Article published online: 2021-04-26

Response Letter to Editor: In Reference to Letter to Viscosuplementation - Rezende MU, Campos GC. Rev Bras Ortop 2012;47(2):160-164

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Rev Bras Ortop 2021;56(2):272–273.

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Dear Editor,

In the english version of the article Viscosuplementation, Durolane® is cited as a hylauronic acid (HA) of intermediate molecular weight. It was wrongly placed in that reference. Despite Durolane® being the first intra-articular one-shot hyaluronic acid of the european market, it was not so in Brazil. When first introduced in Brazil it was not properly presented.

Durolane is a non-animal stabilized hyaluronic acid (NASHA) that was developed in an attempt to overcome the limitations of existing formulations, by increasing residence time within the joint and providing a higher concentration of HA.[1]

NASHA was the first to be produced by bacterial synthesis and the first to be biocompatible as well as cross-linked (into a solution containing 1, 4-butanediol diglycidyl ether).[2] This cross-linking agent reacts with hydroxyl groups of the repeating disaccharide unit, restricted to ∼0.5–1.0% (∼1 in every 100 disaccharide units is joined to another unit). The process joins the HA molecules to one another, forming a three-dimensional gel. Each gel bead is effectively one enormous molecule of HA, which increases the molecular weight by a factor of around ten thousand billion (i.e., ten to the power 13, or 10^{13}).[1] That is the HA product with the highest molecular weight in the Brazilian market at present.

The true half-life of NASHA is believed to be 4 weeks.[3] The NASHA gel is slowly degraded, most likely by free radicals, with a gradual release of free HA molecules, which are dispersed into the synovial fluid then degraded in the same way as naturally occurring HA molecules.[4]

When considering density, the dose of HA delivered by each injection of NASHA is 60mg (3mL; 20 mg/mL HA).[1]

Since the publication of this review, there are other HA launched (and some were retrieved) in the Brazilian market (all hyaluronan, i.e., without cross-linking such as Durolane® or Synvisc®): Euflexxa®, Cristalvisc®, Synovium® 20, 40 and 75, Synolis V-A®, Renehavis®, Opus Joint®.

Density (concentration), rheologic properties, intra-articular residence time and biocompatibility are all properties of HA that affect final outcomes and not all these aspects were considered in the 2012 revision that should be updated.

From the clinical point of view, similar to Hylan G-F20 that has shown greater short-term effectiveness in underweight, male gender, shorter time since diagnosis, and severe baseline pain,[5] NASHA is more effective in single knee OA than bilateral knee OA that is also more effective than generalized OA.[6] Both medications are useful interventions in patients with mild to moderate OA of the knee, can produce sustained pain relief at 6 months, and can reduce the requirement for analgesia and anti-inflammatory medication during this time with a significant advantage to the NASHA group ($p = 0.001$). At 6 months, this difference is extended even further. Adverse reactions occur significantly less with the more effective product.[7] No studies were performed with NASHA as to prove if effectiveness is improved by adding triamcinolone as it has been shown with Othovisc®[8] and Synvisc One®.[9]

DOI https://doi.org/10.1055/s-0041-1728705.
ISSN 0102-3616.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

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