

Do Glucosamine Hydrochloride and Sodium Chondroitin Sulphate Reduce OA Knee Pain?



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Introduction

- ❑ Osteoarthritis may be defined as joint failure
 - Pathologically – as a condition of synovial joints characterised by –
 - Focal loss of articular hyaline cartilage
 - Proliferation of new bone and remodeling of bone contour

 - Clinically OA is characterised by –
 - Joint pain
 - Crepitus
 - Stiffness after immobility
 - Limitation of movement

Impact of OA on the individual

- ❑ Limitation of activities
- ❑ Affects independence and psychosocial functioning
- ❑ Leads to financial loss

Goals of Treatment of Osteoarthritis

- ❑ Relief of symptoms (pain)
- ❑ Preservation of function (daily activities in life)
- ❑ Delay of joint damage (cartilage and bone)

Interventions

- ❑ Lifestyle interventions – to reduce stress on the affected joint
 - Activity Modification
 - Weight Reduction

- ❑ Pharmacological interventions
 - Reduce pain and may reduce joint damage.
 - Improves function, activities and participation.
 - **Drugs used are:**
 - Simple analgesics, NSAIDs/Coxibs and topical therapies
 - **Disease modifying anti-osteoarthritic drugs**
 - Intra-articular injections with glucocorticoids or hyaluronic acid

- ❑ Surgical interventions

- ❑ Rehabilitative interventions

Disease modifying anti-osteoarthritic drugs

- Glucosamine Hydrochloride/Sulphate
- Chondroitin Sulphate
- Diacerein

Glucosamine

- ❑ **Glucosamine** has the ability to –
 - Provide basic raw material necessary to maintain a healthy cartilage
 - Prevent degeneration of the cartilage

- ❑ **Glucosamine Sulfate** seems to be capable of – interfering with various pathological mechanisms of osteoarthritis,
 - Stimulating **synthetic activity** of the chondrocytes
 - Inhibiting the **chondrolysis** provoked by the degrading enzyme released into the articular cavity during osteoarthritis
 - **Attenuates** subchondral bone turnover, structure, and mineralization

Chondroitin Sulphate (CS)

❑ Chondroitin Sulphate – in joints

- Relieves pain
- Restores cartilage cells
- Supports production of new collagenous fibres
- Influences the regeneration of joint cartilage

Chondroitin Sulphate (contd....)

- ❑ Therapeutic activity of CS in osteoarthritis may be due to –
 - Anti-inflammatory activity
 - Metabolic effects on the –
 - Synthesis of hyaluronate
 - Cartilage proteoglycans
 - Direct anti-degradative actions –
 - Inhibition of some proteolytic activities (collagenase, elastase, proteoglycanase)
 - Decreases the dangerous effects on matrix molecules determined by reactive oxygen species

Results of some meta-analyses

Meta-analysis 1 - Towheed et al. (2005)

- ❑ The **effectiveness** and **toxicity** of Glucosamine sulphate/hydrochloride in the treatment of OA
- ❑ 20 RCTs from 1966 through January 2005
- ❑ Total number of patients – 2570
- ❑ Mean age – 61.1 years
- ❑ 67% female
- ❑ All were double-blind, randomized trials
- ❑ Most were 2–3 months long, with the exception of two more recent RCTs that were 3 years (Pavelka et al., 2002; Reginster et al., 2001).
- ❑ **Conclusion** - Collectively, studies showed glucosamine to be superior to placebo for pain and function

Meta-analysis 2 - Richey et al. (2003)

- ❑ The **structural** and **symptomatic** efficacy of oral GS and CS in treating knee and hip OA
- ❑ Systematic review of randomized, double-blind, placebo-controlled trials
- ❑ Duration - between January 1980 and March 2002
- ❑ Number of trials – 15
- ❑ Number of patients – 1775
- ❑ Mean age – 62.1 years
- ❑ The data showed –
 - Highly significant efficacy of GS on all outcomes measured including joint space narrowing, pain and mobility
 - CS was found to be more efficacious than placebo

Meta-analysis 3 - McAlindon et al. (2000)

- ❑ Meta-analysis of clinical trials to evaluate the **benefit** of GS, GH, and CS in treating knee or hip OA
- ❑ Number of trials – 15
- ❑ Published between 1966 and 1999
- ❑ Number of patients – 1710
- ❑ All were double-blind, randomized, and placebo-controlled lasting four or more weeks
- ❑ **Conclusion** - the trials “**demonstrate moderate to large effects**”
 - However, methodological quality issues and publication bias indicate that results may be **overstated**

Meta-analysis 4 - Leeb et al. (2000)

- ❑ Studied the **efficacy** of CS in the treatment of OA through a meta-analysis of controlled clinical trials
- ❑ Seven trials published between 1991 and 1998
- ❑ Randomized and double-blind
- ❑ Number of patients – 703
- ❑ Follow-up period of at least 120 days
- ❑ Analysis – **CS to be superior to placebo** for improvement of function, reduction of pain, and reduction of NSAID or acetaminophen use
- ❑ **Conclusion** – CS may be useful in treating OA, larger and longer trials are needed

