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Glucosamine effects on lipids and blood pressure

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Abstract

Glucosamine has in the past, been recommended for various functions, including the synthesis of synovial fluid, inhibiting degradation, and enhancing the healing of articular cartilage. However, there is no outstanding research that has been done to support these uses. The aim of the study is to examine the effects of glucosamine on lipids and blood pressure. Articles were obtained from reputable databases and used to discuss the glucosamine efficacy in osteoarthritis and glucosamine safety profile on lipids and blood pressure. The proposed study hypothesizes that glucosamine causes an increase in cholesterol and blood pressure levels. The authors analyzed past research studies on glucosamine, its efficacy in osteoarthritis, and the safety profile of the compound on lipids and blood pressure. The findings were inconclusive, even though they tended to suggest that glucosamine sulfate does not increase cholesterol levels; neither does it increase blood pressure in humans. Experimental research tended to show that glucosamine sulfate increases the levels of insulin, which might result in an increase in blood pressure. Even so, more recent studies have shown that glucosamine does not increase cholesterol levels; neither does the compound affect the blood pressure levels in human beings. Further studies are needed to ascertain the actual impact of glucosamine on lipids and blood pressure.

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INTRODUCTION

Glucosamine is categorized as an amino sugar that is generated innately in humans. The compound has often been endorsed for synthesizing synovial fluid, inhibiting degradation, and promoting the healing of articular cartilage. In many cases, glucosamine is administered as a mixture of glucosamine HCl and chondroitin sulfate. However, there are several forms of glucosamine, the most popular being glucosamine hydrochloride, glucosamine sodium sulfate, and glucosamine potassium sulfate. Glucosamine hydrochloride is often used for osteoarthritis, glaucoma, rheumatoid arthritis, joint pain, temporomandibular disorder, and various other related conditions (Papich, 2016). However, no decent scientific evidence exists to support these uses. With this in mind, the study seeks to examine the impact of glucosamine on lipids and blood pressure. According to a consumer lab report, there have been a few cases reports in the past that have shown that glucosamine can increase low-density lipoprotein cholesterol levels (Consumer Lab, 2019). The present paper reviews past literature on glucosamine and its effects on lipids and blood pressure.

LITERATURE REVIEW

Glucosamine Efficacy in Osteoarthritis

A number of past studies have investigated the usefulness of glucosamine sulfate in the managing of osteoarthritis. (Bruyère *et al.*, 2016) provide evidence from actual trials and surveys. The study findings showed cumulative evidence of the therapeutic effects of various glucosamine formulations. An analysis of high-quality clinical trials by the authors revealed that a prescription patented crystalline GS (pCGS) prescription was effective as a symptomatic slow-acting drug for osteoarthritis. The effect size of the prescription on pain was much greater than shown by paracetamol and oral non-steroidal anti-inflammatory drugs (NSAIDS). The effect size for the other preparations of glucosamine was consistently about zero. As a result of the findings, there is proof that chronic administration of pCGS can result in disease-modifying impacts and delay structural changes in the joint.

In a more recent study, (Bruyere *et al.*, 2019) evaluated the cost-effectiveness of using glucosamine for osteoarthritis. Among the 10 studies used in the simulation, four featured glucosamine sulfate in crystalline form, while the others used other types of formulations. In general, crystalline glucosamine sulfate was found to be cost-effective at all times when equated to the placebo. The other formulations were found not to be cost-effective. To some extent, these findings tend to confirm the significance of the formulation of glucosamine products.

(Harrison-Munoz *et al.*, 2017) also examined whether glucosamine was effective for osteoarthritis. The authors obtained data from the Epistemonikos database, which includes various systematic reviews and supporting primary studies. The effects of glucosamine were dependent on 21 randomized trials, featuring a total of 2,691 patients. In sum, the study showed that the certainty of the evidence was quite low. As a result, it was unclear whether glucosamine reduced pain in osteoarthritis. Also, it is not clear from the study findings whether glucosamine enhances functionality in osteoarthritis. It was also highly certain from the study findings that glucosamine did not have any unpleasant effects. Even though the evidence presented focused more on knee osteoarthritis, it can be applied extensively to patients with osteoarthritis.

