Radiosynoviorthesis of the knee: a doubleblind trial of 1 versus 5 mCi Gold-198

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SUMMARY Since the minimal effective dosage for radiosynovectomy is not known, we have performed a doubleblind controlled trial of 1 mCi vs. 5 mCi 198 Au in 60 knees of 46 patients with persistent rheumatoid synovitis. The therapeutic effect was assessed with a clinical score, 99mTc pertechnetate uptake measurements and plain X-rays. With regard to clinical parameters no statistical differences between the two groups were found, but results indicate a trend towards a better outcome in patients treated with 5 mCi. 99mTc uptake improved significantly in patients treated with the higher dose and not in the low dose group. Weighing ease of treatment and risk of side effects against the small difference in effectiveness, we conclude that the use of less than 5 mCi of 198 Au may be justified. During the study the injection technique was changed, enabling a comparison of two methods. Leakage to lymph nodes and liver decreased when the needle was flushed with normal saline after administration of the radiocolloid.

Key words: Radiosynoviorthesis - Gold 198 - Rheumatoid Synovitis.

INTRODUCTION

Irradiation of the synovium by intra-articular administration of radionuclides (radiosynoviorthesis, radiation synovectomy or radiosynovectomy) was introduced in the 1950s and first described by Ansell et al. in 1963 (1). Since then many open studies concerning the use of different radionuclides in various joints and administration of repeated injections of radionuclides have been reported (2-7).

In controlled trials radiosynoviorthesis was found to be equal to surgical synovectomy and injections of osmic acid or corticosteroids (8-13). Later trials, however, have cast some doubt on the effectiveness of radiosynovectomy (14-16). Presently intra-articular administration of radionuclides has a modest place in the treatment of persistent synovitis especially of the knee joint.

Apart from the possibility of local damage to cartilage, the risk of induction of malignant disease has been the main drawback for radiosynovectomy. The demonstration of leakage of radionuclides from the joints to lymphnodes, liver and blood has increased this anxiety (17). Chromosomal damage was indeed found in patients treated with radioactive Yttrium (90Y) and radio-
active gold \(^{198}\text{Au}\) \((18,19)\). However, reports of cancers, that were clearly induced by radiation synovectomy have yet to be published. The absence of radiation injury in the liver of patients with cancer treated with high intravenous doses of \(^{198}\text{Au}\) is also reassuring \((20)\). As a consequence of this potential risk, radiation synovectomy has generally been restricted to patients over 45 years. A further sequel of the use of radionuclides may be the necessity to admit a patient to hospital isolation facilities for a number of days after administration of a radionuclide, dependent on local legislation.

To reduce the risk of induction of malignancies the use of nuclides with a shorter half-life-time and also of larger particles, to prevent leakage, has been proposed. Dysprosium 165-Ferric Hydroxide macroaggregate, with a half-life-time of 2.3 hours is preferrable to \(^{198}\text{Au}\) and \(^{90}\text{Y}\) (both 2.7 days) in these respects, but not available to every hospital. \(^{90}\text{Y}\) Yttrium has a greater effective range of irradiation (about 5 vs. 1 mm, estimates dependent on the method of assessment), does not emit therapeutically undesirable gamma radiation and may have a greater retention in the joint than \(^{198}\text{Au}\). Although these theoretical considerations have not been substantiated by practical proof of superiority, most authors prefer radioactive Yttrium for these reasons.

A disadvantage of this purely beta-emitting radionuclide is that accurate quantitative assessment of the radiation burden to lymphnodes and liver is not possible. The distribution of \(^{198}\text{Au}\), emitting both beta and gamma radiation, can be monitored with a gammacamera. Monitoring of treatment with radioactive open sources, of which considerably higher doses are administered, is common practice in oncology.

Apart from a shorter half-life-time and greater particle size, dose reduction is a method of reducing the risks of radiosynovectomy. Assuming that appropriate measures of immobilisation can be taken, a lower dosage may also enable administration of radioactive colloids in outpatient settings. In all reported studies dosages for knee injections were between 3 and 12 mCi. Reports of comparisons of different dosages are scarce. Menkes did not find a difference between 4 and 6 mCi of \(^{90}\text{Y}\) and Gumpel mentions unpublished results indicating that 5mCi is more effective than 2mCi \(^{198}\text{Au}\) \((2,4,6)\). To evaluate the effectiveness of a lower radioactive dose we have performed a double-blind trial of 1 versus 5 mCi \(^{198}\text{Au}\) in chronic arthritis of the knee.

**PATIENTS AND METHODS**

Between 1979 and 1984 sixty knees of 46 patients (34 female, 12 male) with active arthritis were injected with radioactive gold \((^{198}\text{Au})\). Inclusion criteria were: 1) Persistent synovitis of at least 6 months in spite of treatment with nonsteroidal anti-inflammatory (NSAID) and/or disease modifying antirheumatic drugs (DMARD); 2) Age over 45 years. Exclusion criteria were: 1) Injection of the knee with corticosteroids within 1 month before entering the study; 2) Severe radiologic abnormalities of the knee: joint space narrowing, erosions or leaking synovial cysts (in order to reduce the risk of leakage). All patients gave informed consent to take part in the study.

The age of the patients ranged from 46 to 82 (mean 65) years. Definite or classical rheumatoid arthritis (RA) was present in 44 patients, 30 of whom were seropositive. Two patients had psoriatic arthritis. Disease duration was between 1 and 34 (mean 9) years. Duration of synovitis prior to entry in the study varied from 6 months to 2 years. Treatment with DMARD's and NSAID's was continued during the study.

Fourteen patients were injected in both knees, receiving 1 mCi in one and 5 mCi in the other. Patients with unilateral synovitis were randomly divided into two groups receiving 1 and 5 mCi colloidal \(^{198}\text{Au}\) (Amersham International plc, Amersham UK).

The radioactive gold was diluted with nor-