

Efficacy and safety of **hyaluronic acid**

Due to adverse reactions related to treatment with non-steroidal anti-inflammatory drugs (NSAIDs), treatment with hyaluronic acid is increasingly considered as the therapy of choice in patients suffering from osteoarthritis (OA), according to Gydek *et al.*

OA is one of the leading causes of disability

in the elderly and involves destruction of the articular cartilage. Damage on the collagen network and an increased production of proteoglycans by chondrocytes cause inflammation and thickening of the cartilage.

The course of the disease involves a decreased content of water and proteoglycans, metalloproteinase activation, an increase of pro-inflammatory cytokine activity, subchondral degenerative bone cysts and development of subchondral sclerosis. Osteophytes (bone projections) are formed on the bone-cartilage border. Joint capsule and ligaments become harder and lose elasticity.

Main symptoms of OA include primarily pain and inflammation of the affected joints. Sometimes, there is restricted mobility of the affected joint, muscular atrophy and, in more advanced cases, irreversible stiffness of the joints affected. The disease leads to the increase of disability and hinders the autonomy in the patient's life.

INTRA-ARTICULAR INJECTIONS OF HA

Over the past few years, intra-articular injections of HA have become one of the most popular therapies. HA is a natural component of the synovial fluid responsible for its elastic properties, thus, it is essential for the regular function of articular surfaces.

Studies have shown that intra-articular HA and hylan are an effective, safe, and tolerable treatment for symptomatic knee OA. Symptoms of knee OA are primarily related

to inflammation of the synovial membrane and other articular structures, as well as in the synovial fluid, where hyaluronate level decreases.

Administration of HA in injections efficiently supplements this deficit and prevents its depolymerisation, a process that facilitates leukocyte migration into the synovial fluid.

The restoration of rheological properties of the synovial fluid reduces the development of inflammation through the inhibition of leukocyte migration from synovial membrane capillaries into the synovial fluid.

80.6%
declared an improvement at **six-months** post-injection

EFFICACY AND SAFETY HA INJECTIONS

In their study, Gydek *et al* reconfirmed the efficacy and safety of intra-articular use of HA (suplasyn) in the treatment of knee OA. This was a one-year observational study enrolling 4519 patients (59% females, 41% males) diagnosed with OA. Mean age was 54.2 years.

Each patient received a mean of three intra-articular injections of suplasyn (20mg of sterile HA) and followed for a 30-day period. During the study, measures of intensity of symptoms

were checked before and after treatment, including pain at rest and pain during walking (using visual analogue scale [VAS] score).

Changes in pain intensity (basic scored characteristic for OA degree) and symptoms like morning stiffness, after rest stiffness, pain after ascending stairs and walking on the surface level were evaluated. Evaluation also included changes in the range of motion of the knee joint based on evaluation of extension and extension restrictions.

RESULTS

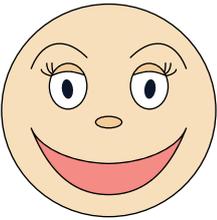
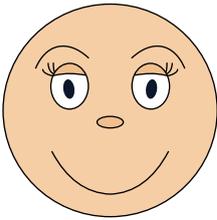
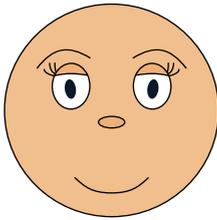
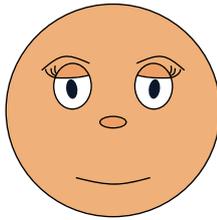
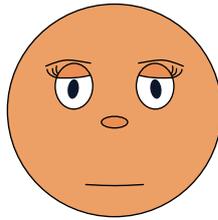
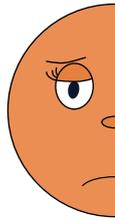
Patients scored the pain level at rest and during walking before treatment was 3.4 and 5.0, respectively. After treatment the scores for pain level at rest and during walking decreased to 1.5 and to 2.2 respectively.

Mean scores of the morning stiffness intensity before and after treatment were 3.5 and 1.8 respectively. Score of stiffness at rest also decreased from 3.0 to 1.5. The treatment also showed some improvement in walking on surface level and walking up and down stairs. Ability to extend and range of extension after treatment changed significantly compared to the baseline.

CONCLUDING REMARKS BY THE RESEARCHERS

Numerous previous multicentre trials confirmed the efficacy of HA in knee OA treatment, including the American College of Rheumatology and European League against Rheumatism.

