ABSTRACT
Objective: To assess whether viscosupplementation with hyaluronic acid in patients with severe hemophilic arthropathy associated with triamcinolone after washing with saline improves joint pain, stiffness, function and quality of life. Methods: Eleven patients with hemophilic arthropathy of the knee with and without involvement of other joints (elbows and ankles) underwent joint lavage with saline and subsequent injection of Hylan and triamcinolone in all affected joints. The patients answered the algo-functional (Lequesne and WOMAC), visual analog scale for pain (VAS) and SF-36 (quality of life) questionnaires preoperatively, and at one and three months postoperatively. Results: Pain (VAS and WOMAC pain) and stiffness (WOMAC stiffness) did not show significant improvement (p = 0.3, p = 0.2, p = 0.1, respectively). However function had significant improvement given by WOMAC total and function (averaging 11 points, p = 0.04 and p = 0.001). There was no significant variation in scores in Lequesne’s questionnaire (p = 0.1), yet both mental and physical components of SF-36 presented clinically relevant and significant improvements (p = 0.002). Conclusion: Joint lavage with saline followed by injection of corticosteroids and Hylan is effective in the treatment of hemophilic arthropathy, functionally and in quality of life. Level of Evidence IV, Case Series.
Keywords: Hemophilia. Osteoarthritis. Knee. Hyaluronic acid/ administration & dosage. Hyaluronic acid/therapeutic use.

INTRODUCTION
Hemophilia is a recessive X-linked genetic blood clotting disorder. It affects about one in every ten thousand people, the vast majority of whom are men. Heterozygous women carrying the gene do not usually manifest the disease, yet can transmit it to their descendants.1 There are two main types of hemophilia. Hemophilia A (factor VIII deficiency) and hemophilia B (factor IX deficiency). Hemophilia can also be classified according to severity (mild, moderate, severe), depending on the amount of circulating factor VIII or IX.2 Patients with hemophilia A or B have the same clinical presentation. Cases with moderate or severe hemophilia exhibit a tendency to bleed spontaneously or after minimum trauma, while the joints are the most frequent hemorrhage sites. The joints affected most often are the knees, followed by the elbows, ankles, shoulders and hips.3 Recurrent hemarthrosis quickly leads to degenerative alterations of the articular cartilage, known as hemophilic arthropathy.3 According to Post et al.,4 there are three stages (1-bleeding or acute phase; 2-inflammatory or sub-acute; 3-chronic phase) in the development of the arthropathy. The physiopathology of hemophilic arthropathy appears to result from the persistent presence of blood inside the joint. High levels of proteolytic enzymes (acid phosphatase and cathepsin-D) and cytokines, (IL-1, IL-6 and TNF-α) in the synovial fluid cause this synovial fluid, when added to cartilage in vitro, to inhibit the production of cartilage matrix. Moreover, siderosomes in the cytoplasm of the synoviocytes and of the chondrocytes, stiffness and an increase in articular pressure also favor cartilage destruction. The treatment of acute hemarthrosis in hemophiliac patients is clinical, while clotting factor replacement is the cornerstone of the treatment.1,2 Methylprednisolone can be used for short periods, as can ice packs, braces or other types of immobilization, always avoiding the use of circular plaster casts. Articular puncture can be performed in cases of voluminous hemarthroses, and can be associated with intra-articular injection of corticosteroid, with the objective of reducing synovitis. When there are recurrent hemarthroses, synoviorthesis...
or synovectomy may be indicated in an attempt to reduce the recurrence of hemorrhathoses.

Nowadays, through adequate clotting factor replacement, hemophilia patients have a near-normal life expectancy. Therefore, other methods of treatment, be they palliative or modifiers of the natural history of the disease, should be researched in an attempt to postpone the need for arthroplasty.

