

Intra-Articular Hyaluronic Acid in Treating of Hemophilic Knee Arthropathy

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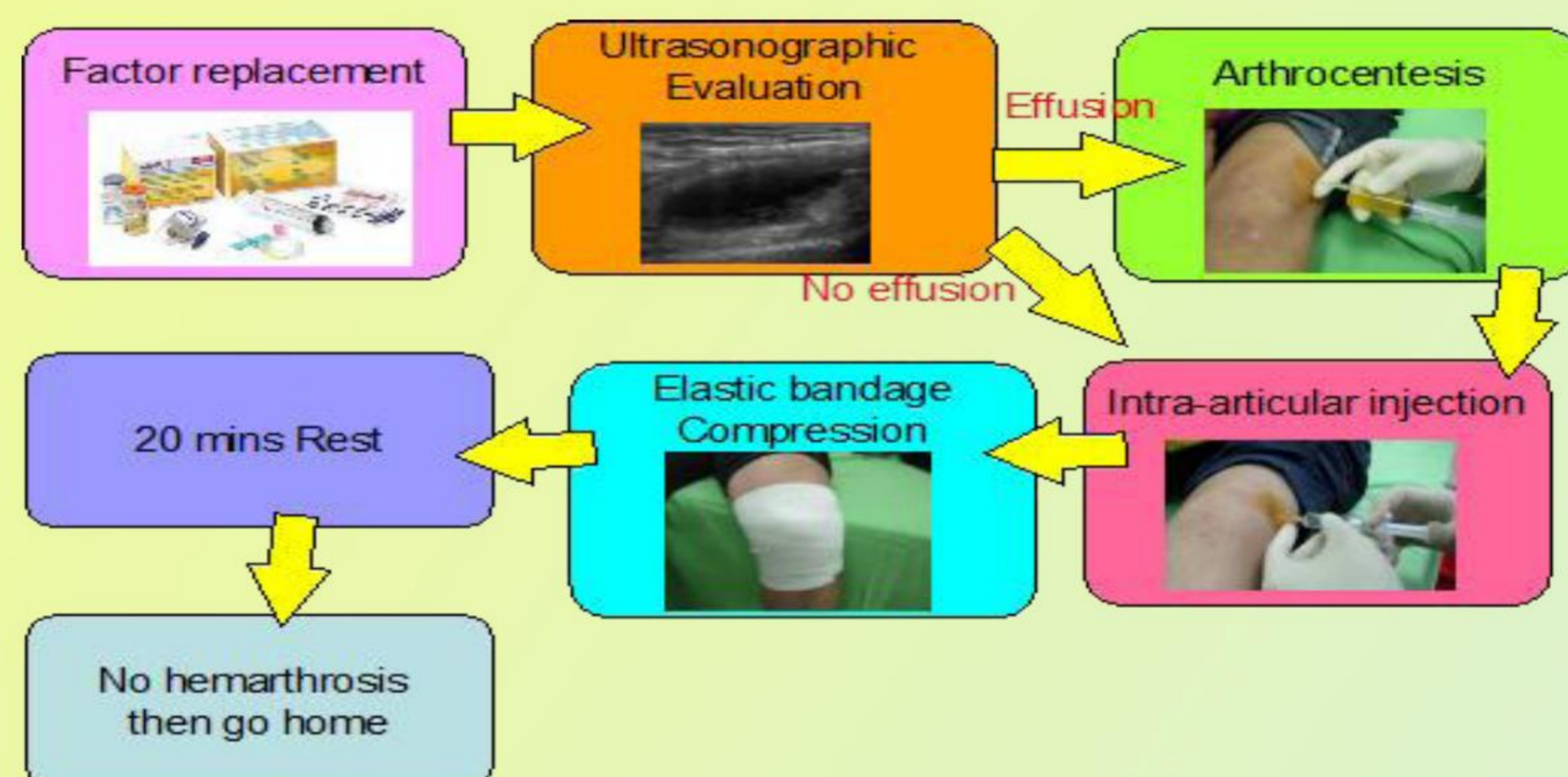
Introduction