Comparative pain scale chart (Pain Assessment Tool)

					
0 Pain free	1 Very mild	2 Discomforting	3 Tolerable	4 Distressing	5 Very dis
No Pain	Minor Pain				
Feeling perfectly normal	Nagging, annoying, but doesn't interfere with most daily living activities. Patient able to adapt to pain psychologically and with medication or devices such as cushions.			Interferes significantly with daily living but patient remains independent	

➤ This study results confirms the benefits from the administration of HA (suplasyn) in the treatment of knee OA. The functionality of the affected knee after treatment with suplasyn improved, with the resolution of pain at rest and during walking.

Extension ability and extension range were improved. Patients reported less frequently complaints on morning stiffness and stiffness after rest. Also, problems with daily activity, such as walking on surface level and walking up and down stairs were reduced.

ASKOT STUDY

The ASKOT study confirmed the findings of Gydek *et al.* The aim of this study was to evaluate the effectiveness and safety in real-life conditions of a viscoelastic solution of HA for intra-articular one-shot injection in OA.

This was an international multicentre, non-interventional, observational study with 411 patients who were attending rheumatology/orthopaedics units for pain due to knee OA.

PAIN SCORES

Mean VAS pain at rest was significantly lower three and six months after treatment compared to the baseline (18.97 versus 30.79 and 18.50 versus 30.79). Also, patients had a significantly lower mean VAS pain while walking after three and six months compared to baseline (37.91 versus 57.56 and 35.87 versus 57.56)

Patients had a significantly lower Lequesne mean overall score at three and six months compared to baseline (7.25 versus 10.60 and 6.85 versus 10.60). Furthermore, the mean subscore pain and discomfort was significantly lower at baseline compared with the subscore at three and six months respectively (2.79 versus 4.47 and 2.65 versus 4.47).

The walking distance sub score improved significantly after three and six months of

treatment compared with baseline (1.48 versus 2.10 and 1.37 versus 2.10). Also, the daily activities subscore decreased significantly after three and six months of treatment compared with baseline (3.01 versus 4.05 versus 4.05).

86.7%
of patients declared an improvement in their health at **three-months** post-injection and a lower number and intensity of pain exacerbations

EXACERBATIONS

Overall, 86.7% of patients declared an improvement in their health at three-months post-injection and 80.6% declared an improvement at six-months post-injection. Improvement in clinical status measured at three and six months was accompanied by a decrease in the number and intensity of pain exacerbations between baseline and three months for 65.2% of patients and between three and six months in 48.8% of patients.

CONCLUDING REMARKS BY THE RESEARCHERS

This study, performed in four European countries in patients suffering from knee osteoarthritis confirmed the safety profile and effectiveness of the therapy with hyaluronic acid with a dosing regimen of one administration of 6ml.

The increased volume of administration (three times more than a conventional injection) did not have any effect on the

safety of the injection. The adverse events reported, which were restricted to minor and transient local events, did not require specific treatment and occurred with less frequency to that described in the literature for this dosing regimen and for the 2ml dosing regimen.

All the parameters used to measure the efficacy of the treatment (pain, quality of life) were significantly improved after three months and six months of treatment. An overall decrease in the Lequesne-index greater than two is considered clinically meaningful.

In this study, more than half of the patients had a clinically meaningful decrease in the Lequesne-index. The mean overall decreases were 3.35 and 3.75 after three and six months respectively.

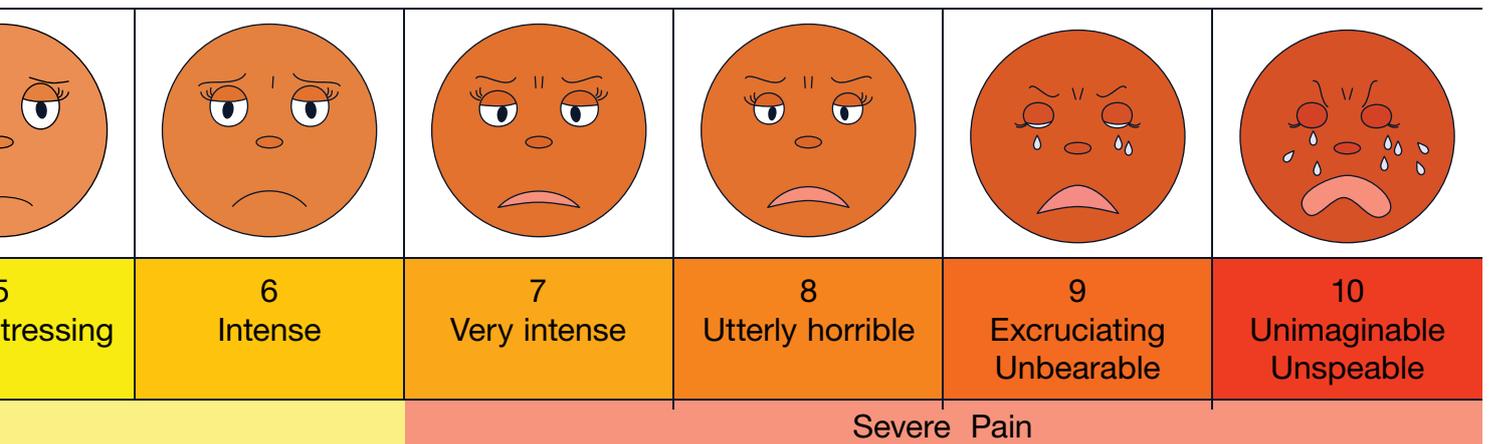
In addition, the study results confirm the efficacy of a single injection and maintenance of the therapeutic benefit over a period of at least six months.

