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Studies of lipid lowering treatment support NICE guidance

A large meta-analysis (26 randomised controlled trials, n=169,138) has confirmed the results of earlier meta-analyses regarding the benefits of standard dose statin therapy on cardiovascular outcomes. It also suggests additional benefits from more intensive statin therapy in selected high-risk populations.[1] However, it did not fully explore the potential harms associated with more intensive statin therapy or examine the cost-effectiveness of this approach. In addition, the studies included were dissimilar and it is a matter of judgment whether combining them in a meta-analysis is entirely appropriate.

The SEARCH study (n=12,064) found no statistically significant difference in major vascular events among people randomised to take either simvastatin▼* 80mg or 20mg per day for secondary prevention. The higher dose was associated with an increased risk of muscle side effects. Myopathy occurred in 53/6,031 patients taking simvastatin 80mg compared with 2/6,033 taking 20mg and rhabdomyolysis was seen in 7/6,031 patients taking simvastatin 80mg compared with 0/6,033 taking 20mg.[2]

*Note: The MHRA has advised that the black triangle (▼) refers to intensive monitoring being requested only when simvastatin is used in children and adolescents (10–17 years), in line with the recently licensed paediatric dosing recommendation.

Action

Health professionals should continue to follow NICE guidance and use simvastatin▼ 40mg per day for most people in whom a statin is indicated, in accordance with NICE guidance on lipid management and care of people with type 2 diabetes. More intensive statin therapy should **not** be automatic but may be **considered** in certain circumstances, taking into account the patient's informed preference, including the benefits and risks of treatment. The results of these studies support this. Health professionals should also note MHRA guidance on the use of simvastatin 80mg per day, which is entirely consistent with NICE guidance.

See *MeReC Rapid Review No. 2127* for more details of the meta-analysis and its limitations, and how it relates to the important questions, 'what initial dose of which statin should I offer?' and 'what are the pros and cons of using more intensive statin therapy and what dose of which statin should I use in that situation?'. See *MeReC Rapid Review No. 2138* for more information on the SEARCH study and how it fits with what we know already. Further information summarising the place in therapy of simvastatin 80mg is available in *MeReC Rapid Review No. 1423*. More information can also be found on the lipids floor of NPCi.

References

1. Cholesterol Treatment Trialists' Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. Lancet 2010;376:1670–81
2. SEARCH Collaborative Group. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12 064 survivors of myocardial infarction: a double-blind randomised trial. Lancet 2010;376:1658–69

More data on the risk of VTE with antipsychotics

A UK case-control study (25,532 cases and 89,491 matched controls) suggests an increased risk of venous thromboembolism (VTE) with the use of antipsychotics. This increased risk equates to about four extra cases of VTE per year for every 10,000 patients treated of all ages and 10 extra cases among people aged 65 years or over. The risk may be greater for new users and those prescribed second-generation (atypical) antipsychotics.[1]

Action

Health professionals should identify risk factors for VTE before and during treatment with antipsychotics and take appropriate preventative measures. Where antipsychotics are prescribed, not forgetting that they may also be used for nausea and vomiting or vertigo, this information should be considered when discussing the risks and benefits of antipsychotic treatment with patients (and their carers if appropriate).

What is the background to this?

A risk of VTE with the use of antipsychotics has been suspected for some time. In 2009, the MHRA led a Europe-wide review of UK Yellow Card data and worldwide published epidemiological studies on antipsychotics and VTE, and concluded that an increase in the risk of VTE could not be excluded. For more information see *MeReC Rapid Review No. 1997*. Information on uses and adverse effects of antipsychotics can be found on the MHRA website, and on the NPCi floors for schizophrenia, bipolar disorder and

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

dementia. More information on VTE can be found on the VTE floor of NPCi and in NICE guidance on reducing the risk of VTE.

Reference
1. Parker C, et al. Antipsychotic drugs and risk of venous thromboembolism: nested case-control study. BMJ 2010;341:c4245

NICE guidance on liraglutide▼ for type 2 diabetes

NICE has issued guidance on the use of liraglutide▼ for the treatment of type 2 diabetes. Liraglutide 1.2mg given via daily subcutaneous injection, is a dual therapy option only in very limited circumstances in people who are unable to take metformin or a sulphonylurea AND are unable to take pioglitazone AND are unable to take a gliptin. Treatment with liraglutide in a dual therapy regimen (with metformin or a sulphonylurea) should only be continued if HbA1c is reduced by at least one percentage point (11mmol/mol) at six months.

Liraglutide 1.2mg daily is a triple therapy option for people whose HbA1c is ≥7.5% (59mmol/mol) (or other higher level agreed with the individual) AND:

- a body mass index (BMI) ≥35 kg/m^2 in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight, OR
- A BMI <35 kg/m^2 and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.

Treatment with liraglutide in a triple therapy regimen (with two of metformin, a sulphonylurea or pioglitazone) should only be continued if HbA1c is reduced by at least one percentage point (11mmol/mol) and body weight is reduced by at least 3% at six months.

NICE does not recommend liraglutide at a dose of 1.8mg daily for type 2 diabetes.[1]

Action

Healthcare professionals managing the care of people with type 2 diabetes should familiarise themselves with this technology appraisal, and base their management on this, alongside the diabetes guideline from NICE. The NICE guideline on type 2 diabetes recommends metformin as the usual first-line hypoglycaemic drug; dual therapy with metformin and a sulphonylurea as the usual second-line therapy; and triple therapy with NPH insulin added to metformin and a sulphonylurea as the usual third-line option.

The role of newer hypoglycaemic agents in the management of type 2 diabetes, particularly in the pursuit of ever tighter blood glucose control, is controversial, as we have previously discussed (*MeReC Rapid Review No. 1017, MeReC Rapid Review No. 435, MeReC Rapid Review No. 336*). There is no evidence that these newer hypoglyaemic agents reduce the likelihood of patient-oriented outcomes such as cardiovascular disease or other complications of diabetes; long-term safety data are also limited. More information can be found in *MeReC Rapid Review No. 2033* and on the type 2 diabetes floor of NPCi.

Reference
1. NICE. Liraglutide for the treatment of type 2 diabetes mellitus. Technology Appraisal 203. October 2010

Tiotropium in asthma – no good evidence of benefit

A US exploratory study found that adding tiotropium to an inhaled corticosteroid (ICS) compared with doubling the dose of ICS improved the disease orientated outcome, morning peak expiratory flow rate, in 210 patients with poorly controlled asthma. While hypothesis generating, the study does not provide grounds for clinicians to include tiotropium in their management of people with asthma. The possible role of tiotropium in asthma needs to be explored in larger studies of longer duration, as certain methodological problems limit the conclusions that can be drawn from the study.[1]

Action

Tiotropium is currently **not** a licensed or a recommended option for the management of asthma. Health professionals should follow the BTS/SIGN guideline on the management of asthma. Before adding or changing treatment, practitioners should check concordance with existing therapy, check the patient's inhaler technique and seek to eliminate trigger factors. More information on asthma can be found on the asthma floor of NPCi. For more information on the details of this study and its limitations see *MeReC Rapid Review No. 2010.*

Reference
1. Peters SP, et al. Tiotropium bromide step-up therapy for adults with uncontrolled asthma. N Engl J Med 2010;363:1715–26

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