Hyaluronic acid is a molecule found physiologically in the synovial fluid. Today it is widely used to treat osteoarthritis. It is believed that its effect is owing to an improvement in the characteristics of the synovial fluid, of the layer of hyaluronic acid in the surface of the articular cartilage and of the increase in protein production by the chondrocyte. In addition, it has viscoelastic properties that play a vital role in maintaining the homeostasis of the synovial fluid and contributes to the lubrication, shock absorption, elasticity, hydration and nutrition of the joint tissues.5,6

The use of hyaluronic acid in hemophiliac patients was described by Wallny et al.7 and Fernandez-Pallazzi et al.8 for the treatment of chronic arthropathy. Fernandez-Pallazzi et al.8 gave an account of the use of hylan in 29 joints of 25 hemophiliac patients, including knee, elbow, shoulder, ankle and hip, reporting excellent or good results in 75% of the patients, with a one-year follow-up. Wallny et al.7 reported the use of hyaluronan in 21 knees of 20 patients, observing improvement in 70% of the cases with a three-month follow-up, and of about 50% with a two-year follow-up. It was concluded, based on these studies, that hyaluronic acid infiltration can act as a palliative therapy in patients with hemophilic arthropathy, postponing more aggressive treatments.

The joint lavage of products of enzymatic degradation of the articular cartilage, nitric oxide, cytokines and pro-inflammatory enzymes, can reduce synovitis.9 The association of triamcinolone with Synvisc® One™, given by injection in patients with knee arthritis improves vicosupplementation results in the first month.10 Synvisc® One™ is the only drug on the market with proof that single-dose application provides results that are equal or superior to the injection of one ampoule of Synvisc® per week for three weeks, allowing a single treatment in patients who should receive clotting factor before each procedure, a factor that involves a higher cost than the cost of complete vicosupplementation (Synvisc® One™).

The aim of this study is to assess the efficacy of the treatment, consisting of joint lavage followed by an injection of corticosteroid and hylan G-F 20, then by a program of exercises to be done at home and/or in a gym depending on the previous level of the hemophiliac patient, in relation to pain relief and improvement of function and of quality of life.

METHODS

Fourteen hemophiliac patients with recurrent hemorrhathosis of the knee, associated or not with recurrent hemorrhathosis of other joints, were included in the study. Three patients who did not have at least one knee joint involved were disregarded in the final evaluation of results. All the patients had the joints involved x-rayed and classified according to the Kellgren and Lawrence (KL) classification.11

The procedure was carried out under anesthesia in a surgical environment under aseptic conditions and surgical paramen-

or synovectomy may be indicated in an attempt to reduce the recurrence of hemorrhathoses. Nowadays, through adequate clotting factor replacement, hemophilia patients have a near-normal life expectancy. Therefore, other methods of treatment, be they palliative or modifiers of the natural history of the disease, should be researched in an attempt to postpone the need for arthroplasty.

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The procedure was carried out under anesthesia in a surgical environment under aseptic conditions and surgical paramen-
profoundly affected with osteophytes and subchondral cysts but with joint space still preserved, perhaps more by some meniscus function than the cartilage thickness itself, and were classified as grade 3. All the others (seven) had grade 4 arthritis of the knees. Neither the age nor the degree of arthritis was related to any of the functional results obtained (VAS, WOMAC Pain, WOMAC stiffness, WOMAC function, WOMAC total and Lequesne) through the lavage and hylan G-F20 and triamcinolone injection procedure.

The pain assessment using the visual analog scale (VAS) showed improvement of six patients at one month and seven patients at three months. The analysis of the entire group did not show significant clinical and statistical improvement (p= 0.293). (Table 1)

Similar to the pain assessment using VAS (Table 1), the pain analysis using WOMAC pain (Table 2), and that of stiffness using WOMAC stiffness (Table 3), did not show significant clinical or statistical improvement in the patients with hemophilic arthropathy due to the lavage and hylan and triamcinolone procedure. Seven patients were better in terms of stiffness after one month and six after three months.

The most important improvement was that of WOMAC function. (Table 4) Ten patients were better at one month and seven remained functionally better at three months. We found one statistically significant p (p=0.0435). Dunn’s test showed a statistically significant difference between before the procedure and one month after (p<0.05), not showing a difference between one and three months postoperatively (p>0.05).

The sum of the three variables (WOMAC pain, stiffness and function) of the WOMAC algofunctional questionnaire (Table 5) revealed that one month after the performance of the procedure, 10 patients out of the total of 11 patients had presented some degree of improvement and seven maintained the improvement after three months with statistically significant result (p=0.0129). In the same way as the WOMAC function, the improvement of the WOMAC total was significantly different between the preoperative period and the first postoperative month (Dunn’s Test, p<0.05) and there was no significant difference between the first and the third month (p<0.05).