(Runhaar *et al.*, 2017) also evaluated the efficacy of oral glucosamine among subgroups of individuals with hip or knee osteoarthritis. The authors conducted their evaluation using pain severity, sex, body mass index, evidence of inflammation, and the existence of structural abnormalities. The authors reviewed all randomized controlled trials that had evaluated the use of glucosamine among patients with defined hip or knee osteoarthritis. The study findings showed that glucosamine did not perform any better than the placebo for pain; neither did the compound perform any better when reviewed for short and long-term follow-up. The study findings showed that there is no decent proof to support the use of glucosamine for knee or hip osteoarthritis.

In another study by (Lubis *et al.*, 2017) the researchers compared the use of glucosamine-chondroitin sulfate in the treatment of knee osteoarthritis. The authors carried out a double-blind, randomized controlled trial, and their sample size consisted of 147 patients with knee osteoarthritis. The sample size was divided into three – 49 were subjected to glucosamine-chondroitin sulfate (GC), 48 were subjected to glucosamine-chondroitin sulfate-MSM, and 50 were placed in the placebo. The study findings showed a somewhat lower WOMAC score in the GC group, even though these findings were not statistically significant. In general, WOMAC scores were better in all three groups during the 4^{th}, 8^{th}, and 12^{th} weeks. Even so, significant scores were only reported during week 12 as compared to the baseline. Overall, a mixture of glucosamine-chondroitin sulfate-MSM resulted in a significant clinical improvement in pain relief among patients with grade I-II Kellgren Lawrence of knee osteoarthritis. Hence, it is possible to conclude that glucosamine-chondroitin sulfate could have measurable improvements in this category of patients.

Similarly, (Zhu *et al.*, 2018b) carried out a network meta-analysis seeking to equate the use of oral glucosamine, chondroitin, and a mixture of these compounds. The researchers searched for suitable studies from PubMed, Cochrane Library, and Embase. The results showed that celecoxib was probably the best choice for pain, followed by a mixture of glucosamine and chondroitin. In terms of physical function, all the interventions performed well when compared to the oral placebo, except for acetaminophen. Considering stiffness, glucosamine and celecoxib performed better than the placebo. Also, celecoxib and acetaminophen showed substantial differences in terms of safety when compared to the placebo. In sum, the study findings showed that celecoxib was the most effective option for relieving pain and enhancing physical function, closely followed by a mixture of glucosamine and chondroitin.

(Naumov and Tkacheva, 2018) investigated the

use of glucosamine sulfate among patients with osteoarthritis and comorbidity with high risks of the side effects of NSAIDs. The authors cited randomized trials that showed that the use of glucosamine sulfate in microcrystalline form could have a positive impact on the symptoms of keen osteoarthritis in its early stages. However, the study also noted pharmacokinetic evidence, which suggested that the regular intake of glucosamine sulfate in microcrystalline form can cause an increase of the compound in synovial fluid. Hence, these observations tend to suggest that the need for osteoarthritis biomarkers to be monitored during treatment with microcrystalline glucosamine sulfate. Besides, the authors recommend that the use of this compound must be combined with suitable physical exercise.

(Lomonte *et al.*, 2018) evaluated the usefulness and safety of mixing glucosamine sulfate and chondroitin sulfate capsules in the treatment of knee osteoarthritis. The sample in the study was randomized to receive a combination of these capsules for a period of 12 weeks. Primary evaluation entailed analgesic efficacy, while secondary evaluation focused on joint pain and swelling and the use of rescue medication. Additionally, the study examined adverse events and the tolerability of the drug. The analgesic efficacy of the group with the mixture compound was 88.9, while that of the glucosamine DS group was 85.4%. The intensity of the pain reduced significantly in the two groups, and there were improvements in the other efficacy outcomes measured by the researchers. Also, the adverse events resulting from the experiment were similar between the groups, and each resulted in good tolerability. These findings can be interpreted to mean that a mixture of glucosamine sulfate and chondroitin sulfate is useful in knee osteoarthritis management.

