Important New Evidence Service

In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch™ Rapid Update 3 – September 2017

Osteoarthritis: systematic review and individual patient data meta-analysis finds no good evidence to support the use of glucosamine

A new systematic review and individual patient data meta-analysis has considered the evidence for glucosamine effectiveness in subgroups of people with osteoarthritis (OA) based on pain severity, body mass index (BMI), sex, structural abnormalities and presence of inflammation. The review found no good evidence to support the use of glucosamine in any subgroup. These findings are consistent with NICE guidance on OA in suggesting a lack of symptomatic benefit with these supplements, which are commonly now listed as 'non-formulary' items by CCGs.

Glucosamine is included in the NHS England's consultation document on drugs that should not routinely be prescribed in primary care. The consultation document is open for comments until 21st October 2017.

Reference: Runhaar J, Rozendaal RM, van Middelkoop M, et al. Subgroup analyses of the effectiveness of oral glucosamine for knee and hip osteoarthritis: a systematic review and individual patient data meta-analysis from the OA trial bank. Ann Rheum Dis. 2017. doi:10.1136/ annrheumdis-2017-211149

What do we know already?

- Glucosamine is available for prescribing within the NHS and it may also be purchased over the counter. There is an annual spend of around £445K per annum in primary care in England, which also includes chondroitin products.
- The BNF states that the mechanism of action of glucosamine is not understood and there is limited evidence to show that it is effective.
- In the UK, glucosamine is available in two forms: glucosamine hydrochloride and glucosamine sulphate. NHS Choices advises patients that the hydrochloride salt has not been shown to have any beneficial effects, but there is some evidence glucosamine sulphate may help symptoms to a small degree.
- The National Institute for Health and Care Excellence (NICE) has issued a "do not do" recommendation for glucosamine products for the management of OA.
- In 2010, a meta-analysis of high quality, large randomised controlled trials (RCTs) found that oral glucosamine was not superior to placebo in reducing pain and joint space narrowing in OA.

What does this evidence add?

- This is the first individual patient data meta-analysis to investigate potential subgroup effects of glucosamine for people with OA.
- Based on the five trials that were eligible and provided access to the individual patient data for analysis, there is no good evidence to support the use of glucosamine for hip or knee OA.
- Also there is an absence of evidence to support specific consideration of glucosamine for any clinically relevant OA subgroup according to baseline pain severity, BMI, sex, structural abnormalities or presence of inflammation.

Study details

This systematic review and meta-analysis aimed to summarise the evidence on the effectiveness of oral glucosamine in subgroups of people with hip or knee OA.

Eligibility criteria for studies:

- All RCTs evaluating the effect of any oral glucosamine substance in participants with knee or hip OA were included. Studies solely testing a combination of glucosamine with chondroitin were not included.
- Studies which included co-interventions were allowed as long as they were identically applied to the glucosamine and control groups.
- The minimum criterion for inclusion of RCTs was adequate reporting of pain as an outcome measure.

Identified studies:

- Corresponding authors of 21 trials were contacted. The authors/institutes of six studies agreed to participate and provide trial data. However, one of these did not use placebo as a comparator and so was excluded leaving five trials to be included in the analysis. The five studies were all defined as having a low risk of bias.
- From the five trials included there was a total of 1,625 participants, of which 64% were female. Of the 1,625 participants, 815 were randomised to glucosamine and 810 to placebo.
- Of the five studies, four considered knee OA only. The other considered knee and hip OA. The hydrochloride salt was used in three studies and the sulphate salt in two of the five studies.
- Pain and physical function was measured across all of the five included studies using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire. Scores were rescaled to a 0 to 100 scale
- In common with other studies, the authors found that the open access to clinical trial data was far from accepted practice.

Meta-analysis:

- The primary outcome measures were pain severity in the short-term (three to six months) and at long term (at least one year) follow-up. Secondary outcomes included physical function at the same time points. Pre-defined subgroups were: WOMAC pain < 70 *vs.* ≥ 70, BMI < 27 kg/m^2 *vs.* ≥ 27 kg/m^2, sex, less *vs.* more severe structural abnormalities (Kellgren and Lawrence grade 0-2 *vs.* 3-4) and absence *vs.* presence of inflammation.
- Glucosamine was not found to be more effective than placebo in reducing pain. The estimated pooled differences and accompanying 95% confidence intervals (CI) between glucosamine and placebo for pain at short and long-term follow-up were 0.60 (-1.80 to 3.00) and 0.98 (-1.76 to 3.73) respectively.
- Glucosamine was not found to be more effective than placebo in improving function. The estimated pooled differences and accompanying 95% CI for glucosamine *vs.* placebo for function at short and long-term follow-up were 1.74 (-0.45 to 3.96) and 1.40 (-1.27 to 4.06) respectively.
- None of the interaction terms of the predefined subgroups, e.g. sex; structural abnormalities; inflammation, reached statistical significance. Stratification for participants with knee OA only or for the type of glucosamine did not result in any differences in the outcomes.
- The only outcomes where further research may be warranted were the interactions with BMI among knee OA on short-term function and long-term pain, when receiving glucosamine sulphate.

Level of evidence:
Level 2 (limited quality patient-orientated evidence) according to the SORT criteria.

Study funding:
Dutch Arthritis Foundation, National Institute for Health Research