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Original article

# Effects of glucosamine sulphate on spinal height: a randomized, double-blinded, placebo-controlled pilot study

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It has been widely reported that glucosamine sulphate can benefit suffers of arthritis by affecting the biochemistry of the articular cartilage. As such, these changes may be a beneficial adjunct in chiropractic management. However, little previous work has been performed to assess the effectiveness of this supplement on spinal characteristics. A randomized, double-blinded, placebo-controlled study was conducted to determine whether the supplement glucosamine sulphate could affect spinal height. Two independent assessors were used to assess this parameter in all subjects. Both examiners reported similarly significant increases in spinal height over the 8-week experimental period. Although there may be some concern with respect to the accuracy of spinal height assessment, the concurrence between the two independent assessors strengthens the significance of the changes reported.

## Introduction

The neuro-biomechanical integrity of vertebral joint complex components is at the heart of chiropractic assessment and management. Ageing is known to adversely affect these structures at both the neurological and biomechanical levels. Primarily with respect to the latter, the ageing annulus shows an increase in its collagen content, especially at lower spinal levels (Adams *et al.* 1977). Both the ratio of type I to type II collagen (Nerlich *et al.* 1997) and the thickness of the collagen lamellae appear to increase in older relative to younger annulus fibrosi (Marchand & Ahmed 1990). However, there appears to be no difference between the collagen types of the degenerated intervertebral disc (IVD) when compared to that of a similarly aged 'normal' IVD (Stevens *et al.* 1982). This suggests that the type of collagen does not necessarily affect or relate to an IVD's degeneration. With increasing age, the lamellae of the annulus fibrosus become frayed and split (Bernick *et al.* 1991). Radial tears develop and appear to be present in as many as 50% of spinal specimens examined between the ages of 30 and 40 years (Krismer *et al.* 1997). The gap in these tears becomes filled with non-aggregated proteoglycans from the nucleus pulposus (Bernick *et al.* 1991), which has little ability to attract and retain water.

With increasing age, there is an increase in collagen and a decrease in the glycosaminoglycan content within the IVD (Sether *et al.* 1990; Olczyk 1993). The functional diameter of the nucleus pulposus and pressure within it are also reduced as age increases (Adams *et al.* 1996). The reason for this could be that the ageing process is correlated with a slightly decreased volume of the nucleus pulposus (Lyons *et al.* 1981; Cole *et al.* 1986; Bishop 1988; Urban & McMullin 1988), which might be related to a decrease in proteoglycan. There is also an increase in keratan sulphate relative to chondroitin sulphate (Adams & Muir 1976; Adams *et al.* 1977; Olczyk 1993); however, this is influenced by pH within the IVD (Kitano *et al.* 1993). Therefore, since chondroitin sulphate has two negative charges compared to the one of keratan sulphate, the concentration of the fixed negative charge

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within the proteoglycan decreases, leading to a reduction in the osmotic pressure within the IVD (Urban & Roberts 1986). This change will reduce the pull on water, and hence, there is a reduction in the potential for maintaining pressure inside the IVD. This mechanism could be one factor that limits the loss of disc height following loading (Reilly *et al.* 1984; Beynon & Reilly 2001). In addition, the convoluted nature of the proteoglycan aggregate creates a mechanism to protect against deformity. As the matrix becomes dehydrated, the 'pores' which have been created by the convoluted proteoglycan aggregate become smaller, and therefore, the hydraulic permeability and fluid losses are reduced (Urban & Roberts 1986).

Although, no direct studies have been performed to date to the present authors' knowledge, the literature would suggest that glucosamine sulphate supplementation could affect the properties within the nucleus pulposus of the IVD. The ground substance found in joint surface cartilage and that of the nucleus pulposus are similar. Therefore, it seems likely that glucosamine sulphate may have some influence on the function and structure of the IVD. Although the extent of this effect is unclear, it has been suggested that glucosamine sulphate supplementation may increase the synthesis of proteoglycans and their ability to combine with hyaluronan to form an aggregate (Bassleer *et al.* 1998). This is one mechanism by which the aggregate could retain its hydrophilic properties. Such a change in the IVD could reasonably be expected to increase the IVD height, which should be reflected in a general change in spinal height. Additionally, glucosamine sulphate has been demonstrated to inhibit the actions of collagenase, a key enzyme in cartilage destruction (Piperno *et al.* 2000).

## Subjects and methods

Ethical permission was obtained from the Bro Taff Medical Ethics Committee prior to commencing the present research. Both the glucosamine sulphate and the placebo were supplied by Health Perception (UK) Ltd and were identical in appearance and packaging. The active tablets contained 500 mg of glucosamine sulphate with potassium chloride. In addition, both the active tablets and the placebo contained microcrystalline cellulose, di-calcium phosphate and magnesium stearate. It was necessary for all participants to take three tablets per day of their respective treatments so that those in the glucosamine group would be taking 1500 mg $day^{-1}$ of the active substance.

Forty healthy, asymptomatic subjects between the ages of 18 and 40 years were randomly apportioned into two groups by drawing a letter appropriate to the group from a bowl containing 18 pieces of paper for each letter. One group was to be given 1500 mg of glucosamine sulphate daily and the other placebo. The supplements were assigned a letter code by a third examiner, who held the code and was authorized to break it in case of an adverse reaction by any of the participants. The subjects were requested to take the supplementation daily for 10 weeks.

