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Original article

Treatment Response Evaluation using Yttrium-90 in Patients with Rheumatoid Arthritis of Knee Joint

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Abstract

For radiosynovectomy, we have measured the retention time of yttrium-90 (^{90}Y) hydroxyapatite (particle size 1–10 μm) within the knee joint space and evaluated the treatment responses in knees with rheumatoid arthritis. Radioactive measurements in the region of knee after injection of ^{90}Y hydroxyapatite into the joint space were made with a single prove system designed to monitor radioactivity and showed retention of ^{90}Y in the knee ranged 76.6% ±5.4% after 4 days of injection. The clinical improvements in rheumatoid arthritis of knee joint with steinbroker Stages I and II were increased as time goes by, the improvement ratio is in 72% at 6th months and 76% at 12th months after injection of ^{90}Y 185 MBq (5 mCi) per joint.

Keywords: Knee joint, radiosynovectomy, yttrium-90 hydroxyapatite

Introduction

In rheumatoid arthritis, pain, swelling, and functional disorder of joints are often satisfactorily treated by oral anti-inflammatory or immunosuppressive drugs when symptoms are mild. However, in chronic, persistent inflammation, additional local treatment must be used. Well-established local treatment options are surgical resection, intra-articular steroid application, and radiosynovectomy. Surgical procedures, ranging from open-joint surgery to minimally invasive arthroscopic synovectomy, are associated with risks of surgery and anesthesia, need for hospitalization, and a prolonged period of rehabilitation. Intra-articular injection of corticosteroids is the most frequently applied and widespread therapeutic approach in the local treatment of synovitis. However, many studies have described negative effects on articular cartilage metabolism and vitality. Furthermore, repeated intra-articular steroid applications often result in increasingly shorter time periods of effective pain relief.[1-3] Owing to the limitations of local treatment modalities, radiosynovectomy has become an alternative and supplementary therapeutic approach for the treatment of painful inflammatory joint diseases or chronic recurrent joint effusion.

For radiosynovectomy, β-emitting radiocolloids are used for intra-articular application. Immediately after administration, the colloids are taken up by phagocytosis by Type-A synoviocytes which partly build the surface layer in the synovial membrane as well as by phagocytosing immunocompetent cells such as macrophages. Therefore, radiosynovectomy using, yttrium-90 (^{90}Y) with β-particle emission is based on the well-documented phenomenon that the internal radiation technique is to destroy the diseased pannus (hyperplasia of the villous synovium) and inflamed synovium by direct and highly selective irradiation and with the exception that following synovium destruction, the regenerated synovium will be free of disease.[4]

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^{90}Y is presently being considered as a suitable radionuclide for in the knee joint with rheumatoid arthritis because of its deep tissue penetration (mean = 3.6 mm; maximum = 11 mm).[5] At list, the particle sizes of ^{90}Y 5 ± 10 nm or 2–5 μm are enough to be taken up by the synovial cells and to achieve a homogeneous distribution within the whole joint. If a particle diameter is not large enough to avoid leakage out of the joint cavity by venous or lymphatic drainage, it would result in an increased irradiation of the whole body and particularly of the locoregional lymph nodes, the liver, and the spleen.[6,7] For radiosynovectomy of the knee joint, the recommended activity per joint is usually 185–222 MBq (5–6 mCi). The clinical outcome of radiosynovectomy in meta-analysis including 2190 treated joints was successful in 66.7% ±15.4% of rheumatoid arthritis.[7] There was a difference according to the steinbrocker stages (Steinbrocker I: 72.8% ±12.3%; Steinbrocker II: 64% ±17.3%; Steinbrocker III and IV: 52.4% ±23.6%).[8]

Materials and Methods

Materials

A total of 25 patients (13 males and 12 females) with 40 rheumatoid knees and Stage I and II classified according to the American Rheumatoid Association classification were selected for the study. The age range was 45–60 years old with mean age of 49.9 years old. These patients were mandatory adequate standard baseline pharmacotherapy with anti-inflammatory drug or intra-articular steroid application for at list 6 months before radiosynovectomy and failed in those.

Methods

Each patient was treated with ^{90}Y hydroxyapatite 185 MBq (5 mCi) per joint for intra-articular therapy of the knee of which a particle size was 1–10 μm. Knee joint puncture for radiosynovectomy has done following the rules of strict asepsis and intra-articular needle placement has been ensured by aspiration of joint fluid through the needle which is being used to inject ^{90}Y-colloid. Moreover, the puncture was made 1–2 cm medial to the margin of the patella using an 18-gauge by 1.5-inch in a supine position of the patient with the knee fully extended. Absolute immobilization of the treated joints for 48 h using splints or bed rest is recommended as this will reduce transport of ^{90}Y hydroxyapatite through the lymphatics to the regional lymph nodes. Radioactive measurements to detect bremsstrahlung in region of knee were made with a single prove system designed to monitor radioactivity at 0, 24, 48, 72, 96 h after injection of ^{90}Y hydroxyapatite into the joint space. Physical half-life of ^{90}Y (2.7 days) is considered in the calculation of the regional radioactivity in percent.

