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MeReC Publications

Cochrane review supports the use of paracetamol in acute migraine

A Cochrane review of 10 studies with over 2,700 adults, found that a single oral dose of paracetamol 1000mg was effective in relieving moderate to severe migraine symptoms, compared with placebo. Paracetamol 1000mg plus metoclopramide 10mg was as effective but better tolerated than sumatriptan 100mg for moderate to severe migraine pain.[1]

Action

Health professionals should continue to follow the recommendations from Clinical Knowledge Summaries (CKS) that paracetamol 1000mg used alone is an appropriate first-line analgesic for the treatment of acute migraine headaches that are not very severe and disabling. In particular, community pharmacists advising people on over-the-counter treatment for acute migraine should consider these new data in discussion with patients. Furthermore, if nausea or vomiting is troublesome, paracetamol 1000mg plus metoclopramide 10mg is an option that appears to be as effective as, but better tolerated than, sumatriptan 100mg.

What did this study find?

When taken for moderate to severe pain, paracetamol was superior to placebo for all efficacy outcomes including being pain free at two hours (n=717; risk ratio [RR] 1.80, 95% confidence interval [95%CI] 1.24 to 2.62; number needed to treat [NNT] 12), and having headache relief at two hours (n=717; RR 1.55, 95%CI 1.32 to 1.83; NNT 5). Furthermore, the addition of metoclopramide 10mg to paracetamol provided short-term efficacy equivalent to oral sumatriptan 100mg alone. When taken for moderate to severe pain, there was no significant difference in headache relief at 2 hours between paracetamol plus metoclopramide and sumatriptan (n=1,140; RR 0.93, 95%CI 0.81 to 1.10). The proportion of patients experiencing adverse events was significantly lower with paracetamol plus metoclopramide, compared with sumatriptan (n=1,328; 28% vs. 47%; RR 0.61, 95%CI 0.53 to 0.71; number needed to harm [NNH] 5).[1]

As paracetamol has a good safety profile and is well tolerated, it may offer advantages over aspirin and other NSAIDs, particularly for those at high risk of gastrointestinal or cardiovascular adverse events. If nausea or vomiting is troublesome, paracetamol plus metoclopramide is a reasonable option. CKS recommends an individualised, stepwise approach, using the least expensive drugs with known efficacy first, before advancing up the treatment ladder to migraine-specific drugs (i.e. triptans).

For more details of this meta-analysis and its limitations see MeReC Rapid Review No. 2520. More information on managing migraine and the evidence to support the use of other drug treatments can be found in the NPC migraine e-learning materials.

References

1. Derry S, et al. Paracetamol (acetominophen) with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD008040. DOI: 10.1002/14651858.CD008040.pub2

All information was correct at the time of publication (April 2011)

Inhaled corticosteroids and the risk of diabetes

A Canadian cohort study (n=388,584) found that, in patients treated for respiratory disease using inhaled corticosteroids (ICS), current use of an ICS was associated with, on average, a 34% relative increased risk of both new-onset diabetes and diabetes progression over 5.5 years, compared with patients not treated with an ICS in the previous 30 days. This risk increased with the dose of ICS: patients treated with high doses of ICS, equivalent to fluticasone 1000microgram/day or more, had a relative risk increase of 64% for developing diabetes compared with patients not treated with an ICS.[1]

Action

Prescribers should follow the British guideline for the management of asthma with regard to the use of ICS in patients with asthma. The dose of ICS should be titrated to the lowest dose at which effective control is maintained. In COPD, an ICS should be used only in combination with a long-acting beta-agonist and only in accordance with the NICE guideline for the management of COPD.

Further information

The potential for ICS to increase the risk of diabetes is another possible adverse effect to consider when reviewing the risks and benefits of ICS with patients, particularly if high doses are being considered for a prolonged period. Based on an estimated baseline risk of 1.36% per year, and an increased relative risk of 64%, we calculate that the NNH for patients taking a high-dose ICS is approximately 21 over 5.5 years. Or putting it another way, if 21 patients are treated with high-dose ICS for 5.5 years, one of them will develop diabetes requiring drug treatment who otherwise would not have done if they had not been prescribed high-dose ICS.

Systemic side effects are of crucial importance when considering the benefits and risks for individuals with asthma or COPD for whom an ICS is being considered, and healthcare professionals should be prepared to discuss these with patients. Pending further data and/or formal consideration by the regulatory authorities, among the other side effects of ICS (e.g. adrenal suppression, osteoporosis), prescribers may need to be aware of the potential for ICS to increase the risk of, and be vigilant for, the development of diabetes, particularly if used at high doses for prolonged periods.

For more information on this study and its limitations see MeReC Rapid Review No. 2485. Further information on COPD and asthma can be found in the NPC respiratory e-learning materials.

References

1.Suissa S, et al. Inhaled corticosteroids and the risks of diabetes onset and progression. Am J Med 2010;123:1001–6

Antihypertensives and cancer: A2RA use with ACE inhibitors may increase risk

An analysis of randomised controlled trials (RCTs, n=324,168)) found no evidence of an increased risk of cancer and cancer-related deaths with drugs commonly used for the treatment of hypertension, including angiotensin II receptor antagonists (A2RAs). However, an increased risk of cancer with the combined use of an A2RA and an ACE inhibitor could not be ruled out.[1]

Action

Health professionals should follow the NICE guideline for the management of hypertension. A2RAs are an alternative to ACE inhibitors only where a renin-angiotensin drug (RAD) is indicated, but an ACE inhibitor is not tolerated.