Although the assessment using Lequesne’s algofunctional questionnaire shows that eight patients improved in the assessment at one month and seven at three months, it did not show significant improvement. (Table 6)

The physical component of SF-36 showed an improvement with the procedure, but the mental component of SF-36 was the one

| Chart 1. Joints affected by repeated bleeding and clinical complaint. |
|--------------------------|--------------------------|--------------------------|
| Knee | Ankle | Elbow |
| Right | Left | Right | Left | Right | Left |
| 6 | 8 | 4 | 5 | 4 | 0 |

| Table 1. Results of the VAS (Visual Analog Scale of Pain) of the hemophilic patients one day before the procedure (0m), 1 month after (1m) and 3 months after the procedure (3m). Difference between the values of VAS 1 month after the procedure (VAS10) and 3 months after the procedure (VAS30). |
|--------------------------|--------------------------|--------------------------|
| VAS0m | VAS1m | VAS3m | VAS10 | VAS30 |
| Mean | 44.6 | 44 | 46.2 | -0.6 | 1.5 |
| Standard error | 7.9 | 7.6 | 7.7 | 7.5 | 10 |
| Median | 51 | 35 | 42 | 0 | -3 |
| Standard deviation | 26.3 | 25 | 25.6 | 24.8 | 33.1 |
| Minimum | 10 | 19 | 17 | -37 | -35 |
| Maximum | 97 | 97 | 94 | 41 | 71 |
| Number | 11 | 11 | 11 | 11 | 11 |

Friedman Test p=0.293.

| Table 2. Results of WOMAC Pain, of the hemophilic patients one day before the procedure (0m), 1 month after (1m) and 3 months after the procedure (3m). Difference between the values of WOMAC Pain 1 month after the procedure (WD10) and 3 months after the procedure (WD30). |
|--------------------------|--------------------------|--------------------------|
| WD0m | WD1m | WD3m | WD10 | WD30 |
| Mean | 6.6 | 4.7 | 5.5 | -1.9 | -1.1 |
| Standard error | 1.2 | 1.2 | 1.5 | 0.9 | 0.8 |
| Median | 7 | 3 | 5 | -1 | 0 |
| Standard deviation | 4.2 | 3.9 | 4.9 | 2.9 | 2.6 |
| Minimum | 2 | 0 | 1 | -7 | -5 |
| Maximum | 16 | 14 | 18 | 1 | 2 |
| Number | 11 | 11 | 11 | 11 | 11 |

Friedman Test p=0.2557.

| Table 3. Results of WOMAC Stiffness of the hemophilic patients one day before the procedure (0m), 1 month after (1m) and 3 months after the procedure (3m). Difference between the values of WOMAC Stiffness 1 month after the procedure (WR10) and 3 months after the procedure (WR30). |
|--------------------------|--------------------------|--------------------------|
| WR0m | WR1m | WR3m | WR10 | WR30 |
| Mean | 3.9 | 2.5 | 3.1 | -1.4 | -0.8 |
| Standard error | 0.6 | 0.5 | 0.6 | 0.5 | 0.6 |
| Median | 4 | 3 | 3 | -1 | -1 |
| Standard deviation | 2.1 | 1.7 | 1.9 | 1.8 | 2 |
| Minimum | 0 | 0 | 1 | -4 | -5 |
| Maximum | 7 | 6 | 8 | 1 | 2 |
| Number | 11 | 11 | 11 | 11 | 11 |

Friedman Test p=0.1165.

| Table 4. Results of WOMAC Function of the hemophilic patients one day before the procedure (0m), 1 month after (1m) and 3 months after the procedure (3m). Difference between the values of WOMAC Function 1 month after the procedure (WF10) and 3 months after the procedure (WF30). |
|--------------------------|--------------------------|--------------------------|
| WF0m | WF1m | WF3m | WF10 | WF30 |
| Mean | 27.7 | 16.3 | 17.91 | -11.4 | -9.8 |
| Standard error | 5.5 | 3.9 | 3.73 | 3.8 | 4 |
| Median | 23 | 12 | 14 | -7 | -9 |
| Standard deviation | 18.3 | 13 | 12.4 | 12.7 | 13.1 |
| Minimum | 9 | 7 | 5 | -41 | -35 |
| Maximum | 68 | 51 | 51 | 2 | 6 |
| Number | 11 | 11 | 11 | 11 | 11 |

Friedman Test p=0.0435*. Dunn Test WF0m vs. WF1m p<0.05*.
that improved the most, in fact more so at three months than at one month after the procedure. (Table 7)

Despite the team’s efforts to shed light on the importance of physical exercises, this population did not adhere to these exercises. The delivery of didactic material to be read and incorporated into the routine did not do anything to change the patients’ past habits.

