be use – e.g. nortriptyline.

**Topiramate**
Topiramate is effective at reducing monthly migraine frequency and monthly migraine days in trials. It is associated with a number of side effects including nausea, paraesthesia, anorexia and weight loss. In particular cognitive side effects are common, vary in severity, are dose related and often define drug tolerability. Topiramate is associated with an increased risk or abnormal oral cleft development in infants during the first trimester of pregnancy. Hence women who may become pregnant should be advised of the risks of topiramate during pregnancy, the need for effective contraception and the need to seek further advice on migraine prophylaxis if pregnant or planning a pregnancy. It is recommended as a first line treatment by NICE guidelines at a dose of 50-100mg daily (titrated as per licence). There is no benefit to doses greater than 100mg daily (minimal further reduction in migraine and increased risk of side effects).

**Flunarizine**
Flunarizine is a calcium channel blocker which is unlicensed in the UK. It has a similar efficacy to propranolol, topiramate and valproate. It is generally well tolerated. Depression is a potential adverse drug reaction; so is not recommended in patients with a history of depression. As it is a calcium channel blocker must check blood pressure 2 weeks after initiation. Flunarizine dose is 10mg daily.

**Botulinum toxin type A**
Is commissioned as per NICE TA for chronic migraine. Botulinum toxin type A is recommended as an option for the prophylaxis of headaches in adults with chronic migraine (defined as headaches on at least 15 days per month of which at least 8 days are with migraine):
- that has not responded to at least three prior pharmacological prophylaxis therapies and
- whose condition is appropriately managed for medication overuse.

**Erenumab/ Fremanezumab**
These are new class of agents with direct action on the calcitonin gene-related peptide (CGRP) receptor. This is a novel action which is relevant to migraine pathophysiology. They are not currently commissioned in Hull or East Riding. NICE has reviewed erenumab and it did not fulfill cost effectiveness requirements.

**Menstrual migraine**
A drop in oestrogen prior to menstruation is a known trigger for migraine. Triptans reduce the occurrence of migraine both menstrually related and pure menstrual migraine from 2 days before the start of bleeding and 3 days after. Frovatriptan 2.5mg twice a day is the triptan of choice (low NNT/high patient numbers). It is also effective at reducing migraine severity and need for rescue medication.
Cluster Headache and other trigeminal-autonomic cephalalgias
All these headache syndromes have two features in common: short-lasting, severe headaches and accompanying typical cranial autonomic symptoms. There are differences in duration of attack, frequency and rhythmicity of the attacks and in the intensity of pain and autonomic symptoms.

Episodic and chronic cluster headache
Cluster headache (CH) is defined as a paroxysmal, strictly unilateral, very severe headache, typically with a maximum of pain focused in the retro orbital area. Even though the attacks are short-lasting, CH is excruciatingly painful and patients suffer badly. During a cluster period frequent attacks can be disabling to patients. The goal of treatment is attack cessation or suppression until the next episode.

Attack treatment
Oxygen.
Inhalation of 90% oxygen via a non-rebreathing face mask with a flow rate of at least 7L/min (sometimes more than 15 L/min is required). The oxygen should be inhaled for 10-20 minutes. About 60% of all cluster headache patients respond to this treatment with significant pain reduction.

Non-oral triptans
Sumatriptan subcutaneous (6mg), sumatriptan 20mg intranasal and zolmitriptan 5mg intranasal are effective in the acute treatment of cluster headache. The quantity supplied needs to match usage. There is no evidence supporting the use of oral triptans for cluster headache.
Doses:
- zolmitriptan intranasal 3 doses/24 hours,
- sumatriptan s/c max 12mg/24 hours,
- sumatriptan intranasal 10-20mg/dose max 100mg/24 hours.

Cluster headache prophylaxis
Verapamil
Verapamil in a total daily dose of 240-960mg is the first line choice in the prophylaxis of episodic and chronic cluster headache. Initially it should be started at a dose of 80mg TDS and titrated upwards usually every 14 days. Modified release formulations can be used to reduce tablet burden and aid compliance. The full efficacy of verapamil can be expected within 2-3 weeks.

Lithium carbonate
Lithium carbonate in a total daily dosage between 600 and 1500mg has been studied in multiple open trials. It is used in both episodic and chronic cluster headache if verapamil is ineffective or contraindicated. Monitoring of the lithium level is required (should be between 0.3 and 1.2mmol/l). Monitoring requirements are in the SCF for lithium carbonate.

Corticosteroids
Corticosteroids may be recommended for short term treatment (2-3 weeks) high dose prednisolone 30mg or greater. Initial dose may be as high as 60-100mg prednisolone for 2-5 days. Prednisolone may be used while titrating other prophylactic drugs to therapeutic dose.

Melatonin
As cluster headache is thought to be related to circadian effects melatonin has been tried as prophylaxis with varying results. As it is well tolerated with limited side
effects then it may be tried in combination with other therapies at a dose of 10mg at night. Modified release preparations can be used.

Other treatments:

- **Greater occipital nerve block** – Lidocaine with or without corticosteroids can be used in an outpatient setting by specialist teams. It is often used instead of oral steroids as a bridging treatment while awaiting preventative medicine such as verapamil to take effect.

- **gammaCore**: this is an innovative medical device treatment for cluster headache. It is a non-invasive vagus nerve stimulator which enables the patient to ‘zap’ their vagus nerve to reduce pain from cluster attacks. It is NHS England funded and NICE approved. It is prescribed by specialist teams following failure of first line prophylactic treatment i.e. verapamil. It can be used as a daily prophylaxis and an acute treatment.

**APPROVAL PROCESS**

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