EARLY EFFICACY OF A NOVEL VISCOSUPPLEMENT COMBINING HYALURONIC ACID AND SORBITOL, ANTI-OX-VS (SYNOLIS) IN PATIENTS WITH KNEE OSTEOARTHRITIS

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ABSTRACT

Title: EARLY EFFICACY AND SAFETY OD A NOVEL VISCOSUPPLEMENT COMBINING SODIUM HYALURONATE AND SORBITOL (ANTI-OX-VS) IN PATIENTS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS.

Objective(s): ANTI-OX- VS is an innovative viscosupplement (VS) made of a high concentration (20 mg/ml) of a > 2MDa Sodium Hyaluronate (NaHA) from non animal origin, combined with a high concentration of an oxygen free radical (OFR) scavenger, the Sorbitol (40mg/ml). The high ability of Sorbitol to scavenge and neutralize OFR has already been proven to delay the degradation of the gel. We hypothesis the antioxidant effect of a Sorbitol may also play a role to reduce the time to onset of analgesia.

Materiel and Methods : 26 patients with symptomatic KOA were included in a 13 weeks prospective open pilot study. Treatment regimen consisted of 3 IA injections of 2 ml of ANTI-OX-VS on week apart. Pain and function (WOMAC scale, walking pain (WP), patient and physician global assessment (GA) using a 5 points Likert scale were obtained at W1, W2 and W13. Between W2 andW14 patients were asked to complete a weekly self evaluation questionnaire (WP, WOMAC A between W0 and W1, w2, W8, W13. The treatment efficiency was also evaluated at W13.

Results : Mean age was 71+10, BMI 27.9???3.9. KL grades 1,2,3,4 in 0, 6, 8, 12 cases respectively. At W0 mean WP was 2.1 and WOMAC A 8.3. At W3 mean WP to 1.5(p<0.0003). As early as W1 WP was already reduced to 1.6 (p<0.0003) and decrease again 1.0 (p<0.0001) at W13. Variation of mean MP between W0 and W1, W2, W3, W8, W13 was resp. -0.5; -0.4; -0.5 and -1.1. Variation of mean WOMAC A between W0 and W1, W2, W8, W13 was resp. -2.1, -2.0, -2.0, -3.9. At W13, 82% of the patients considered ANTI –OX-VS treatment is moderately to extremely effective. There was no advice related adverse event reported.

Conclusion(s) : This study suggests a quick and strong pain relief occurring immediately after the first injection on ANTI-OX-VS followed by continuous improvement until W13. Pain decreases much faster than what obtained with other VS probably because of the presence of a high concentration of Sorbitol through its antioxidant activity.

Viscosupplementation by intraarticular injections of hyaluronic acid (HA) reduces pain and improves function in patients with knee osteoarthritis (KOA) but the improvement is delayed and occurs usually 6 to 8 weeks after the injections.

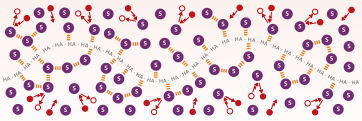

Figure 1

Rationale

ANTI-OX-VS (Synolis™) is a new innovative viscosupplement made of a high concentration (20 mg/ml) of a 2mDa hyaluronic acid (HA) from non animal origin, combined with a highconcentration of a free radical-scavenger, the sorbitol (40 mg/ml).

Figure 2

The high affinity between HA and sorbitol, stabilizes the complex through a very dense network of hydrogen bonds (figure 1).

Furthermore the high ability of sorbitol to scavenge and neutralize oxygen free radicals (OFR) has been demonstrated to delay the degradation of the gel, compared to linear and cross-linked HA viscosupplements (Figure 2).

OBJECTIVES

To evaluate the short term pain-relief effect of ANTI-OX-VS in patients suffering from knee osteoarthritis.

Study design

Prospective, open-label 13 week study 26 outpatients fulfilling the American College of Rheumatology clinical criteria for the diagnosis knee OA.

