National Prescribing Centre
Provided by NICE

MeReC Monthly

No.43 October 2011

MeReC Publications

'Glitazone' use associated with pneumonia in meta-analysis

The RECORD study (rosiglitazone) and the PROactive study (pioglitazone) raised concerns about a possible increased risk of pneumonia with these medicines. This meta-analysis[1] of 13 published and unpublished randomised controlled trials (RCTs) which compared 'glitazones' with controls (n=17,627) found that their use was associated with an increased risk of pneumonia or lower respiratory tract infection (LRTI) in patients with type 2 diabetes (1.59% vs. 1.06%; relative risk 1.40, 95% confidence interval [CI]1.08 to 1.82). Based on the average control event rate in the included trials, the number needed to harm over 3.7 years was 239 (95% CI 117 to 1191).

Action

Healthcare professionals should continue to follow NICE guidance on type 2 diabetes, which places pioglitazone usually as a third-line hypoglycaemic option for patients in addition to metformin and a sulfonylurea. However, prescribers should be aware of several safety concerns with this class of drugs: notably heart failure, fractures, and now, possibly, pneumonia. Also see the following article regarding the increased risk of bladder cancer with pioglitazone.

So what?

There are limitations with this meta-analysis, mainly reflecting the quality of the reported data, as discussed in MeReC Rapid Review No. 3909. However, it provides a safety signal about glitazones and a possible association with an increased risk of pneumonia and LRTI. This is in addition to previous concerns with this class of drugs and regulatory authorities continue to review the safety of pioglitazone. Further information on glitazones can be found on NHS Evidence and the type 2 diabetes e-learning materials on the NPC website.

* Glitazones are also known as thiazolidinediones

Reference

1. Singh S, et al. Long-term use of thiazolidinediones and the associated risk of pneumonia or lower respiratory tract infection: systematic review and meta-analysis. Thorax 2011; 66:383–8

MHRA advice on pioglitazone and risk of bladder cancer

The August 2011 edition[1] of Drug Safety Update (DSU) highlighted that the use of pioglitazone is associated with a small increased risk of bladder cancer. It outlined new warnings and precautions for use in at-risk patients.

Action

Healthcare professionals should follow the MHRA advice below:

- Patients with a current or past history of bladder cancer and those with uninvestigated haematuria should not receive pioglitazone.
- Individuals receiving pioglitazone should be reviewed after 3 to 6 months to ensure treatment continues only in those deriving benefit. (NICE guidance recommends pioglitazone should only be continued if there is a reduction in HbA1c of at least 0.5 percentage points in six months).
- Known risk factors for development of bladder cancer should be assessed before starting pioglitazone: age; any history of smoking; exposure to some occupational or chemotherapy agents; previous pelvic region irradiation.
- Elderly patients should be considered carefully before and during treatment with pioglitazone, using the lowest possible dose because of associated increased risks of bladder cancer and heart failure, which also increase with age.

Further information

This MHRA advice follows a Europe-wide review by the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP). This found a small increased risk of bladder cancer in patients taking pioglitazone. However, it concluded that the benefits continue to outweigh the risks for those who respond to treatment where there are no identified risk factors for bladder cancer, and that the small increased risk could be reduced by appropriate patient selection.

Further discussion is available in MeReC Rapid Reviews Nos. 4241, 4090 and 3977. The place of pioglitazone in the overall context of care for people with type 2 diabetes is discussed in MeReC Rapid Review No. 3909.

Reference

1. MHRA. Drug Safety Update Vol 5, Issue 1, August 2011

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

Treating pain to reduce behavioural disturbances in people with dementia

An RCT[1] suggests that a systematic approach to the management of pain in people with dementia reduces agitation and may reduce the number of unnecessary prescriptions for antipsychotic drugs.

Action

Underlying health problems, such as pain, should be considered as one of the potential causes of 'behavioural problems' in people with dementia and should be managed appropriately. The WHO pain ladder provides a useful basis for pain management.

As summarised in MeReC Rapid Review No. 3471, there are useful resources building on the NICE/SCIE guideline for the management of people with dementia who develop behavioural and psychological symptoms. A Best Practice Guide, 'Optimising treatment and care for people with behavioural and psychological symptoms of dementia', is endorsed by the Department of Health and recommends analgesics, such as paracetamol, as one treatment option that may be attempted on a trial basis where other specific interventions have been unsuccessful. The Banerjee report emphasised that antipsychotic drugs are often used inappropriately as first-line treatment for behavioural and psychological symptoms in people with dementia.

What does this study claim?

This study was a cluster RCT of 352 nursing-home residents with moderate to severe dementia. It compared daily treatment of pain for eight weeks according to a stepwise analgesic protocol with usual treatment. Followed over 12 weeks, agitation scores (Cohen-Mansfield agitation inventory) were statistically and clinically significantly reduced in the intervention group, compared with the control group. In the intervention group, 69% of patients received only paracetamol (Step 1).

A more detailed discussion of this study is available in MeReC Rapid Review No. 4119. Further information can be found on NHS Evidence and in the dementia and pain management e-learning sections of the NPC website.

Reference

1. Husebo BS, et al. Efficacy of treating pain to reduce behavioural disturbances in residents of nursing homes with dementia: cluster randomised clinical trial. BMJ 2011;343:d4065

'High risk' prescribing in primary care – how prevalent is it?

A cross sectional analysis[1] of 315 general practices in Scotland found that 14% of the patients defined as particularly vulnerable to adverse drug events because of age, pre-existing disease, or co-prescription had received at least one 'high risk' prescription in the past year. 'High risk' prescribing included medicines such as non-steroidal anti-inflammatory drugs, warfarin, methotrexate and antipsychotics. Considerable unexplained variation in the levels of high risk prescribing between practices was found.

Action

As discussed in the NPC's recently published 10 Top tips for GPs, the risks associated with adverse drug events are particularly high in the following vulnerable groups of patients:

- the old, particularly when frail
- those with multiple serious morbidities
- those taking several potentially hazardous medications
- those with acute medical problems
- those who are ambivalent about medication taking or have difficulty understanding or remembering to take medication

In these groups it is important to take particular care when first prescribing, to prioritise medication review, and to specifically check that patients (and carers) understand how the medicines need to be used. Clinicians need to monitor patients ensuring that essential laboratory tests are undertaken periodically; side effects are detected; patients are given essential information and are involved in decisions about their medicines; and that therapy is optimised.

A more detailed discussion of this study is available in MeReC Rapid Review No. 4019. Further information is available in the NPC's 10 Top tips for GPs, guide to medication review and e-learning materials on evidence-informed decision making. Prescribing and safety information for individual drugs can be found on NHS Evidence.

Reference

1. Guthrie B, et al. High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice. BMJ 2011;342:d3514

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.

National Prescribing Centre, Ground Floor, Building 2000, Vortex Court, Enterprise Way, Wavertree Technology Park, Liverpool, L13 1FB
Tel: 0151 295 8691 Fax: 0151 220 4334 www.npc.nhs.uk