Yttrium-90 silicate radiosynovectomy treatment of painful synovitis in knee osteoarthritis. Results after 6 months

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Abstract

Our aim was to evaluate the response of radiation synovectomy (RS) with yttrium-90 silicate (^{90}Y-S) treatment of synovitis in patients with knee osteoarthritis (OA) and to derive factors that influence this response. The RS treatment response *was assessed* prospectively in 74 painful OA knees of 74 patients during a period of 6 months follow up. The duration of the disease was 24 ± 9 months. Forty-four of the 74 knees had pain during the night and 43/74 had abnormal flexibility. Knee joints were graded according to the Steinbrocker radiological system. RS was performed according to the European Association of Nuclear Medicine guidelines. RS response was assessed considering the pain improvement from baseline values in terms of a 100-point visual analogue scale (VAS), the improvement of knee flexibility and the pain remission during the night. RS response was classified as poor (VAS < 25), fair (VAS ≥ 25 - 50), good (VAS ≥ 50 - 75) and excellent (VAS ≥ 75), with excellent and good results considered as success, while fair and poor as failure. *Our results* show that 6 months after RS treatment, the percentage of VAS from baseline values was 66.0% ± 24.8% and found to be significantly related to patients' age (P = 0.01), duration of the disease (P = 0.04) and to radiographic grading of OA (P = 0.001). Knees without or with mineral type OA radiographic changes (Steinbrocker's grades 0-I) responded better than those with more advanced changes (Steinbrocker's grade III-IV) in terms of VAS improvement (77.9% versus 53.8%) (P < 0.001). The overall success rate (VAS ≥ 50) was 83.8%. Remission of pain during the night was achieved in 88.6% and knee flexibility was improved in 65.1%. RS side effects assessed for the whole follow-up period were minor and not significant. *In conclusion*, RS with a single injection of ^{90}Y-S in patients with knee OA seems to have a significant therapeutic effect after a six months follow-up period with no significant side effects. Six months after RS treatment, clinical improvement was inversely related to radiographic knee damage, patients" age and duration of the disease. RS also induced remission of OA pain during the night.

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Introduction

Radiation synovectomy or radiosynovectomy (RS), also known as radiosynoviorthesis was first described in 1950's as an adjuvant treatment for rheumatoid arthritis (RA) [1]. RA is effective and safe for the management of persistent synovitis, combined with various chronic inflammatory joint disorders [2-4]. RS may relieve synovitis, joint pain, knee flexibility and joint effusion in about 60%-80% of the cases [5-8]. RS is based on the irradiation of the joint synovium by the intra-articular administration of various β-emitting radiopharmaceuticals and its effectiveness depends on the kind of the joint and the location of inflammation [1, 3]. Yttrium-90 (^{90}Y), in the form of citrate or silicate (^{90}Y-S) colloid solution, is the radiopharmaceutical of choice for RS of knee joint synovitis caused by several arthropathies [3] and recently, recommended for persistent synovitis in cases of osteoarthritis (OA) [8-12]. The European Association of Nuclear Medicine (EANM) included the RS treatment of OA synovitis in the revised RS guidelines [4], suggesting that more results of RS treatment on specific joints and arthropathies are needed [3]. Many of the RS treatment results of synovitis in knee OA include a small number of cases [13-16]. So far the RS efficiency in patients with OA advanced radiographic knee damage and pain at night and the study of other factors that may influence its efficiency, have not been extensively studied. We have studied prospectively in patients with knee OA, factors that may have influenced the response to RS after a single ^{90}Y-S injection and a follow up period of 6 months.

Material and methods

We have prospectively studied 74 patients (62 women, 12 men) with an average age of 67.8±8.5yr (range 49-82yr) and 74 knee joints with knee osteoarthritis, as recorded in their medical files. All patients were referred to us by their medical physician complaining of chronic knee pain, inadequately controlled by systemic or local pharmacotherapy, and were treated with a single RS after they gave their informed consent. The mean duration of the disease was 24±9 months (range 6-127 months). All 74 knee joints (64 right and 10 left knees) studied, had a history of knee pain at exercise, severe enough to limit their normal physical activity over the preceding 3 months, while 44 out of the 74 knee joints (58%) had also night pain. The knee flexibility was normal in 31 out of 74 joints (41.9%) and reduced less than 20° in 12/43, between 20° and 40° in 16/43 and more than 40° in 15/43 knees.