Inclusion criteria

- Patients suffering from symptomatic knee OA and considered by the physician as requiring viscosupplementation
- 30 ≥ Age < 85 years
- Kellgren-Lawrence grade (KL) II to IV on standing AP view, Lyon schuss view, profile, skyline view of the patella.

Main exclusion criteria

- Flare at any joint.
- VS of any knee within 6 months prior to the initiation of treatment.
- Intra-articular steroid injection of any knee within 3 months prior to the initiation of treatment.

Treatment procedure

Three 2mL intra-articular injections of ANTI-OX-VS (Synolis™) were performed 1 week apart by an experienced rheumatologist.

Authorized treatments

- Paracetamol < 4 g/jour
- NSAIDs if taken before inclusion
- SYSADOAs *(chondroïtin sulfate, diacerhein, avocado/soja unsaponifiables, glucosamin , diacerhein)* if taken at stable doses at least 3 months before inclusion and during the whole follow-up period.

Evaluation

At baseline, W1, W2 and W13 : WOMAC A, WOMAC aggregate, walking pain (WP), patient and physician global assessment (PGA) using a Likert 5 points scale.

Between the third injection and end-point patients were asked to complete once a week **a self evaluation questionnaire** for WP, WOMAC A, patient GA and adverse events.

At W1, W2 and W13 : Percentage of improvement since the first injection were obtained (figure 4).

Treatment satisfaction was also evaluated at the end of the follow up period (Likert 4 points scale).

Primary criteria : Variation of WP between first injection and W3.

Secondary criteria : Variation of WP, WOMAC A, PGA between baseline and W1, W2, W3, W8, W13. Variation of WOMAC between baseline and W13. Percentage of improvement between baseline and W1,W2,W13.

RESULTS

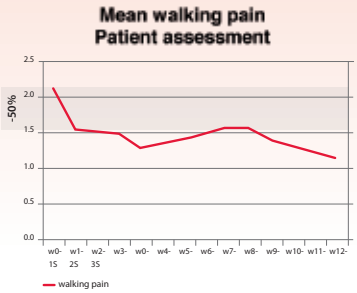

Figure 3

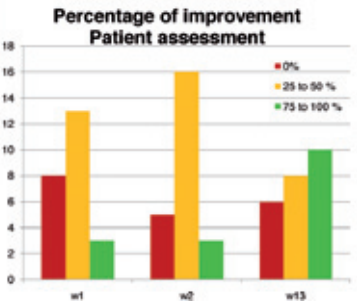

Figure 4

Mean age 71 ± 10
Mean BMI 27.9 ± 3.9
KL (grade /N): II/6; III/8; IV/12

At baseline:
- Mean WP = 2.1
- Mean WOMAC A = 8.3

At week 1:
- Mean WP 1.6 (p<0.0003)
- Mean WOMAC A = 6.2 (p<0.0000)

At week 3:
- Mean WP 1.5 (p<0.0003)
- Mean WOMAC A = 7.5 (p<0.05)

At week 13:
- Mean WP 1.0 (p<0.0001)
- Mean WOMAC A = 4.9 (p<0.0000)
- Variation of WP between baseline and W1, W2, W8 and W13 was respectively -0.5, -0.4, -0.5 and -1.1 (figure 3)
- Variation of WOMAC A between baseline and W1, W2, W8 and W13 was respectively -2.1, -2, -2 and -3.9. At W13, 82 % of the patients considered ANTI-OX-VS moderately to extremely effective.

No device-related adverse event was reported.

CONCLUSION

This exploratory study demonstrates a quick and strong pain relief occurring immediately after the first injection of ANTI-OX-VS, followed by a continuous improvement until the end of follow-up (W13) .

Improvement was achieved much faster than that usually obtained with other commercial viscosupplements probably because of the presence of a high concentration of sorbitol acting through its antioxidant activity.

These data support the need for a large scale, prospective clinical trial comparing the safety and long term efficacy of Synolis™ to regular viscosupplement.