These findings are relevant for the physician in daily practice, because decreasing the number of injections into the osteoarthritic joint decreases the risk of infection associated with any intra-articular procedure and improves patient compliance and convenience. Also, there is significant economic benefit to be gained from reducing the number of injections required to complete the treatment as physician time, patient time, clinic overheads, and medical disposable costs could all be reduced.

REFERENCES:

Blanch Rubió J, Badstübner R, Schnee B *et al.*
ASKOT STUDY: Effectiveness and safety of a 1-shot injection of sodium Hyaluronate for knee osteoarthritis treatment. *Springer Experience & Drug Evidence*, 2012.

Gydek A, Kowiczek K, Wordliczek J, Liszka H.
Efficacy and safety of intra-articular use of hyaluronic acid (suplasyn) in the treatment of knee osteoarthritis. *Przegl Lek*, 2011. **SF**



g activities. Requires lifestyle changes
nt. Patient unable to adapt pain.

Disabling; unable to perform daily living activities. Unable to engage in normal activities. Patient is disabled and unable to function independently.



Multiple choice questions

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- 1 What causes inflammation and thickening of the cartilage in OA?
 - a. Damage on the collagen network. A
 - b. An increased production of proteoglycans by chondrocytes. B
 - c. All of the above. C
- 2 The course of the disease involves:
 - a. A decreased content of water and proteoglycans, metalloproteinase activation, an increase of pro-inflammatory cytokine activity, subchondral degenerative bone cysts and development of subchondral sclerosis. A
 - b. An increase of proteoglycans, metalloproteinase activation, an increase of pro-inflammatory cytokine activity, subchondral degenerative bone cysts and development of subchondral sclerosis. B
 - c. A decreased content of water and metalloproteinase activation, an increase of pro-inflammatory cytokine activity, proteoglycans, subchondral degenerative bone cysts and development of subchondral sclerosis. C
- 3 Main symptoms of OA include:
 - a. Primarily distortion of affected joints. A
 - b. Primarily pain and inflammation of the affected joints. B
 - c. Inhibition of the mobility of the affected joint and muscular atrophy. C
- 4 HA is a natural component of the:
 - a. Synovial fluid responsible for its elastic properties. A
 - b. Articular surfaces. B
 - c. Collagen network. C
- 5 In the Gydek *et al's* study, patients scored the pain level at rest and during walking before treatment as 3.4 and 5.0 respectively. What were their pain level scores after treatment?
 - a. Decreased to 1.9 and 2.6 respectively A
 - b. Decreased to 1.5 and 2.5 respectively. B
 - c. Decreased to 1.5 and 2.2 respectively. C
- 6 HA treatment also showed some improvement in walking on surface level and walking up and down stairs.
 - a. True A
 - b. False B
- 7 The main aim of the ASKOT study was to evaluate the effectiveness and safety in real-life conditions of a viscoelastic solution of HA for intra-articular one-shot injection in OA.
 - a. True A
 - b. False B
- 8 What percentage of patients in the ASKOT study declared an improvement in their health at three-months post-injection?
 - a. 86.6% A
 - b. 87.7% B
 - c. 87.2% C
- 9 What percentage of patients in the ASKOT study declared an improvement at six-months post-injection?
 - a. 80.6% A
 - b. 80.3% B
 - c. 80.8% C
- 10 According to the researchers of the ASKOT study, why are their findings relevant for the physician in daily practice?
 - a. Because increasing the number of injections into the osteoarthritic joint decreases the risk of infection associated with any intra-articular procedure and improves patient compliance and convenience. A
 - b. Because decreasing the number of injections into the osteoarthritic joint decreases the risk of infection associated with any intra-articular procedure and improves patient compliance and convenience. B
 - c. Because decreasing the number of injections into the osteoarthritic joint increases the risk of infection associated with any intra-articular procedure and improves patient compliance and convenience. C

This is to state that I have participated in the CPD-approved programme and that these are my own answers.

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