**Table 5. Results of WOMAC Total of the hemophilic patients one day before the procedure (0m), 1 month after (1m) and 3 months after the procedure (3m). Difference between the values of WOMAC total 1 month after the procedure (WT10) and 3 months after the procedure (WT30).**

|       | WT0m | WT1m | WT3m | WT10 | WT30 |
|-------|------|------|------|------|------|
| Mean  | 38.3 | 23.5 | 26.5 | -14.7| -11.7|
| Standard error | 7.1  | 5.4  | 5.4  | 5    | 4.7  |
| Median | 33   | 18   | 21   | -10  | -12  |
| Standard deviation | 23.6 | 18   | 18   | 16.5 | 15.7 |
| Minimum | 16   | 8    | 8    | -52  | -41  |
| Maximum | 91   | 71   | 77   | 2    | 7    |

Friedman Test p = 0.0129*. Dunn Test WT0m vs. WT1m p < 0.05*.

**Table 6. Results of LEQUESNE of the hemophiliac patients one day before the procedure (0m), 1 month after (1m) and 3 months after the procedure (3m). Difference between the values of LEQUESNE 1 month after the procedure (LQ10) and 3 months after the procedure (LQ30).**

|       | LQ0m | LQ1m | LQ3m | LQ10 | LQ30 |
|-------|------|------|------|------|------|
| Mean  | 10.9 | 7.9  | 9.2  | -3   | -1.7 |
| Standard error | 1.2  | 1.2  | 1.2  | 0.9  |
| Median | 12   | 7    | 8.5  | -2.5 | -2   |
| Standard deviation | 4    | 4    | 3.2  | 3.9  | 3.1  |
| Minimum | 5    | 3    | 2.5  | -10  |
| Maximum | 17   | 18   | 14.4 | 1    |
| Number | 11   | 11   | 11   | 11   |

Friedman Test p = 0.1165.

**Table 7. Results of the SF-36 of the hemophilic patients, physical component (PCS) and mental component (MCS) one day before the procedure (0m), 1 month after (1m) and 3 months after the procedure (3m).**

|       | PCS0m | PCS1m | PCS3m | MCS0m | MCS1m | MCS3m |
|-------|-------|-------|-------|-------|-------|-------|
| Mean  | 32    | 38    | 36.3  | 48.3  | 54.4  | 55.8  |
| Standard error | 2.4  | 2.4   | 2.9   | 3.1   | 2.2   | 2.6   |
| Median | 32.7  | 36.3  | 38.6  | 50.6  | 55.2  | 54.2  |
| Standard deviation | 8    | 7.9   | 9.5   | 10.3  | 7.5   | 8.8   |
| Minimum | 22.6  | 23.1  | 22.9  | 25.2  | 44.4  | 45.9  |
| Maximum | 43.5  | 50.8  | 48.6  | 61.8  | 67.3  | 74.8  |
| Count  | 11    | 11    | 11    | 11    |

Friedman Test p = 0.020*. Dunn Test MCS0m vs. MSC1m p < 0.05*. MCS0m vs. MSC3m p < 0.01*.

**DISCUSSION**

Hemophilia is a disease that can greatly diminish the quality of life of patients from childhood. Hemophilic children are often deprived of common childhood games to avoid bleeding of the joints. The bleeding of lower limbs starts when these children start to walk. Clotting factor replacement is without a doubt the prophylaxis and the main treatment of the joints. However, due to several factors, Brazil still presents a large group of cases of youths with severe hemophilic arthropathies. These youths have repeated bleeding, important muscular atrophy, reduced bone density (far below normal for the age), no cartilage and intense synovitis that leads to the repeated bleeding. Specifically the knees of hemophiliacs show hypertrophic epiphyses. Arthroplasties should be performed with care, reducing the size of the implants to avoid limiting the range of motion (ROM) in the postoperative period. They are patients with low bone mineral density that can lead to early loosening, in spite of the patients’ low physical demand. Nowadays, with factor replacement, these patients have a long life expectancy. Thus it is important to adequately assess the patient’s quality of life and to try to find ways of improving it, leaving arthroplasty as a last resort, if all else fails.

