Use of Metoclopramide in the Cancer & Palliative Care Service

Background:

The European Medicines Agency (EMA) Committee on Medicinal Products for Human Use (CHMP) has reviewed published studies and meta-analyses on the efficacy of metoclopramide and reports of suspected adverse reactions in children and adults. The review confirmed the risks of neurological effects, such as short term extrapyramidal disorders and tardive dyskinesia, and that these risks outweigh the benefits in long term or high dose treatment. Subsequently, new recommendations on the use of metoclopramide containing medicines in the European Union were issued in July 2013.

The new recommendations would affect the use of metoclopramide in Cancer & Palliative care and include the following:

- Restricted to prescribe for a maximum of 5 days
- No longer recommended to be used in chronic conditions including gastroparesis, dyspepsia and gastro-oesophageal reflux disease
- Restricted to a maximum dose of 0.5mg/kg in 24 hours. For adults the maximum recommended does is 10mg up to 3 times daily (all routes).

Actions taken:

1. In response to these new restrictions, an attempt was made to contact the Medicines on Healthcare Products Regulatory Agency (MHRA). Unfortunately the MHRA was unable to reveal further details on the evidence used to support the recommendations. As a result the Cancer & Palliative care service was unable to fully review the significance or relevance of the risks identified in relation to their patient group.

2. In order to clarify the use of metoclopramide in palliative care, a consultant in palliative medicine in Cheshire had written to the EMA. The EMA responded and acknowledged the following points:

    - The CHMP recommendations were based on careful analysis of evidence of efficacy and safety of metoclopramide in its licensed indications.
    - The aim of the review was to examine the evidence for efficacy and safety in the licensed indications and to restrict the use of metoclopramide to those existing indications in which reliable evidence supported a favourable benefit to risk balance.
    - Since the use of metoclopramide in palliative care was not a licensed indication, the CHMP evaluation did not specifically examine such use.
    - Since few medicines are specifically studied and licensed for use in terminally ill patients, palliative care often requires the use of medicines outwith their standard licensed indications when the balance of risks and benefits may differ from other patient groups.
    - If off label metoclopramide was previously recognised as standard practice by specialists in palliative care, that should not necessarily change as a consequence of the CHMP review

Current practice in NHS Lothian:

Domperidone and metoclopramide are two approved prokinetics currently available in NHS Lothian. Metoclopramide is the only prokinetic that is currently available in injectable form. In some patients it is often necessary to give drugs subcutaneously (SC) and to exceed the usual indicated doses in order to achieve symptom control.

Main indications of metoclopramide use in the Cancer and Palliative care service are:

- Impaired gastric emptying secondary to drugs or tumour infiltration
- Severe reflux due to past surgery or oesophageal stenting
- Gastroparesis caused by autonomic neuropathy or spinal cord compression
- Bowel obstruction in patients without colic

Metoclopramide doses used are:

- PO 10mg-20mg 6 – 8 hourly
- SC 10mg 6-8 hourly or SC infusion 20-120mg/24 hours

Recommendations by the Cancer and Palliative Care Service:

Based on the EMA's recommendations on the use of metoclopramide, the Cancer and Palliative Care service recommend that the current practice of using a higher dose or longer duration of metoclopramide than those advised by the EMA is to be maintained. These practices are carried out if they are deemed necessary by the specialists for certain patient groups for whom the benefit outweigh the risks.

Each patient, as per current routine practice, is reviewed and monitored very closely ensuring the benefits for the use of metoclopramide continues to be carefully evaluated.

Revisions summary	
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