

RADIOISOTOPE SYNOVECTOMY IN PATIENTS WITH HEMOPHILIA: SINGLE CENTER EXPERIENCE

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Background:

Hemophilia is a congenital blood defect consisting of a partial or total absence of clotting factor VIII (hemophilia A) or factor IX (hemophilia B). This defect leads to abnormal bleeding in the musculoskeletal system, causing joint disability. If the bleeding is not correctly treated, this abnormal position leads to recurrent bleeding and progressive destruction of the joint. Chronic hemophilic synovitis is characterized by persistent joint swelling (1-4).

In children, total joint replacements are absolutely contraindicated and surgical synovectomies are not cost-effective procedures. Hence, noninvasive procedures can be used to reduce progression (3-7). Among these, the one is intra-articular injection of corticosteroid, rifampicine and hyaluronic acid (8,9). Previous studies have shown that radioisotope synovectomy (RS) is an effective treatment for chronic hemophilic synovitis. RS is both less invasive and inexpensive procedures. RS is a good non-surgical option for reducing synovial membrane size and thus the number of hemarthrosis episodes. RS is accepted as the gold-standard therapy before surgical synovectomy (2,4,10).

Aim

We aimed to investigate the efficacy and complications of RS in the patients, who treated at our center, with hemophilia.

Patients and Method

For the last 5 years, from 2008 to 2013, 27 RS Yttrium 90 (⁹⁰Y) and Erbium ¹⁶⁹ (Er¹⁶⁹) in 12 patients with hemophilia A and B, age ranging 6-21 (mean 11) years at the time of RS have been performed at our center, Erciyes University Medical Faculty of Turkey. Of 27 joints, 12 were knees, 9 were ankles and 6 were elbows. All patients had severe type of hemophilia (FVIII < 1% and F IX < 2%). Eleven of them had hemophilia A and 1 had hemophilia B. No patients had anti-HIV, anti-HBs and anti-HCV antibodies.

No patients had the FVIII and F IX inhibitor. For clinical classification of synovitis, grading system developed by Fernandez-Palazzi was used for evaluation (3,7). RS was preferred in the stage of grade-II (permanent synovitis) and grade-III (chronic hemophilic arthropathy). Firstly, written informed consent had been for each patient. Factor supplementation was started 2 h before injection. For patients, >50% correction dose because of non-inhibitor was the accepted level. Midazolam (0.5 mg/kg) was used orally 15 min before procedure for sedation of children. Injection site is prepared for aseptic application in fluoroscopy unit of Radiology Department. Inserting 20 (for knees) or 22-gauge needle (for small joints) into joint and aspirating the synovial fluid if it is possible. Yttrium ⁹⁰ (⁹⁰Y) was preferred for knees and ankles, and Erbium ¹⁶⁹ (Er¹⁶⁹) for elbows. Yttrium dosimetry: 5 mCi (4 mCi for ages below 10 years) for knees and 2 mCi ankle. Erbium ¹⁶⁹ dosimetry: 2 mCi for elbow. Isotope was injected into the joint in a volume of 1 mL, using a separate syringe. Following injection of isotope, analgesic drug was injected into the joint. Manual pressure upon the puncture site for 5 min and passive flexion of extremity for dispersing the material in joint space was applied. Factor supplementation is continued for 3 days with two bolus injections in operation day and one bolus injection for the next two days. The patients were immobilized for a period of 3 days. After 3 days elastic bandage was applied for 2 weeks for supporting the joint. Physical therapy initiated if clinically indicated. All patients should be followed-up for at least 1 year.

Table 1 The clinical classification of synovitis in 12 patients

	Number of Knee	Number of Ankle	Number of Elbow
Grade I	-	-	-
Grade II	4	8	4
Grade III	8	1	2
Grade IV	-	-	-

Table 2 The success of RS in different joints

	Number of Knee	Number of Ankle	Number of Elbow
Good	11	9	4
Poor	1	-	2

Results

We considered that the study includes 6 elbows, 9 ankles and 12 knees, and a total of 27 RS procedures. Two patients were in secondary continuous prophylaxis regimen before RS. In 12 patients (4 patients: Grade II and 8 patients: Grade III), RS was applied to knees. In 9 patients (8 patients: Grade II and 1 patient: Grade III), RS was applied to ankles. In 6 patients (4 patients: Grade II and 2 patients: Grade III), RS was applied to elbows (Table I).

Radioisotope injections were three times repeated in right ankle of one patient after 6-month interval. After RS, two mild complications were observed. In 3 patient, there was a minimal hematoma of the ankle and hematomas were been drained. Two patient had minimal pain on injection site. Therefore, intra-articular steroids were used after the procedure. After 2 years of follow-up, the marked reduction in frequency of bleeding was observed. In 24 procedures (11 knees, 9 ankles and 4 elbows), good results were obtained. But, the outcome was poor for 3 different procedures (1 knee, 2 elbow) (Table II).

Discussion

In patients with hemophilia, the relationship between repeated hemarthroses, chronic synovitis and hemophilic arthropathy has been well documented in literature (1-5). Hemophilic arthropathy can be prevented by primary prophylaxis. Secondary prophylaxis and aggressive on-demand treatment might not be preventive of arthropathy. In the previous years, most patients had no social security for the need to be operated in hospital, long rehabilitation periods and high cost of factor concentrates in Turkey (2,4). Hence, we try to use episodic treatment for target joints or sometimes 6 months of secondary prophylaxis for reducing synovitis.

If the patients have recurrent bleedings with chronic synovitis in their target joints, they are eligible for local therapy such as surgical synovectomy or RS. It is accepted that the first-line therapy should be RS before operative synovectomy. Compared with surgical synovectomy, RS is less invasive and has a lot of advantages (1-4,11-13). In using RS, neither articular nor neoplastic complications have been reported in the literature. RS can be performed at any age in the hemophilic patients (12).

The different radioisotopic materials such as Rhenium 186, Y90, Er¹⁶⁹ could be use for the procedure of RS (2,4,12). We preferred Y90 for knee and ankle, Er¹⁶⁹ for elbow, respectively. Because Y90 and Er¹⁶⁹ are the chemically pure, non-toxic isotope, which are easy to obtain, Kavakli et al. found excellent outcome rates in grade-II synovitis (84% for knees, 93% for elbows and 50% for ankles) with Y90 after 6 months. In grade-III synovitis rates were 73%, 66% and 27%. Regarding excellent plus good results, notes were 100% for knees and elbows and 92% for ankles (2). Jahangier et al. also reported one case of acute pain even when using steroid plus Y 90 (14). We also found a good outcome in grade-II and III synovitis (11 for knees, 9 for ankles and 4 for elbows 9) with Y90 and Er¹⁶⁹ after two years.

Most studies have shown that RS procedure is rather safe. The risk of malignancy is the major problem, especially in children. Exposure to radioisotopes may cause chromosomal abnormalities and oncologic transformation and increase the risk of neoplasia. There are the published reports of malignancy-associated RS in rheumatoid arthritis patients. But, in the patients with hemophilia, there is no single report of neoplasia after RS (2,4,12). In conclusion, Y90 and Er¹⁶⁹ are effective and safe in the treatment of chronic synovitis of children with hemophilia. Compared with surgical alternatives, RS is cost-effective and easy to perform.

Literature

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