Hemophilia is characterized by frequent and lifelong bleeding, and more than 60% of bleeding occurred into joints.¹ Repeated joint bleeding leads to chronic synovitis, cartilage damage and bony destruction, which is associated with range of motion (ROM) limitation, pain, muscle atrophy and functional impairment.^{2,3} Approximately 80% of all spontaneous joint bleeds occur in the ankles, knees and elbows. Prophylactic replacement⁴, physical therapy, COX2 inhibitors^{5,6}, corticosteroids, chemical synovectomy⁷, and radionucleotide synovectomy⁸ should be considered to manage hemophilic synovitis and arthropathy. Hemophilic patients are either not good candidates for surgery or prefer not to have surgery. Some studies showed Hyaluronic acid (HA) to be safe and effective for the treatment of pain associated with osteoarthritis.⁹⁻¹¹ HA has been used successfully in the treatment of osteoarthritis since 1989. Fernandez-Palazzi was the first who used intra-articular HA injection in hemophiliacs in 1994 and reported good response in arthropathy of hemophilic patients in 2002¹². Wallny *et al.* also reported 14 of 20 hemophilic patients improved in knee pain, WFH score and walking distance after 5 times weekly injection of HA¹³. However, we are not aware of any studies focus on the synovial thickness and vascularity after intra-articular HA injection for the treatment of hemophilic arthropathy.

The aims of the study were (1) to investigate the efficacy, safety and effective duration of three weekly intra-articular injections of HA in patients with hemophilic knee arthropathy (2) to evaluate change of synovial thickness and vascularity by ultrasonography after intra-articular HA injection.

Materials and methods

From Aug 2010 to Dec 2011, 15 hemophilic patients who had painful arthropathy of knee joint with synovitis at our hemophilia center were enrolled. Patients received three weekly intra-articular injections of 2 mL HA (Hyalgan). Synovial thickness and vascularity assessed by ultrasonography. Visual analogue pain scale (VAS), range of motion (ROM), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and SF-36 were compared before treatment and at 1, 2, 3 and 6 months after the first injection.



Results

There were 14 hemophilia A and one hemophilia B patients. Their median age was 41 years (range, 21 to 58 years). Twenty knee joints were given HA viscosupplementation therapy and average Pettersson score was 8.4±3.66 (range, 1 to 13). (Table 1) Significant improvement in VAS (F=20.48, p<0.001), WOMAC score (F=10.77, p<0.001), SF-36 score (F=14.24, p<0.001), thickness of suprapatellar recess synovium (F=16.49, p<0.001) and synovial hyperemia (F=12.96, p<0.001) as compared to baseline values were noted at all follow-up visits from one to six months after intra-articular HA injection (Fig 1-4). No severe injection related adverse events or hemarthrosis was observed.

Table 1. Demographic features of hemophilic patients

Characteristic	Average	Range
Patient number	15	
Age, y/o	41.53±8.88	21-58
Height (cm)	167.61±6.16	159-177
Body weight (kg)	68.66±15.79	47.7-113.6
BMI (kg/m ²)	24.33±5.35	19.1-40.3
Severity		
A, severe	12	
A, moderate	2	
B, severe	1	
HIV	2	
Inhibitor	1	
Injected knee	20	
right/left	7/13	
Short Form 36	49.72±16.07	28-93
WOMAC	38.9±19.96	3-79.1
Pettersson score of knee joint	8.4±3.66	1-13
VAS	4.83±2.03	3-9