Owing to the fact that there is no correlation between the degree of arthritis and the symptoms, as well as the fact that hemophilic patients are young, arthritic and low-demand individuals, the initial hypothesis of this study was that viscosupplementation (associated with a joint lavage to wash cytokines, cartilage fragments and blood from the joints involved, as well as the addition of 1ml of triamcinolone) would improve the function and the quality of life of these patient regardless of the degree of arthritis.9,10

The Hemophilia Outpatient Sector of the Hematology Discipline of HCFMUSP referred 14 patients with severe hemophilic arthropathy in order for us to wash from one to four symptomatic joints with frequent bleeding. Of these, 11 had at least one knee involved.

In this case series, they all received clotting factor and were sedated. The joint lavage with one to two liters of saline, as described previously, has various objectives. The main objective is the removal of products of the enzymatic degradation of the articular cartilage, nitric oxide, cytokines and pro-inflammatory enzymes present in the synovial fluid and in the affected joint. These substances perpetuate the synovitis already installed by hemosiderin deposits. The lavage also ensures the correct intra-articular injection of one ampoule of Synvisc™ One™, in the case of the knee, and of Synvisc® in the ankles and elbows.9,12

It is known that viscosupplementation improves pain, function and quality of life. A meta-analysis of 76 studies (including 40 placebo-controlled studies with hyaluronan or Hylan) conducted by Cochrane showed that viscosupplementation is effective in the treatment of knees osteoarthritis for pain relief, improvement of function and of the overall evaluation of the patient. The efficacy of hyaluronic acid is comparable to that of the non-hormonal anti-inflammatory agent and its benefits are more long lasting than the articular injection of corticosteroids. Few adverse effects were reported with viscosupplementation.13,14

The exact mechanism of action of hyaluronic acid injection is not fully known. It is believed that several mechanisms contribute to the positive clinical results in osteoarthritis treatment.15

The first mechanism of action of viscosupplementation would be the purely mechanical effect due to the viscosity of the product (restoration of the viscoelasticity of the synovial fluid: damping, lubrication and elasticity).15

A second mechanism of action of viscosupplementation would be an anti-inflammatory, analgesic, anabolic and chondroprotective biological action. The term visco-induction has been used to describe this biological action and would explain the
maintenance of the positive effects of viscosupplementation for several months even though the half-life of hyaluronic acid is just a few days. It is believed that exogenous hyaluronic acid induces the synthesis of endogenous hyaluronic acid, possibly stimulating the joint regeneration process. In actual fact, in vitro, studies of synoviocytes of joints with osteoarthritis exposed to exogenous hyaluronic acid showed new synthesis of hyaluronic acid. 16

Finally, hyaluronic acid may have a structure modifying action with benefits for the evolutionary process of the disease. The structural benefit of viscosupplementation for the cartilage was proven through biopsy and magnetic resonance imaging. 17,18 We opted for Synvisc® One™ because at the time the project was conceived it was the only medication with proven and authorized indication of single intra-articular injection for arthritis, which is important if we consider that the patient is supposed to receive clotting factor (much more expensive than the medications injected in the joints) before each injection. Its high molecular weight, its prolonged half-life and its high analgesic power also corroborated its choice. With high molecular weight (6 million Daltons), Hylan G-F 20 is a hyaluronic acid mixture with chemically modified molecule. The efficacy of the intra-articular injection of hyaluronic acid can be partly dependent on the viscoelastic properties of the injected mixture determined by its molecular weight. 19 Accordingly, it was initially believed that mixtures with high molecular weight presented better clinical results. 20 We associated triamcinolone as we have experience in the association of these two medications in knee arthritis. Optimizing the results in the first month of treatment with the triamcinolone, what remains, after one month, are the results of the viscosupplementation. And this showed itself to be true in hemophilia as well, with the best results of the first month of treatment (the numbers are always better in the first month of treatment even though there is no statistical difference between the first and the third month after the procedure in an of the variables studied).

As the sample is small, all the tests were non-parametric, possibly lacking strength to demonstrate statistical significance of differences that were clinically obvious.

