

## Glucosamine in diabetic patients

Query: Is it safe for people with diabetes to take glucosamine?

Concerns have been expressed that administration of glucosamine, a commonly used dietary supplement taken for osteoarthritis, might adversely affect glycaemic control in diabetic subjects [1]. This was based on theoretical considerations and on some animal studies indicating that glucosamine has a role in cellular glucose uptake..

The metabolic sequence of events which lead to glucose and free fatty acid-induced reduction / inhibition of cellular glucose uptake has now been clarified and indicates a role for glucosamine [2]. In addition, glucosamine - a product of the hexosamine biosynthetic pathway - appears to be a molecular energy sensing device involved in signalling the energy status of peripheral tissues. In 1991, Marshall et al [3] advanced the hypothesis that routing of incoming glucose through the hexosamine biosynthetic pathway plays a role in the development of insulin resistance. Glucosamine, which enters the hexosamine pathway at a later stage could induce insulin resistance without the presence of high glucose or glutamine levels. In vivo studies in rats [4] showed glucosamine infusions to induce insulin resistance in normoglycaemic, but not hyperglycaemic rats. Using IV infusions of glucosamine 0.1mg/kg/minute, a 17% reduction in the rate of glucose uptake was noted [5]. A second study described this effect as “marginal” [6]. In addition to the effects via the hexosamine pathway on insulin action, storage of glucose as glycogen may be influenced by glucosamine [7].

Correspondence following the initial article in the Lancet [1] has provided reassurance for diabetic patients who wish to take glucosamine. Rovati et al [8] and Russell and McCarty [9] comment that the animal studies used IV regimens of glucosamine which gave plasma glucosamine levels of 1-2 mmol/L. These are levels greatly in excess of those achieved by the oral route [10].

To date, there are no reports that oral glucosamine affects insulin sensitivity in animals or humans. Following oral administration, a substantial percentage of absorbed glucosamine is taken up by the liver as a result of first-pass metabolism. If glucosamine does have any clinically relevant effect on insulin, it is likely that this effect would take place in the liver [9].

Two studies cast doubt on the hypothesis that glucosamine is a mediator of hyperglycaemia-mediated insulin resistance [11,12]. Fasting plasma glucose levels were not affected in a 4 week placebo-controlled study of glucosamine for osteoarthritis [11]. No effect was detected in a subset of patients whose plasma glucose at enrolment was greater than 7mmol/L. Mean plasma glucose concentrations fell in both the 9 patients on glucosamine and in the 14 given placebo. In a larger, 3-year placebo-controlled, study of glucosamine sulphate on progression of knee osteoarthritis [12], only a slight decrease in fasting blood glucose was noted in the glucosamine group (n=106), whereas it remained stable in the placebo group (n=106). Few diabetic patients participated in this study; however, analysis of a

subset of patients with high baseline glucose levels at entry showed a similar pattern, with a tendency for a fall in plasma glucose in those taking glucosamine.

Whilst further long-term safety studies are needed for glucosamine, existing data does not indicate that oral administration adversely affects hyperglycaemic control in diabetes. Nevertheless, it would be prudent to monitor the diabetic patient for altered response if they start taking glucosamine.

### **References**

1. Adams ME. Hype about glucosamine. *Lancet* 1999; 354: 353-354
2. Hussain MA. A case for glucosamine. *Eur J Endocrinol.* 1998; 139: 472-475
3. Marshall S et al. Discovery of a metabolic pathway mediating glucose-induced desensitization of the glucose transport system. Role of hexosamine biosynthesis in the induction resistance. *J Biol Chem* 1991; 266: 4706-4712
4. Rossetti I et al. In vivo glucosamine infusion induces insulin resistance in normoglycaemic but not hyperglycaemic rats. *J Clin Invest* 1993; 96: 132-140
5. Baron AD et al. Glucosamine induces insulin resistance in vivo by affecting GLUT4 translocation in skeletal muscle: implications for glucose toxicity. *J Clin Invest* 1995; 96: 2792-2801
6. Miles PD et al. Troglitazone prevents hyperglycaemia-induced, but not glucosamine-induced insulin resistance. *Diabetes* 1998; 47: 395-408
7. Crook ED and McClain DA. Regulation of glycogen synthase and protein phosphatase-1 by hexosamine. *Diabetes* 1996; 43: 322-327
8. Rovati L C et al. Glucosamine in osteoarthritis. *Lancet* 1999; 354: 1640
9. Russell AI and McCarty MF. Glucosamine in osteoarthritis. *Lancet* 1999; 354: 1640
10. Setnikar I et al. Pharmacokinetics of glucosamine in the dog and in man. *Arzneim Forsch* 1986; 36: 729-735
11. Noack W et al. Glucosamine sulfate in osteoarthritis of the knee. *Osteoarthritis Cart* 1994; 2: 51-59
12. Reginster JY et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet* 2001; 357: 251-158

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