BMI, body mass index; VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

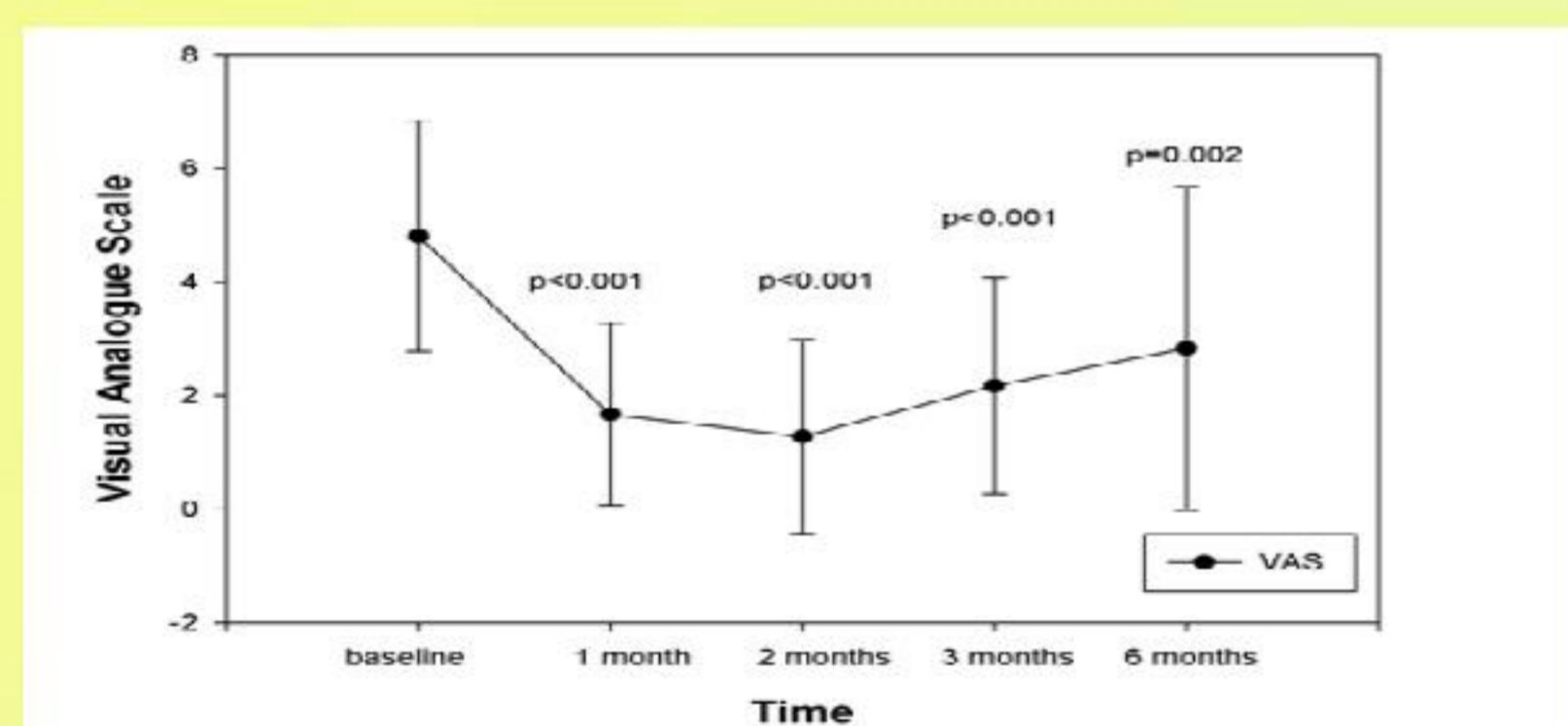


Fig 1 VAS pain scale

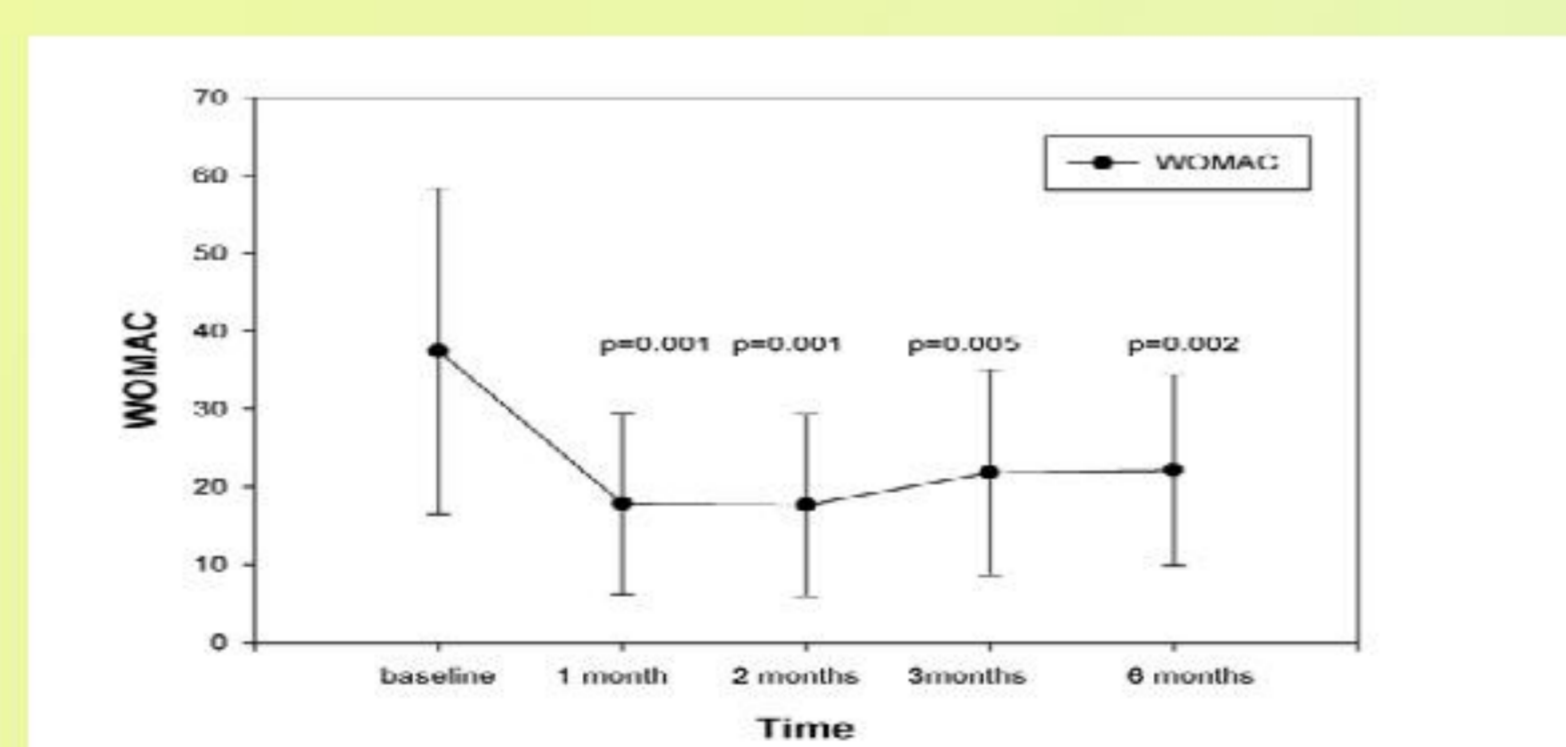


Fig 2. WOMAC scale

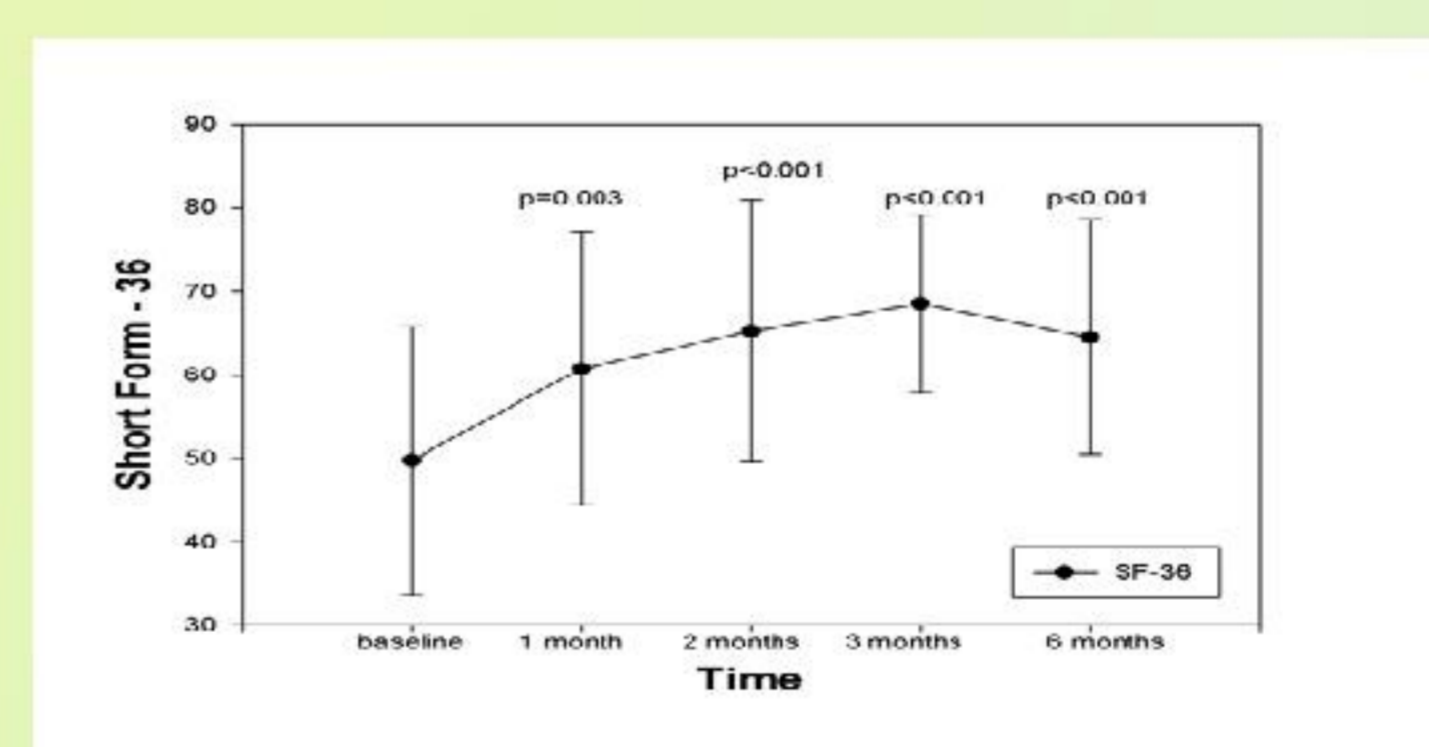


Fig 3. Short Form-36

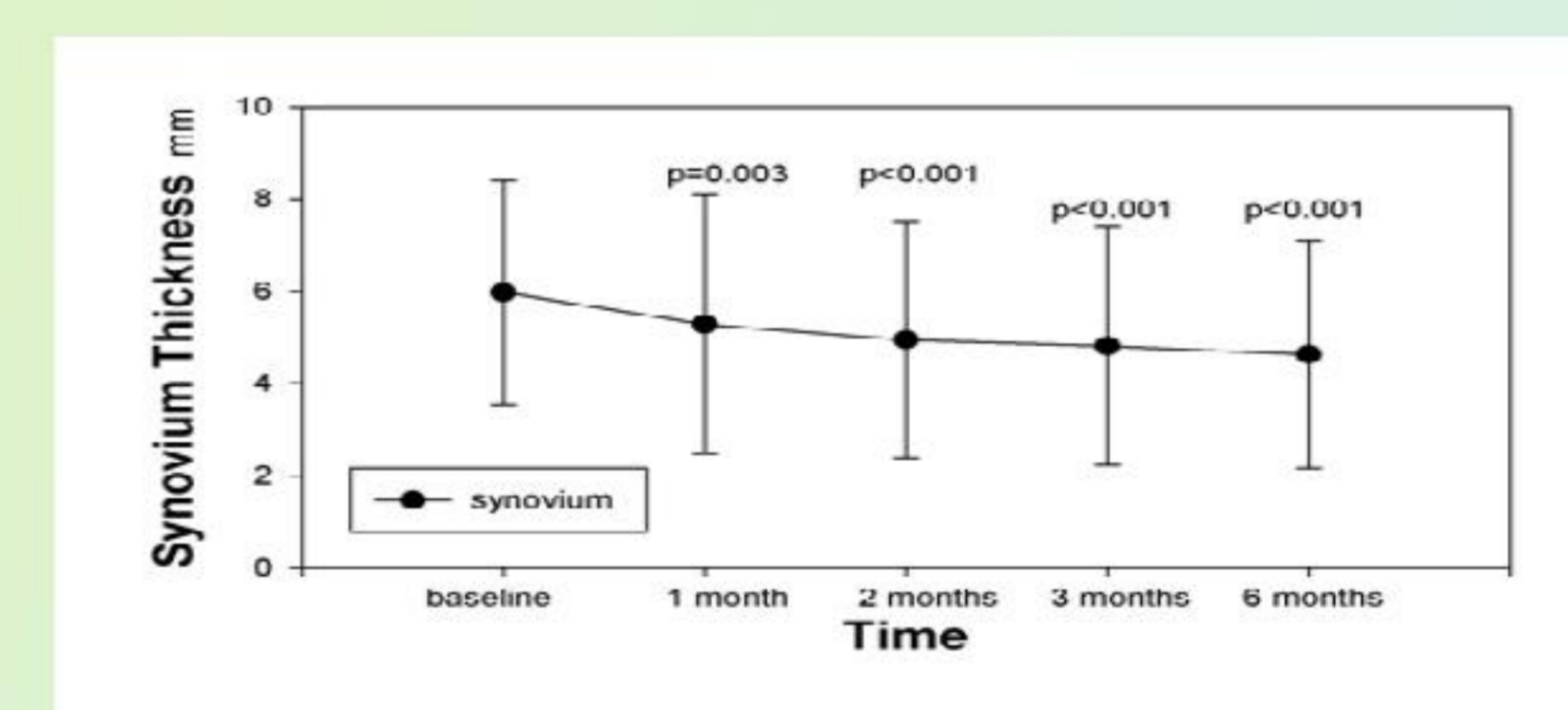


Fig 4. Synovial Thickness

Conclusion

This study demonstrates that three weekly intra-articular HA (Hyalgan) injections are safe and effective in treating of hemophilic knee arthropathy with synovitis. It can not only improve quality of life, relieve pain and restore function of knee in hemophilia patients with painful arthropathy, but also decrease synovial thickness and hyperemia. Hyaluronic acid viscosupplementation therapy could be an alternative therapy if conservative treatment failed or could be an adjunctive therapy before surgical interventions such as arthroscopic synovectomy and total knee arthroplasty.