Further information

This study provides some reassurance that A2RAs and other antihypertensive agents (ACE inhibitors, diuretics, beta blockers, and calcium channel blockers) are not associated with a significantly increased risk of cancer. There is little robust evidence of a clinically significant benefit of combining an ACE inhibitor and an A2RA, except as a specialist second-line treatment for some patients with heart failure (see NICE clinical guideline 108). In addition, use of this combination increases the risk of side effects e.g. renal impairment.[2] Even though the increased risk of cancer seen in this study with an ACE inhibitor and an A2RA used together was not significant in every analysis, and was driven mainly by one study,[2] the remaining uncertainty provides another good reason for limited use of this combination, and then only with careful monitoring.

See MeReC Rapid Review No. 2491 for details on this analysis and how it relates to other studies. More information on hypertension can be found in the cardiovascular disease — hypertension e-learning materials. More information on the use of ACE-inhibitors and A2RAs can be found in the RADs national support materials.

References

1.Bangalore S, et al. Antihypertensive drugs and risk of cancer: network meta-analyses and trial sequential analyses of 324 168 participants from randomised trials. Lancet Oncol 2011;12:65–82

2.The ONTARGET investigators. Telmisartan, ramipril or both in patients at high risk for vascular events. New Engl J Med 2008;358:1547–59

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Further improvement possible in the drug management of heart failure

The National Heart Failure audit 2010 confirms there have been improvements in the use of key treatments for heart failure, such as ACE inhibitors and beta blockers. However, more could still be done to ensure patients are provided with the full range of effective treatments to manage their symptoms and improve their quality of life. Beta blockers, in particular, seemed to be underused. Mortality rates were significantly lower in those who had access to specialist care.[1]

Action

Health professionals should continue to follow the recently updated NICE guideline for the management of chronic heart failure in adults. **ACE inhibitors and beta blockers licensed for heart failure** should both be considered as first-line treatments, using clinical judgement to decide which drug to start first. Second-line options should be started only after specialist advice. This audit recommends that all secondary care service providers should streamline the heart failure care pathway to ensure all patients, regardless of admission ward, have access to the medication recommended by NICE and are managed by specialist staff.[1] For primary care providers, this highlights the importance of thorough follow-up of patients with heart failure after discharge from hospital to check that prescribing is in line with NICE guidance and, in particular, that medication doses are adjusted to target doses, where appropriate.

What did the audit find?

The audit suggested that, between April 2009 and March 2010, beta blockers were being underused: of 17,523 patients with recorded data on beta blockers, 10,544 (60%) were prescribed them (see **figure 1**). It also highlighted that of 5,214 patients with a reported dose of a beta blocker, 66% received less than half the target dose. Men and patients aged less than 75 years were likely to receive higher doses.[1]

The audit found that of 19,240 patients, 14,421 (75%) were reported to have been prescribed ACE inhibitors and A2RAs (see **figure 1**). Of 5,929 patients with a reported dose of an ACE inhibitor, 49% received less than half the target dose.[1]

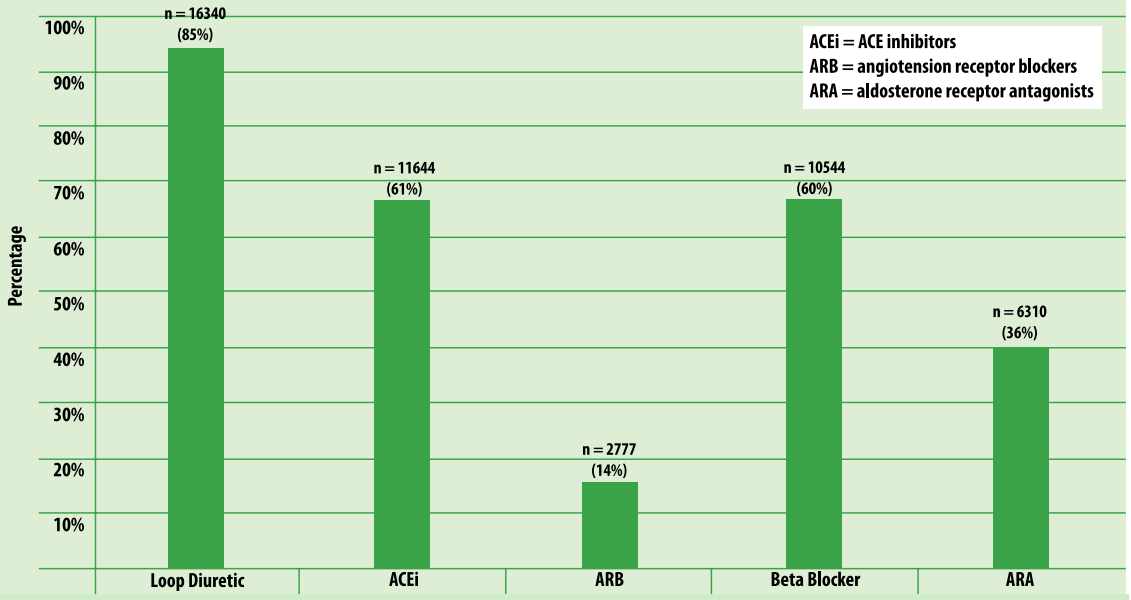
More information on what the audit found is available in MeReC Rapid Review No. 2479. Information on heart failure is available in the NPC heart failure e-learning materials.

References

1. The NHS Information Centre. National Heart Failure Audit. 2010

Figure 1: Drug treatment on discharge from hospital

Note: Percentage of all patients including those with missing data. This is worst case scenario for uptake



Source: National Heart Failure audit. Copyright © 2010, The NHS Information Centre.

The National Prescribing Centre (NPC) is responsible for helping the NHS to optimise its use of medicines. NPC is part of the National Institute for Health and Clinical Excellence (NICE), an independent organisation providing national guidance on promoting good health and preventing and treating ill health.

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