In the same way, (Zhu *et al.*, 2018a) investigated the effectiveness of combining glucosamine and chondroitin in the management of osteoarthritis. The authors obtained their research articles from the PubMed, Cochrane Library, Embase, as well as the reference lists of some of the most relevant articles. The sample size of the study entailed twenty-six articles illustrating 30 trials. The study findings showed that chondroitin had the ability to reduce pain symptoms and enhance function. On the other hand, glucosamine had a noticeable effect only on stiffness. Even so, there was no adequate evidence to suggest that the use of the two compounds together had superior benefits. From these results, it is possible to conclude that oral chondroitin was more effective in the management of pain and enhancement of physical function, while glucosamine was significant in dealing with stiffness. These findings are consistent with observations made in another study by (Aweid *et al.*, 2018) where the authors noted that a combination of glucosamine and chondroitin had the lowest possible unfavorable risk score. The authors recommended the need for more studies to examine the benefits of combining glucosamine and chondroitin.

The combination of glucosamine and chondroitin sulfate is also examined in the study by (Dinubile, 2018). The author noted that individuals suffering from osteoarthritis pain use both glucosamine and chondroitin sulfate, either alone or in combination. However, the study also noted that the few existent intervention trials had done very little to clarify the effectiveness of these compounds. The outcome of the study showed that the findings of the studies are mixed due to the high rate of placebo response resulting from rescue analgesics. These findings suggest the need for objective measurement tools rather than reliance on subjective measurement tools when conducting osteoarthritis trials.

Another study by (Yang *et al.*, 2018) attempted to combine oral glucosamine hydrochloride with hyaluronate sodium in the treatment of joint osteoarthritis. The authors initiated a double-blinded randomized controlled trial meant to examine the efficacy and the safety of combining oral glucosamine hydrochloride and hyaluronate sodium intra-articular injection. 144 participants with temporomandibular joint osteoarthritis were randomized into 4 hyaluronate sodium injections together with oral glucosamine hydrochloride. All the participants, except for 18, were followed for a period of 1 year. In the outcome of pain intensity, group A showed apparently lower visual analog scale scores compared to the second group. Additionally, some participants experienced gastrointestinal tract side effects, rash, as well as fatigue. Of these individuals, 23 had minor side effects that were not associated with glucosamine. These findings suggested that the combination of hyaluronate sodium injection and glucosamine hydrochloride pills did not have any consequential effect on temporomandibular joint osteoarthritis in the short-term. Even so, the combination of these compounds was found to relieve pain and enhance temporomandibular functions in the long-term.

(Ogata *et al.*, 2018) conducted a systematic review and meta-analysis investigating the effects of glucosamine among patients diagnosed with osteoarthritis of the knee. The impact of the compound on the function of the knee was minimal and

not significant. Given these findings, the authors concluded that glucosamine had the potential of relieving knee osteoarthritis pain. Similarly, other researchers conducted a higher-dose trial examining the use of glucosamine in the treatment of osteoarthritis. The authors noted that the response of levels of plasma glucosamine to the intake of higher doses of glucosamine was close to linear (Mccarty *et al.*, 2019). Another study in this realm was conducted, examining the long-term effects of glucosamine sulfate on the progression of osteoarthritis. The authors carried out a randomized double-blind placebo-controlled trial, which involved 212 patients diagnosed with knee osteoarthritis. The findings showed that 106 patients that were on placebo had an advanced joint-space narrowing. Besides, the 106 patients on glucosamine sulfate experienced no significant loss in joint space. These findings tend to suggest that glucosamine sulfate can be used as a disease-modifying agent among patients diagnosed with osteoarthritis (Reginster *et al.*, 2001).