All patients treated between the years of 2004 to 2006 fitted the EANM guidelines for RS [3, 4]. The severity of active, soft tissue inflammation of the joints was evaluated with a 2-phase bone scan using ^{99m}Tc-methylenediphosphonate. All patients had a recent radiography and sonography of the joint, with recorded knee effusion and synovial thickness. All knee joints were assigned in groups according to the radiographic OA changes, using the Steinbrocker's radiological grading system (grades 0, I, II, III and IV) [17], presented in Table 1.

Table 1. *VAS knee joint improvement after 6 months follow up according to Steinbrocker's radiographic classification. Percentage values are shown in parentheses (* P<0.05)*

Total number of treated knee joints	n = 74	VAS improvement (%)
Grade 0 (no, percentage)*	4 (5.4%)	85.0 ± 12.9 (70-100)
Grade I*	27 (36.5%)	76.3 ± 15.6 (50-100)
Grade II*	20 (27.0%)	62.3 ± 25.6 (0-90)
Grade III*	21 (28.4%)	54.2 ± 29.8 (0-100)
Grade IV*	2 (2.7%)	50.0 ± 0.0 (50-50)

* Comparison of VAS improvement between the OA knee grade groups gave a significant difference of P<0.05

RS treatment was performed in all knee joints with precise intra-articular single knee injection of a typical dose of 185MBq ^{90}Y-S (Nycomed Amersham, U.K) under sterile conditions and after as much as possible synovial fluid aspiration. Before joint puncture, local anesthesia was administered with 2% lidocaine-hydrochloride. Immediately after the radionuclide injection, the needle remained in situ and was flushed with 20mg triamcinole hexacetonide, in order to reduce the risk of acute radiation induced synovitis and to avoid skin radiation necrosis [3]. Thereafter the patient was advised to keep the injected joint elastically splinted and partially immobilized for 72h, without weight bearing [3, 18]. Imaging of activity distribution with a dual head gamma camera (Vertex Plus Epic, ADAC, CA, USA), showed appropriate homogeneously intra-articular distribution of the radionuclide within the joint space [3].

The analysis of RS treatment outcome after 6 months follow up, in all knees was based on detailed information from the patient and clinical examination. Treatment outcome was examined in terms of joint pain during exercise improvement measured with a 100-point visual analogue scale (VAS) pain score, before and at 6 months after treatment. Any improvement of the knee pain was measured and calculated as a mean (±SD) percentage change from the baseline VAS score. The RS treatment outcome was assessed as excellent, good, fair and poor [15, 16]. Excellent and good results were considered as treatment success, fair and poor as treatment failure. Patients with excellent results had an improvement of VAS score equal or higher than 75%, patients with good response had VAS scores of 50%-75%. Patients with a fair result had VAS scores 25%-50%, while patients with a poor result, had no benefit from treatment, joint pain continued and VAS score was less than 25%. The presence or absence of pain during the night before and after RS treatment, was recorded according to patients judgment and was used as another treatment response variable, not being studied so far. The improvement of patient's knee flexibility was considered as an objective treatment response, measured by the angle of knee flexion (less than 20°, between 20° to 40°, more than 40°).

We also compared RS influences with patients age, the duration of symptoms and the X-ray grading. Patients were divided into two groups according to their age (45-65 and 66-85 yr) and two other groups according to the duration of the disease (6-23 months and 24-127 months). Knee joints were assigned in groups according to the radiographic OA findings, using the Steinbrocker radiological grading system (grades 0, I, II, III and IV) [17]. Any difference between these groups was tested using the χ^2 distribution and t-Student's tests, considering as statistically significant, the P value of less than 0.05.

Results

Six months after RS, the VAS improvement from baseline values of the knee pain on exercises for the whole group was 66.0%±24.8%. For patients aged 45-65 yr and 66-85 yr, the mean VAS improvement was 75.2%±20.7% and 60.7%±25.9%, respectively. There was a statistically significant difference (P=0.01) between these two groups. Patients with symptoms lasting less than 2 years, had a mean VAS improvement of 73.5%±19.0%, significantly higher than the corresponding value of 62.4%±26.6% of patients with the disease lasting for 2 or more years (P=0.04). The outcome results in terms of VAS for joint improvement related to the radiographic changes, are shown in Table 1. With an adjustment for the number of treated knee joints, the VAS improvement for knees without or with mineral OA (Steinbrocker's grades 0-I), versus knees with more advanced (Steinbrocker's grades III-IV) radiographic changes, was 77.9% versus 53.8% (P<0.001).

