



Therapeutics Today

March 2010

Number 3

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Medication overuse headache (MOH) occurs in 1% of adults and is most prevalent between 40-50 years of age, affecting women 3 times more than men (*DTB 2010; 48: 2-6*). It occurs in patients with a history of primary headache, most commonly those with migraine and/or tension-type headache. MOH occurs with overuse of any acute or symptomatic headache treatment including: NSAIDs, paracetamol, codeine or dihydrocodeine, combination analgesics containing caffeine and codeine, and chronic use of triptans and ergotamine. While many patients with MOH use very large quantities of medication (e.g. 35 doses/week), the **frequency of dosing rather than the absolute quantity of drug is more important**. Evidence suggests that the onset of MOH vs. duration of headache treatment is shortest for triptans (~ 1.7 yrs) and longest for simple analgesics (~ 4.8 yrs). The type of MOH varies with some patients reporting a migraine type headache and others a tension-type headache, which is often present and at its worst on waking in the morning. **Diagnosis** is made from the patient's history and clinical presentation; headache occurring ≥ 15 days/month, regular overuse for >3 months of ≥ 1 acute/symptomatic treatment drugs (ergotamine, triptans, opioids or combined analgesics on ≥ 10 days per month or simple analgesics alone or any combination of ergotamine, triptans and analgesic opioids on ≥ 15 days/month) and the development or marked worsening of headache during medication overuse. Assessment should also include search for possible complications of regular drug intake (e.g. recurrent gastric ulcers, anaemia). **Measures to prevent MOH** include patient education and restriction of medicines, thought to be responsible i.e. restriction of triptans to <10 treatment days/mth, analgesics to <15 days/mth and avoidance of migraine drugs containing caffeine and opioids. Early migraine prophylaxis with medical or behavioural treatment or acupuncture reduces the use of acute medication, which may help prevent MOH.

The management of MOH involves stopping the overused medication, managing withdrawal symptoms, reviewing and assessing the underlying primary headache disorder and preventing relapse. Patients are more successful if they are motivated; they should be warned that withdrawal may initially aggravate symptoms (e.g. withdrawal headache +/- nausea, vomiting, tachycardia, sleep disturbances, anxiety). Withdrawal should be planned in advance, done under supervision and may require leave from work. Most drugs causing MOH can be stopped abruptly apart from drugs such as opioids. The duration of the withdrawal headache depends on the type of overused medication; improvement usually occurs by 10 days with triptans, by 3 weeks with simple analgesics and 4 weeks with opioids. Vomiting, due to withdrawal, can be treated with an antiemetic. While there is limited evidence, some specialists recommend naproxen for withdrawal headaches (unlicensed indication); prednisolone and triptans have also been used with mixed results. Patients should be reviewed 2-3 weeks following withdrawal and if headaches persist, specialist referral should be considered. The mean success rate for withdrawal therapy (i.e. 50% reduction in headaches) at 6 months is approximately 72%; success is better with migraine type headaches, overuse of triptans and shorter duration of medication. Most patients revert to their original headache type within 2 months and may require reintroduction of the overused medication with explicit restrictions on the frequency of medication use. Consideration should be given to using an alternative approach to treatment of the primary headache including: massage, acupuncture and behavioural therapies. Patients with frequent headache may find that previously ineffective prophylactic drugs may become effective following treatment of MOH. Relapses of MOH occur commonly (up to 41% in the first year); these may be prevented by patient education and the avoidance of combination drugs.



Clostridium difficile in Ireland *C.difficile* is increasingly regarded worldwide as one of the commonest healthcare-associated infections. The spectrum of infections ranges from asymptomatic colonisation to potentially fatal colitis. The recently published Epi-Insight looked at the epidemiology of *C. difficile* in Ireland from May 2008-December 2009 (<http://www.hpsc.ie/hpsc/EPI-Insight/Volume112010/>). *C.difficile*-associated disease (CDAD) typically presents as diarrhoea, abdominal cramps, fever and leucocytosis, occurring after recent antibiotic therapy. Pseudo-membranous colitis is the most severe manifestation of disease. The prevention and control of CDAD include good antibiotic prescribing practices, active surveillance and compliance with infection prevention and control measures. Since May 2008, *C.difficile* infection has been notifiable (category of acute infectious gastroenteritis). The report notes a crude incidence rate of 56.9 cases/100,000 population in 2008 and 45.1/100,000 in 2009. Data suggest a decline in the number of new CDAD reported cases for 2009 vs. 2008, however, due to the large weekly variability in the data, it is too soon to decide if this decline is significant. New cases of CDAD were more prominent in female patients (57.6%) and older age groups (mean age of 71 years, range 2-102 years). The majority of cases were notified by hospitals (62.9%), while 7.8% were classified as GP patients, 2.8% as hospital outpatients, 0.2% as hospital day patients and the remainder as "other", "unspecified" or "unknown". The report notes that these classifications represent the location of the patient at time of CDAD diagnosis and therefore don't provide information on the origin or onset of the disease. The HPSC has recently commenced enhanced CDAD surveillance to capture information on recurrent infection and details regarding the origin or onset of disease. Further details of the enhanced surveillance scheme are available on the HPSC website (www.hpsc.ie).