Glucosamine Safety Profile on Lipids and Blood Pressure

A few previous studies have also attempted to find evidence of the impact of glucosamine on blood pressure. (Reis, 2011) also investigated the use of crystalline glucosamine sulfate in the treatment of osteoarthritis. The authors examined safety data from two long-term randomized controlled trials of crystalline glucosamine sulfate. The 428 osteoarthritis patients used in the study had either high normal blood pressure or high cholesterol at baseline. The study findings showed no major changes in the mean blood pressure after the use of crystalline glucosamine sulfate for a period of 6 months. Another similar study by (Eggertsen *et al.*, 2012) was conducted, where the authors examined changes in cholesterol levels among patients treated with lipid-lowering drugs. Specifically, the authors conducted a trial that examined the impact of glucosamine on s-cholesterol levels. The study sample was either treated with glucosamine or Vitamineral, a multivitamin tablet available commercially. The study findings showed that glucosamine did not change the levels of lipids among patients treated with simvastatin.

(Pham *et al.*, 2007) also investigated the impact of oral glucosamine on the resistance of insulin among patients with osteoarthritis. The authors noted that the glucosamine compound had been found to cause insulin resistance in animals. However, few or no studies have attempted to examine insulin resistance among human beings prescribed with oral glucosamine. The study, using a sample of 38 human subjects, showed that individuals with very poor insulin sensitivity could worsen their condition by taking a dosage of glucosamine to treat osteoarthritis. Likewise, (Huang *et al.*, 2015) evaluated the anti-obese effect of glucosamine and chitosan oligosaccharide injected in obese rats. The rats were randomly grouped into 12 units, and each unit received oral treatment for a period of six weeks. The outcome of the study showed that glucosamine enhanced dyslipidemia and hindered a gain in body weight. These findings can be interpreted to mean that glucosamine can be used to control obesity. Another study by (Esfandiari *et al.*, 2017) conducted a randomized clinical trial to examine the impact of glucosamine on intraocular pressure. The study included 88 patients who had been diagnosed with osteoarthritis. The study sample was randomized either into the glucosamine sulfate or the placebo group. The findings showed that glucosamine supplement therapy results in a statistically significant increase in intraocular pressure, and the impact was more evident among elderly patients. Even so, the implication of these findings requires additional investigation. The study by (Veronese *et al.*, 2019) also investigated the effect of type 2 diabetes mellitus on the outcomes of osteoarthritis. The study findings showed that type 2 diabetes mellitus has a pathogenic impact on osteoarthritis through oxidative stress as well as low-grade chronic inflammation. The researchers recommend the need for additional research to comprehend whether the control and prevention of diabetes can modulate the occurrence and progression of osteoarthritis.

The impact of glucosamine on cardiac function has also been examined in the study by (Zou *et al.*, 2009). Before this study, previous experiments on rat models had shown that the administration of glucosamine boosts cardiac functioning. However, the mechanisms through which glucosamine resulted in this impact have never been determined. Hence, the purpose of the study was to determine whether glucosamine reduced the activation of nuclear factor κB (NF-κB). The outcome of the study indicated that the modulation of *O*-GlcNAc levels changed the response of cardiomyocytes to the instigation of the NF-κB pathway. Possibly, this is what contributed to the improvement in cardiac function resulting from the use of glucosamine. (Anderson *et al.*, 2005) also investigated the impact of glucosamine in humans, with a special focus on glucose metabolism. The study findings showed no serious impact of oral glucosamine on urine, blood, or fecal parameters. A review of glucosamine sulfate on WebMD also suggests that this compound does not increase choles-

terol levels in humans, but can cause an increase in insulin (Webmd, 2019). Besides, the review also indicates that more reliable research suggests that glucosamine sulfate does not cause an increase in blood pressure (Webmd, 2019). To be on the safe side, it is important for patients to monitor their cholesterol and blood pressure when taking glucosamine sulfate.

CONCLUSION

Experimental research tends to indicate that glucosamine sulfate increases insulin levels, which might cause an increase in blood pressure. However, more recent studies tend to show that glucosamine does not increase cholesterol levels or blood pressure in human beings. From the reviewed studies, the actual impact of glucosamine on lipids and blood pressure is inconclusive. Hence, there is a need for additional experiments to ascertain the impact of glucosamine sulfate on lipids and blood pressure.

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