The RS overall success rate as a percentage of knee joints studied, is shown in Table 2. Table 2 does not show that no response (complete failure-VAS improvement score 0%) was

Table 2. *Patients' RS response measured by VAS at 6 months. Percentage values are shown in parentheses.*

No of joints	Excellent (VAS ≥75)	Good (VAS ≥50-75)	Fair (VAS ≥25-50)	Poor (VAS < 25)	Success	Failure
74	40 (54.1)	22 (29.7)	7 (9.5)	5 (6.8)	62 (83.8)	12 (16.2)

found in 4/74 knees, while complete response (VAS improvement score 100%) was seen in 7/74 knees. In a further analysis, concerning the radiographic changes, it seems that at 6 months after RS treatment the success rate was 100% for knees without or with mineral OA radiographic changes (Steinbrocker's grades 0-I) and 90% for knees with moderate OA radiographic changes (Steinbrocker's grade II). However in knees with advanced (Steinbrocker's grades III-IV) degenerative changes, the RS success rate was significantly reduced (79.2% in 6 months), compared to the joints with no or minimal radiographic changes.

At 6 months after RS treatment, night pain was absent in 39 out of the 44 knees (88.6%). Knee flexibility was improved on 28/43 knees (65.1%) at 6 months and not improved in the rest. Specifically knee flexibility was reduced to less than 20^{o}, between 20^{o} and 40^{o} and more than 40^{o} in 16/43, 10/43 and 2/43 cases (for direct comparison with abnormal knee flexibility before RS).

The side effects during the follow-up period were minimal: In three cases there was a temporary increase in synovitis, most probably due to the radiation-induced flare up synovitis [3] and was treated with joint fluid aspiration. Symptoms of an allergic reaction occurred immediately after one therapeutic procedure injection and lasted for 2 days after appropriate treatment. No other side effect, occurred, including thromboses or skin radiation necrosis.

Discussion

According to our prospective study, the RS overall success rate (VAS ≥50%) was 83.8% at 6 months, indicating a high short-term beneficial effect in pain remission at exercise of OA knee joints. Other studies reported outcome results mostly at 12 months [8, 13-16]. An equally significant beneficial effect of RS in complete remission of the joint pain during the night was found in 88.6% of the joints. Night pain has not been studied by others. Other RS parameters concerning joint pain are the reduced intake of analgesics and the improvement of patient's quality of life, which although seemed to follow the RS response, were not studied. Improvement of knee flexibility, as we have shown, has also been reported by others [8, 14 -16] and is probably associated with the ablation of the synovial membrane, reduction of knee effusion and pain remission.

The mean VAS improvement at 6 months we have found, was inversely related to patients' age, duration of symptoms and the radiographic grading of OA. Similarly to other studies, RS seemed to be less beneficial in older patients, in cases of long duration of the disease and in advanced OA stages (Steinbrocker's grades III-IV) [6-8]. Similar findings have also been reported when radiographic changes of OA knees were assigned according the Kellgren–Lawrence radiographic grading system [15]. Knee OA with more advanced radiographic changes (grades III and IV) may be considered as a relative RS contraindication [3], but such patients may have no other choice of treatment than RS, especially in cases with burdensome knee replacement. Long lasting joint inflammation accompanied by intense degenerative changes of the synovium can not be subsided by a single RS treatment. In these cases a combination of RS with arthroscopic synovectomy or repeated RS, may be more effective. Repeated RS treatment procedures may be applied in the same joint after a minimum interval of 6 months, according to EANM guidelines [3, 4]. Single RS treatment, response usually has a delay of onset of 3-6 months and lasts up to 24 months. That is why we followed up our patients for 6 months. The co-administration of glucocorticoids immediately after the ^{90}Y-S injection, is considered to have a beneficial effect as early as the first week and up to 4 months and is used to reduce the risk of acute radiation induced synovitis, due to the ^{90}Y injection [3, 18]. The only difference in our RS treatment with the EANM treatment protocol was the partial instead of strict immobilization of the treated joint after RS, in order to avoid thrombosis [18]. The RS side effects and complications observed were minimal and not significant as is usually expected [3, 18].

In conclusion, our findings implicate that the clinical improvement after a single RS treatment, is inversely related to radiographic knee damage, to patients' age and duration of the disease. RS also induced remission of knee OA pain during the night.

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