Spinal height assessment was made using a stadiometer (Cranlea, Birmingham, UK). The assessments of each participant were made at the same time of day (± 30 min). Readings were taken at inception (after obtaining written informed consent), and at weeks 4 and 8. Two independent measures (two blinded assessors) were taken on each occasion. In addition to not knowing which supplement each subject was taking, neither examiner was privy to the results obtained at either of the previous assessments.

The data was analysed following week 8 using the SPSS 11.0 for Windows computer program.

## Results

Out of the 40 subjects who initially volunteered, four were not included in the analysis for either medical or personal reasons. The remaining 36 subjects were subsequently apportioned into the two test groups following a random number sequence.

By week 4 of the trial, the subjects in the glucosamine sulphate group showed a trend towards a change in the results of examiner B and a significant increase in the results of examiner A. However, a statistically significant increase in the subjects height was apparent in the results from both examiners by week 8 (Table 1).

Little change was apparent in the placebo group over this period.

A small number of benign adverse reactions were reported, such as stomach upset and indigestion. This was not restricted to the glucosamine supplementation group, and did not appear to affect either compliance or participation in the present research.

## Discussion

Previous studies have shown the effects of numerous factors such as exercise, loading and other daily activities on spinal height (Reilly *et al.* 1984; Beynon & Reilly 2001). However, to the present authors' knowledge, this report is the first to show an increase in spinal height following any intervention other than lying down for



 

**Table 1.** Changes in spinal height from week 1 to weeks 4 and 8. The data are presented as the mean (± 1 SD). Analysis was by paired Student *t*-test. Significant probabilities ($P<0.05$) are highlighted

| | Change in spinal height (cm) | | | |
|---|---|---|---|---|
| | Glucosamine | | Placebo | |
| Examiner | Mean ± SD | *P*-value | Mean ± SD | *P*-value |
| *Week 4* | | | | |
| A | 0.34 ± 0.48 | 0.008 | 0.00 ± 0.56 | 1.000 |
| B | 0.10 ± 0.51 | 0.407 | −0.02 ± 0.35 | 0.818 |
| *Week 8* | | | | |
| A | 0.39 ± 0.44 | 0.002 | −0.01 ± 0.48 | 0.940 |
| B | 0.24 ± 0.30 | 0.004 | 0.02 ± 0.40 | 0.812 |

prolonged periods (Reilly *et al.* 1984). Considerable effort was made to reduce the effects of diurnal spinal shrinkage. This was crucial since the expected changes were small in magnitude and the variations caused by diurnal change were potentially much larger (Roberts *et al.* 1998). The greatest daily reductions in height are known to occur within the first 3 h of rising in the morning (Reilly *et al.* 1984). Therefore, it was decided to assess the subjects at or around the same time of day on each occasion, with the actual time being at least 4 h after the subject had risen. This protocol was designed to reduce variability and enhance the present authors' capacity to detect smaller changes.

Although diurnal changes were considered when constructing the protocol, they were not the subject of direct assessment. Therefore, the present results cannot be used to directly determine the influence of supplementation on diurnal change. Furthermore, the kinematic influence that these changes may have on the motion segments was also not subject to direct scrutiny in this part of the study. These are two areas of investigation which obviously require further research attention. If the results reported here are confirmed, it is the authors' opinion that the changes may be best explained by a reduction in the diurnal variations in IVD height.

To the present authors' knowledge, the current study is the first to report that the supplementation of glucosamine sulphate may affect physical properties of the spine in normal asymptomatic subjects. The statistically significant increase in the subjects' height followed 8 weeks of daily supplementation. If confirmed in future studies, this represents a potentially important clinical finding. There are two possible interpretations of the results: glucosamine sulphate supplementation may either increase the total body height of the average subject, or alternatively, reduce the amount of normal diurnal spinal shrinkage (Roberts *et al.* 1998). In the absence of any other structural changes, this implies that the increase in height seen in the present study could be caused by changes in the biochemical/biomechanical properties of the IVD (Eklund & Corlett 1984). It does not necessarily imply that an increase in the volume of the IVD has occurred because previous work has shown there is not a close relationship between spinal height and IVD volume (Natarajan & Andersson 1999).

## Conclusion

The results from the present study suggest that glucosamine sulphate supplementation can affect the spinal height of normal, non-arthritic subjects. Glucosamine sulphate supplementation appears to either increase the total body height of the average subject or reduce the amount of diurnal spinal shrinkage. In the absence of any other structural changes, this suggests that the increase in height seen in this study is caused by changes in the properties of the IVD (Eklund & Corlett 1984). Such a change may be expected to have an influence on the kinematics of spinal motion segments.

The results of the present study do not allow the determination of the reason for the underlying changes. However, it is considered more likely that these are the result of a reduction in diurnal spinal shrinkage. This is in addition to glucosamine sulphate's previously documented anti-arthritic properties. The sites of action are probably manifold, and must include the nucleus pulposus of the IVD, the vertebral end-plates and the zygapophyseal joints. In addition, the supplement may have an effect on the soft tissues. From this, it might be surmised that an additional effect of glucosamine sulphate supplementation could be a change in spinal kinematics, i.e. range of spinal motion and spinal curvature. Such effects

may prove to be a useful adjunct in the treatment of those disorders managed by chiropractors and allied professionals.

## Acknowledgements

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