Antiepileptic drugs and contraception The UK Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit (CEU) recently issued a statement regarding antiepileptic drugs and contraception. The metabolism of oestrogen and progestogen is known to be increased by cytochrome P450 inducing antiepileptic drugs (AEDs). The Faculty recommends the consistent use of condoms in women using any enzyme-inducing AED (e.g. carbamazepine, phenytoin) with combined hormonal contraception (CHC) (i.e. combined oral

contraception, vaginal ring, patch), the progestogen-only pill (POP) or progestogen implant. The efficacy of the progestogen-only injectable - depot medroxyprogesterone acetate (DMPA) is not reduced. In view of the potentially serious consequences of contraceptive failure in patients on AEDs, it is recommended that **women on long-term enzyme-inducing AEDs should use an alternative reliable method of contraception including DMPA or intrauterine methods**. Lamotrigine is not thought to induce liver enzymes, however it does appear to reduce levonorgestrel levels, even though the clinical significance of this is unknown. **Ethinylestradiol** is thought to induce lamotrigine glucuronidation, which results in **reduced lamotrigine levels** and which may in turn result in increased seizures in women on lamotrigine and CHC. Due to the risk of drug interactions the use of lamotrigine monotherapy with CHC is a UKMEC Category 3 (risks generally outweigh the benefits). Progestogen-only methods of contraception are not affected by lamotrigine. Studies suggest that the AEDs sodium valproate, levetiracetam, vigabatrin, pregabalin, zonisamide, tiagabine and gabapentin do not affect the pharmacokinetics of oral contraceptives. Regarding **emergency contraception**, women who choose to use progestogen-only emergency contraception, may be advised to double the dose of levonorgestrel (taken within 72 hrs of unprotected sexual intercourse), although there is no evidence to support the need for this (unlicensed use).

DMPA has been associated with reduced bone mineral density (BMD) and there have been recent safety concerns regarding long-term treatment with carbamazepine, phenytoin, primidone and sodium valproate associated with decreased BMD. The CEU recommends that women should be informed about the potential effect of both drugs and the risks/benefits of using DMPA should be assessed on an individual basis. The full CEU document can be viewed on <http://www.ffprhc.org.uk/>



Community acquired MRSA (CA-MRSA) is estimated to account for <0.05% of all MRSA, however, it is increasing in prevalence. A recent paper reviewed this topic (*DTB 2011;48:14-19*). CA-MRSA differs from hospital-acquired MRSA in a number of ways; the typical patient is young, previously healthy, and the organism is isolated in an outpatient or community setting or within 48 hours of hospital admission. CA-MRSA organisms may be

more virulent than hospital-acquired MRSA, as they are more likely to carry Panton-Valentine leucocidin (PVL) genes, which results in lysis of white blood cells. **Diseases** caused by CA-MRSA include skin, soft tissue and bone or joint infections and community acquired pneumonia; CA-MRSA infections may be severe and associated with septic shock. The prognosis for CA-MRSA skin and soft tissue infections is generally good, however recurrence is common. These infections are classified as complicated if the infection spreads to deeper tissues, if surgical intervention is necessary or if the patient has a co-morbid condition (e.g. diabetes mellitus). CA-MRSA pneumonia is most common in young healthy adults and may be preceded by a flu-like illness or associated with a focal skin infection. The most severe cases can lead to acute respiratory distress syndrome; patients with PVL positive CA-MRSA pneumonia have a worse prognosis than those caused by PVL-negative strains.

Diagnosis of CA-MRSA depends on testing appropriate microbiological samples (e.g. pus, exudates, sputum). Cultures should be taken from septic sites if CA-MRSA is suspected, if there are recurrent furuncles or abscesses, if the infection is severe or if there is a history of spread in the family. In cases of severe infection, samples may be sent for toxin gene profiling (if PVL positivity suspected). **Management:** Patients with localised CA-MRSA abscesses are frequently cured with surgical drainage alone; when there is suspected infection by PVL-positive *S. aureus* in deep tissues, surgical management should be guided by repeated imaging. Small abscesses without cellulitis should be incised and drained; systemic antibacterial therapy should not be given to patients with minor skin and soft tissue infections or minor abscesses. Empirical or culture guided antibacterial therapy should be started for large abscesses, co-existing infection in family members, if the patient is immunocompromised, is an infant or is deteriorating clinically. Patients with a suspected serious or deep-seated MRSA infection should be treated in hospital and those with CA-MRSA pneumonia should be referred to intensive care as soon as possible. Antibacterial drugs that have been used to treat both hospital and CA-MRSA infections include: clindamycin, co-trimoxazole, daptomycin, doxycycline, fusidic acid, linezolid, rifampicin, teicoplanin, tigecycline and vancomycin, however the choice of drugs depends on published guidelines, local resistance patterns and patient-specific factors such as culture results. Intravenous immunoglobulins have also been used (although only sparse clinical data are available) for staphylococcal toxic shock syndrome and necrotising PVL-associated staphylococcal sepsis when other treatments have failed. The paper concludes that CA-MRSA is distinguishable from the hospital-acquired MRSA strains by its presentation, virulence factors and anti-bacterial resistance profile. It recommends that personal and environmental hygiene measures be used to control the spread of CA-MRSA in the community.

Every effort has been made to ensure that this information is correct and is prepared from the best available resources at our disposal at the time of issue. References are available on request. This newsletter is produced by the National Medicines Information Centre, St. James's Hospital (SJH) Dublin 8 and Dept of Therapeutics Trinity College, Trinity Centre, SJH. Tel: Direct Line (01) 473 0589 or 1850 727 727 Fax: (01) 473 0596 Email: nmic@stjames.ie