Reference

- Stephensen D, Tait RC, Brodie N, Collins P, Cheal R, Keeling D, et al. Changing patterns of bleeding in patients with severe haemophilia A. *Haemophilia*. 2009 Nov;15(6):1210-4.
- Choudhury MZ, Mann HA, Goddard NJ, Lee CA. An outline of the current orthopaedic management of haemophilic disease of the upper limb. *Haemophilia*. 2007 Sep;13(5):599-605.
- Luck JV, Jr, Silva M, Rodriguez-Merchan EC, Ghalambor N, Zahiri CA, Finn RS. Hemophilic arthropathy. *The Journal of the American Academy of Orthopaedic Surgeons*. 2004 Jul-Aug;12(4):234-45.
- Fernandez-Palazzi F. Treatment of acute and chronic synovitis by non-surgical means. *Haemophilia*. 1998 Jul;4(4):518-23.
- Rattray B, Nugent DJ, Young G. Rofecoxib as adjunctive therapy for hemophilic arthropathy. *Haemophilia*. 2005 May;11(3):240-4.
- Rattray B, Nugent DJ, Young G. Celecoxib in the treatment of hemophilic synovitis, target joints, and pain in adults and children with haemophilia. *Haemophilia*. 2006 Sep;12(5):514-7.
- Fernandez-Palazzi F, Rivas S, Viso R, de Bosch NB, de Saez AR, Boadas A. Synovectomy with rifampicine in hemophilic haemarthrosis. *Haemophilia*. 2000 Sep;6(5):562-5.
- Rivard GE, Girard M, Belanger R, Jutras M, Guay JP, Marton D. Synoviorrhesis with colloidal 32P chronic phosphate for the treatment of hemophilic arthropathy. *J Bone Joint Surg Am*. 1994 Apr;76(4):482-8.
- Petrella RJ. Hyaluronic acid for the treatment of knee osteoarthritis: long-term outcomes from a naturalistic primary care experience. *Am J Phys Med Rehabil*. 2005 Apr;34(4):278-83; quiz 84, 93.
- Charalambous CP. Corticosteroid compared with hyaluronic acid injections for the treatment of osteoarthritis of the knee. *J Bone Joint Surg Am*. 2004 Apr;86-A(4):874; author reply 874-5.
- Lo GH, LaValley M, McAlindon T, Felson DT. Intra-articular hyaluronic acid in treatment of knee osteoarthritis: a meta-analysis. *JAMA*. 2003 Dec 17;290(23):3115-21.
- Fernandez-Palazzi F, Viso R, Boadas A, Ruiz-Saez A, Cavaglia H, De Bosch NB. Intra-articular hyaluronic acid in the treatment of hemophilic chronic arthropathy. *Haemophilia*. 2002 May;8(3):375-81.
- Wallny T, Brackmann HH, Semper H, Schumpe G, Effenberger W, Hess L, et al. Intra-articular hyaluronic acid in the treatment of hemophilic arthropathy of the knee. Clinical, radiological and sonographical assessment. *Haemophilia*. 2000 Sep;6(5):566-70.