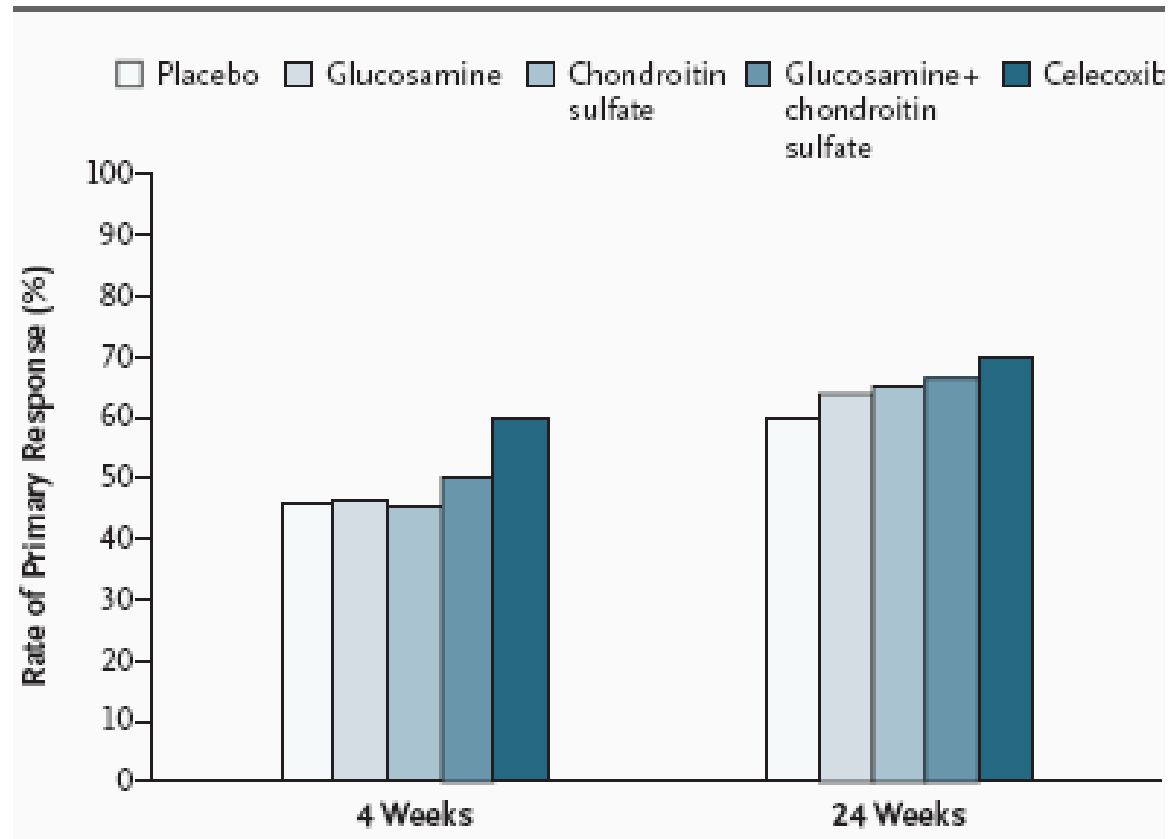
Glucosamine/chondroitin Arthritis Intervention Trial (GAIT)

- ❑ To evaluate rigorously the efficacy and safety of glucosamine, chondroitin sulfate, and the two in combination in the treatment of pain due to osteoarthritis of the knee
- ❑ Study duration – 24-week
- ❑ Randomized, double-blind, placebo- and celecoxib controlled, multicenter trial
- ❑ Sponsored by the National Institutes of Health
- ❑ Mean age of the patients was 59 years
- ❑ 64 % were women

GAIT (contd.....)

- ❑ Assignment was stratified according to the severity of knee pain –
 - Mild = 1229
 - Moderate to severe = 354
- ❑ The primary outcome was a 20 % decrease in knee pain from baseline
- ❑ Glucosamine and chondroitin sulfate alone or in combination did not reduce pain effectively in the overall group of patients with osteoarthritis of the knee
- ❑ Exploratory analyses suggest that the combination of glucosamine and chondroitin sulfate may be effective in the subgroup of patients with moderate-to-severe knee pain.

Rates of a Primary Response at 4 and 24 Weeks



As compared with placebo, celecoxib therapy was associated with a clinically meaningful difference in the primary outcome measure of 15 percentage points, but the difference did not reach statistical significance.

Conclusion

- ❑ Data so far available are inconclusive
- ❑ In patients with OA of the knee, glucosamine and chondroitin, or both do not much differ from placebo for pain relief
- ❑ Continuing research is needed to establish the potential efficacy and increase our understanding of the biology, pharmacology, and pharmacokinetics of these agents

Thank you

A 3D-style graphic featuring the text "Thank you" in a bold, orange, sans-serif font. The text is centered on a blue gradient rectangular banner that is tilted at an angle. The banner has a light blue glow around its edges and a soft shadow cast below it, giving it a floating appearance against a white background.