As we only treated patients with severe hemophilic A arthropathy, all the patients were male. The idea was to treat young individuals to postpone a knee arthroplasty. Only two patients were over 30 years of age. The 37-year-old patient had already been submitted to this procedure at the age of 33. The effects of the procedure had lasted more than 18 months. He wanted to take part in this new study, felt an improvement and this continued throughout the first three months. Only one patient had just one knee involved. The non-treatment of the other joints would not show significant improvement of quality of life since the gait of these patients would still be affected, with continuous pain, and the various forms of function challenges due to the difficulty of ramps, stairs, daily habits, stiffness, etc.

As mentioned above, it is interesting, but somewhat evident, that when both ankles or both knees were not involved, the involvement was crossed, i.e., if the left knee was affected, the patients had the right ankle involved and vice versa, showing that the bleeding of one knee causes the protection of this limb leading to the overburdening of the contralateral side, producing bleeding in the contralateral knee and/or ankle. One of the patients presented important muscular bleeding in the leg considered good in the third postoperative month. His evaluations all showed deterioration in the third month, yet the patient commented that if he had not had the knee procedure done, he would not have managed to bear his weight on the knee with hemophilic arthropathy and move around to protect the contralateral leg. His poor results were due to the leg that bled and not to the loss of the results at three months.

Since most of the patients had severe arthritis, the correlation and regression tests did not show any relation with any of the results obtained (VAS, WOMAC pain, WOMAC stiffness, WOMAC function, WOMAC total and Lequesne). A larger sample may be able to show some relation between age or degree of arthritis, and pain relief or function improvement or even with the extent of the response to the procedure. The visual pain scale (VAS) is somewhat controversial. Despite the constant explanations to the patient, many take the score of ten to mean being in excellent condition and not the worse pain. One patient experienced worse pain in the first month as he presented bleeding in this knee a few days before the assessment (he was the only one whose pain became worse in the first month), returning to preoperative levels in the third month and maintaining the improvement in function). We can say that the procedure did not avoid bleeding, but were also able to observe that the bleeding did not prevent the functional improvement brought about by the procedure, which was best observed in SF-36 (physical and mental). But generally speaking, the pain did not improve. (Tables 1 and 2) Stiffness (WOMAC Stiffness) improved slightly when we analyze the mean. Actually, one K&L 2 patient and the two K&L 3 patients showed a vast improvement in stiffness. Among the seven K&L 4 patients, most improved, 1 deteriorated and 2 maintained the degree of stiffness.

As we expected, the most important improvement was in the patients’ function. The hyaluronic acid interacts with CD44 receptors from the synovial membrane, triggering a series of chemical events, including the maturation of hyaluronic acid of higher molecular weight. Either due to its prolonged half-life, or to the effect of the lavage and of the administration of triamcinolone in the synovial fluid together with the viscosupplementation, this lead to greater autonomy for the patients, improving function and quality of life (WOMAC function, WOMAC total, SF-36 physical and mental components). In all the tests, the improvement obtained in the first month was only slightly lost in the third month and was not statistically significant, as a matter of fact there were patients in which it improved even further in the third month, showing the action of the hyaluronic acid.

Lequesne’s questionnaire has fewer questions and mixes pain, stiffness and function. The degree of improvement here was low and as the sample was small it did not appear statistically significant. In general, Those patients who improved significantly in the WOMAC questionnaire, improved only slightly questionnaire. And those who improved only slightly in the WOMAC questionnaire sometimes obtained even worse scores in the LEQUESNE questionnaire. The WOMAC questionnaire uses a significantly higher number of questions to provide a score for function that of LEQUESNE.
The patients are all satisfied with the procedure. This perhaps justifies the higher score of the mental component of SF-36, which was also higher in the third than in the first month. And although the function is far from ideal, these patients had improvements in day-to-day activities that caused them trouble, such as starting to walk without a limp, improving their ability to descend steps of staircases or ramps, affecting the mental component even more significantly than the physical component. Even though we would have liked these patients to have seized the advantage of the relative analgesia and improvement of function produced by the medication to increase their activity and, consequently, to generate an increase in bone and muscle mass, none of the patients changed habits. Any improvement was provided by the procedure.

CONCLUSION
Joint lavage with saline followed by injection of corticosteroid and hylan is effective in the treatment of hemophilic arthropathy, functionally and in quality of life.

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