

Glucosamine

When the early trials on glucosamine came out I started to suggest patients with arthritis tried it. Later, when it became available on the NHS I offered to prescribe it to those who felt it was making a difference to their symptoms. Then earlier this year the NICE Guidance on osteoarthritis suggested it should not be used and I started to be less encouraging about it's use. So, does it work? Should we recommend it? Should we prescribe it? (Oh, and if you live in Scotland the Scottish Medicines Consortium does not recommend prescribing it either)

This review in the Drugs and Therapeutics Bulletin reviewed the evidence for glucosamine (DTB 2008;46(11):81-84).

What is glucosamine?

- Glucosamine is a naturally occurring amino acid monosaccharide found in cartilage and synovial fluid. Its action in osteoarthritis (OA) is not clearly understood.
- The pharmacokinetics and availability of oral glucosamine is not known and it isn't clear how it interacts with the naturally occurring glucosamine.
- Glucosamine is available as hydrochloride and sulphate. Only studies of glucosamine sulphate are publically available, therefore sulphate preparations are preferred.

Preparations available in the UK

- Only one form of glucosamine (Alateris) is licensed for use in the UK. This is in the form of glucosamine hydrochloride, for which there are no publically available trials. (*Odd don't you think?!*)
- Many other preparations are available to prescribe and buy over the counter (OTC) but are considered a food supplement and therefore may contain glucosamine in variable amounts and of variable purity.
- Alateris is licensed for symptomatic relief of mild to moderate osteoarthritis. It is available as 625mg tablets, with a recommended dose of 2 tablets daily (1250mg). It may take several weeks to start to give pain relief and it is recommended that you re-evaluate 2-3 months after starting and if symptoms have not improved, consider stopping it.
- At 1250mg daily Alateris costs the NHS £224/year. Other non-licensed preparations are available OTC for much cheaper (Online a year's supply can be bought for as little as £7.50).

Side effects and contraindications

- Glucosamine is extracted from shellfish so do not use in those allergic to shellfish!
- Common side effects (1-10% affected):

Nausea	Constipation or diarrhoea	Less common side effects (0.1-1%):
Abdominal pain	Headache	Rash
Indigestion	Tiredness	Itching
		Flushing
- Glucosamine is a sugar and has not been widely studied in those with impaired glucose tolerance or diabetes.
- Very rarely it has been reported to cause hypercholesterolaemia or to worsen asthma.
- It is contraindicated in pregnancy or breastfeeding and in those on warfarin.

Does glucosamine work?

One of the big criticisms of research into glucosamine is that most of the trials have been short lived (6-8w) or small (and often both!).

A Cochrane systematic review in 2005 considered 20 RCTs, mainly of patients with knee OA. The studies included over 2500 patients (Cochrane 2005;CD002946).

- **Results on pain and functioning were equivocal.**

All the studies showed reduction in pain and improved functioning using the Lequesne index (5 questions on pain, 4 questions on activities of daily living and a question on maximum distance walked). However on another, perhaps more widely used index (WOMAC OA Index), none of the trials reached statistical significance.

- **Three studies compared glucosamine with NSAIDs and showed pain relief was similar to or better than that obtained using NSAIDs.**

- **Two long term trials showed a reduction in progression of OA over a 3 year period** (note, a reduction in progression, which is not the same as an improvement!)

- **Adverse events in all these studies were similar to those from placebo, suggesting it is pretty safe.**

- **The Cochrane review concluded that glucosamine does not improve pain by much after 2-3 months use and that function may not improve at all.**

Since this Cochrane review in 2005 two other useful trials have been published:

An RCT of 1500 patients with symptomatic OA (NEJM 2006;354:795-808). Patients were randomised to one of 5 arms (glucosamine, chondroitin, glucosamine and chondroitin, celecoxib or placebo). The trial ran for 24 weeks.

- **No preparation was significantly better than placebo.**

Two criticisms of the study: firstly those enrolled had pretty mild OA and secondly, most had a particularly good result from placebo alone (more than would be expected).

An RCT that ran for 2 years looked at the impact of glucosamine v placebo on hip OA (most trials have been done on knee OA). It was a small trial (222 patients) but the accompanying editorial argues that it is big enough to measure an effect, although do note that many participants had relatively mild disease (Annals of Int Medicine 2008;148:268-77).

- **Over the two years there were no significant improvements in pain or functioning.**

So what does this mean in practice?

The DTB concludes that on the basis of the Cochrane review and the other papers highlighted above:

- **Glucosamine sulphate (1500mg) provides modest pain relief in knee OA and appears to be safe.**

- **But that cost effectiveness of glucosamine makes it difficult to recommend prescribing it on the NHS.**

- **They recommend patients purchase it OTC if they want to give it a try.**

What should we tell patients?

Here are some practical tips gleaned from the papers above and from my own experience:

- **None of the clinical trials have shown glucosamine is particularly effective. It may reduce pain in some people. It probably won't make function any better. It is still unclear whether it has any long term effects (slowing disease progression).**
- **There are no good trials looking at the role of glucosamine with other agents for OA (eg. chondroitin, cod liver oil, omega 3), so I don't recommend them.**
- **Glucosamine is safe in most people (but see the section on contraindications for those who should avoid it).**
- **Glucosamine may take several weeks to start to work and should be reassessed after 2-3 months. If pain is not improved, consider discontinuing it.**

Take home messages: Glucosamine

- **NICE do not recommend the use of glucosamine or other supplements for OA.**
- **Although glucosamine occurs naturally in cartilage and synovial fluid the pharmacokinetics and bioavailability of oral glucosamine is poorly understood.**
- **Only one form of glucosamine is licensed in the UK, but many other forms are available OTC and on prescription.**
- **Glucosamine sulphate is preferred to glucosamine hydrochloride.**
- **Don't use in those allergic to shellfish, pregnant, breast feeding or on warfarin.**
- **There is little evidence that glucosamine improves function.**
- **Glucosamine may provide some pain relief in knee OA although most of the studies are small and short lived.**
- **Any long term benefits on disease progression are still unclear.**
- **The costs of prescribed glucosamine are significant higher than that available OTC and therefore it is not recommended for prescribing on the NHS.**

The GP Update Course – A one day course for GPs and GP Registrars, by GPs.

We trawl through all the journals and do all the legwork to bring you up to speed on the latest issues, research and guidelines in General Practice. **We set all this in the context of the consulting room and the requirements of revalidation.** We focus on actions - getting the literature into practice and ensuring it counts towards revalidation. We make it entertaining too, without compromising the content!

Course delegates receive a copy of **The GP Update Handbook**, a 350 page book outlining the results of the most important research relevant to primary care over the last 5 years, and a year's subscription to the **GP Update Handbook Online**. We will also give you a copy of the **Revalidation Action Pack** which contains step by step guidance on audits, reflective practice and service developments related to the course, so that you have documented evidence of improved care for your next appraisal and for revalidation. We've included lots of material for locums too.

Autumn 2010 dates:

Oxford - Friday October 1
Nottingham - Wednesday October 6
Leeds - Thursday October 7
Manchester - Friday October 8
Birmingham - Saturday October 9
Exeter - Wednesday October 13

Cardiff - Thursday October 14
London - Friday October 15
London - Saturday October 16
Norwich - Tuesday October 19
London - Wednesday October 20
Glasgow - Thursday November 4
Inverness - Friday November 5

GPs £185, GP Registrars £150. For more details see www.gp-update.co.uk.

From www.gp-update.co.uk – one day courses for GPs, by GPs

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature, and this should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular check drug doses, side effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages.

GP Update Limited and Primary Care Education LLP