Calculation of absorbed dose to the synovium is done using the models of Berger.

Treatment responses were evaluated as improvement of clinical signs and symptoms (pain, swelling, effusion, knee motion) at 6 and 12 months after injection. We defined "very good" results as complete disappearance of clinical arthritis; "good" implies a striking improvement of all clinical signs and symptoms; "fair" implies improvement of some clinical abnormalities; and "none" implies to be the same as before the treatment.

Results

Estimation of retention of yttrium-90 hydroxyapatite within the knees

Changes of radioactivity of the injected ^{90}Y hydroxyapatite in the knee at each time are shown in Table 1.

Radioactivity in the knee after injection was 76.6% ±3.6% at 4 days. Assuming a surface area of the synovium of the knee is 250 cm^2 and effective half-life is not equal to physical half-life, a dose of ^{90}Y hydroxyapatite 185 MBq (5 mCi) injected in the joint space of the knee would thus be expected to deliver about 8500 cGy to the synovium using the model of Berger.[9]

Clinical improvement in rheumatoid knees

Reduction of pain in the knee

As shown in Table 2, reduction of pain is above 80% and 77% in the knees with rheumatoid arthritis of Stage I and II, respectively, 12 months after injection. Moreover, some patient did not follow-up the treatment response at 12 months, only 6 months.

Reduction of swelling and effusion in the knee

Reduction of swelling and effusion is above 80% and 76% in the knees with rheumatoid arthritis of Stage I and II, respectively, 12 months after injection [Table 3].

Table 1: Regional radioactivity of the injected yttrium-90 hydroxyapatite in the knee (%)

Number of knees	Time interval after injection			
	1 day	2 days	3 days	4 days
5	92.6±3.0	89.6±3.8	80.5±3.4	76.6±3.6

Table 2: Reduction of pain in the knee

Stage	Number of knees	Months of follow-up	Results (%)			
			Very good	Good	Fair	None
I	15	6	7 (47)	3 (20)	2 (13)	3 (20)
	10	12	5 (50)	1 (10)	2 (20)	2 (20)
II	25	6	11 (44)	4 (16)	4 (16)	6 (24)
	21	12	10 (48)	2 (10)	4 (19)	5 (23)

Improvement of the knee motion

As shown in Table 4, improvement of the knee motion is above 80% and 76% in the knees with rheumatoid arthritis of Stage I and II, respectively, 12 months after injection. The biological effects within the irradiated tissue are caused by both direct damage and indirect interaction.

Secondary oxygen radicals generated by tissue irradiation are known to destroy the cellular membranes by lipid peroxidation and result in DNA strand damage and breaks. All these interactions result in fibrinoid necrosis, sclerosis, and fibrosis of the synovial stroma, the inflammatory cells, and capillaries within the synovial membrane. A significant reduction of the inflammatory pannus tissue and the occlusion of capillaries of the synovial membrane decreasing the secretory activity markedly would be within a few weeks. Thus, the clinical effects of radiosynovectomy for the patient seem to be a reduction of pain, swelling, and effusion.

Discussion

The retention rate of ^{90}Y hydroxyapatite (particle size 1–10 μm) in the joint space of the knee is 76.6% ±3.6% after 4 days. The radiation absorbed dose delivered to the synovial membrane is about 8500 cGy using the model of Berger for calculation after injecting a dose of ^{90}Y hydroxyapatite 185 MBq (5 mCi) in the joint space of the knee.

Radiosynovectomy using ^{90}Y hydroxyapatite showed good clinical improvement in the treatment of rheumatoid knee in steinbrocker Stages I and II.

Table 3: Reduction of swelling and effusion in the knee

Stage	Number of knees	Months of follow-up	Results (%)			
			Very good	Good	Fair	None
I	15	6	8 (54)	2 (13)	2 (13)	3 (20)
	10	12	6 (60)	1 (10)	2 (20)	2 (20)
II	25	6	12 (48)	4 (16)	4 (16)	6 (20)
	21	12	12 (57)	-	4 (19)	5 (24)

Table 4: Improvement of the knee motion

Stage	Number of knees	Months of follow-up	Results (%)			
			Very good	Good	Fair	None
I	15	6	7 (47)	2 (13)	2 (13)	3 (27)
	10	12	6 (60)	1 (10)	2 (20)	2 (20)
II	25	6	11 (44)	3 (12)	4 (16)	7 (28)
	21	12	10 (47)	1 (5)	5 (24)	5 (24)

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Conflicts of interest

There are no conflicts of interest.

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