Assessment of rheumatoid inflammation in the knee joint

A reappraisal

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SUMMARY Subjective pain score, clinical assessment, ^{99m}Tc technetium joint uptake, infrared thermography, and thermistor skin temperature measurements were evaluated and compared in patients with rheumatoid knee treated with intra-articular hydrocortisone. In 11 patients with definite and classical rheumatoid arthritis, 10 of whom had unilateral knee involvement, the affected knee joints were assessed by the above techniques before and at intervals after treatment of 0 to 14 days.

The anti-inflammatory property of the steroid therapy was shown by all the assessment parameters, values having decreased significantly from the pretreatment values. However, the only parameter still showing a statistically significant decrease on the 14th post-treatment day was ^{99m}Tc joint uptake. Correlations were obtained between the two clinical measurements assessed by a physician, i.e. pain score and index of joint inflammation. Both of these also correlated with the ^{99m}Tc joint uptake but not with skin temperature measurements. Using the clinical assessments as a yardstick, ^{99m}Tc joint uptake seemed to provide a useful index of changes in disease activity in the group as a whole. However, skin temperature measurements by infrared thermography and by the thermistor were of considerably less value.

Various methods have been used to assess inflammation in rheumatoid arthritis with regard to the severity of the disease and response to treatment. Clinical evaluation using a number of simple measurements has been described (Boardman and Hart, 1967; Hart and Huskisson, 1972) and work has been done using radioactive technetium uptake (^{99m}Tc -pertechnetate) by inflamed joints (Dick *et al.*, 1970; Huskisson *et al.*, 1973) and infrared thermography (Collins *et al.*, 1974). We evaluated the response to treatment with intra-articular steroids in patients with active knee involvement by (1) the patient's estimate of pain; (2) an examining physician's estimate of joint inflammation; (3) ^{99m}Tc -pertechnetate uptake in the knee joint; (4) knee temperature as determined by infrared thermography and also by direct skin temperature measurement.

Patients and methods

Ten patients who fulfilled the American Rheumatism Association criteria (Ropes *et al.*, 1959) for definite or classical rheumatoid arthritis and who had unilateral knee joint involvement were selected for study. An eleventh patient with bilateral knee joint involvement was also included, giving a total of 11 actively diseased knees for study. Owing to occasional technical difficulties, the number of knee assessments completed varied slightly at different times. Systemic anti-inflammatory drug therapy was not altered during the study.

SUBJECTIVE PAIN ASSESSMENT

On each visit the patients were asked to record the severity of pain in the joint under study on a visual analogue scale (Bond and Pilowsky, 1966; Aitken, 1969).

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INDEX OF JOINT INFLAMMATION

Clinical assessments were made of tenderness on firm pressure over the joint margin (graded 0-3) modified from Ritchie *et al.* (1968), increase in skin temperature over the joint (grade 0-3), and joint swelling (grade 0-3). The sum of these grades was taken as the numerical value for an index of joint inflammation. Clinical assessments were made by the same observer throughout.

^{99m}Tc-PERTECHNETATE UPTAKE IN KNEE JOINTS

A dose of 100 μ Ci ^{99m}Tc-pertechnetate was injected intravenously and the ^{99m}Tc activity in the knees measured 15-20 minutes later using a scanning whole body monitor. The monitor was of the screened room type with a ring of 6 sodium iodide crystal scintillation detectors moving horizontally along the length of the patient, 3 detectors above the patient and 3 below. The outputs from vertically opposed pairs of detectors provided three activity profiles, from head to foot, of different transverse sections of the body, i.e. 2 lateral profiles and 1 midline profile. The sum of the three profile count rates gave a measure of the whole body activity while the peak count rate over the knees obtained from the lateral profiles gave a measure of ^{99m}Tc activity in the knees. The uptake was defined as follows:

$$\text{Normalised } ^{99m}\text{Tc uptake, (NTU)} = \frac{(\text{peak count rate over knee}) 100}{\text{average whole body count rate}}$$

Previous studies of isotope uptake in the knee have been made with single fixed detector systems. One advantage of the whole body monitor method of uptake measurement was the easy normalisation of the results obtained using slightly different amounts of ^{99m}Tc-pertechnetate in each patient since the whole body ^{99m}Tc activity detected by the monitor gave a quantitative measure of the administered dose.

INFRARED THERMOGRAPHY AND THERMISTOR THERMOMETRY

Knee temperatures were measured in a 'draught-free' room used exclusively for thermography with room temperature maintained at $20 \pm 1^\circ\text{C}$. The patients were allowed to cool for approximately 15 minutes, supine with knees bared, on a couch fitted with an overhead mirror. Thermograms of both knees were recorded using a Bofors thermography unit interfaced to a Varian 620L computer system (Shimmins *et al.*, 1977). The knee/thermal scanner distance was fixed at 1 m and a life-sized hard copy image with a grid superimposed was printed out by the computer. A 10 cm square was drawn on each copy, the grid

co-ordinates were input to the computer and the mean temperature of each square calculated. The system was calibrated using black body references. Skin temperatures medial, lateral, and superior to each patella were also directly measured using an Ellab DU-3 Thermistor probe thermometer.

After initial assessment the rheumatoid knees were injected with hydrocortisone acetate 50 mg. The anatomical site of injection in each patient was uniform and this site and the identical site on the untreated knee were covered by small patches so that the treated knee was known only to the injector. After the initial visit and treatment the patients were again assessed on days 3, 7, and 14 of the study.

Results

The group mean values and standard deviations for the assessment parameters recorded on each evaluation day are shown in Tables 1-6. Tests for significant differences in the parameters relative to pretreatment values were performed using the sign test on paired differences.

Table 1 gives the subjective pain score information, indicating that significant decreases were recorded on days 3 and 7 ($P \leq 0.01$), but not on day 14. The data on index of joint inflammation in Table 2 show a similar pattern with a significant decrease on day 3 ($P \leq 0.01$), and on day 7 ($P \leq 0.05$), again becoming nonsignificant by day 14. Tables 3 and 4 give the normalised ^{99m}Tc knee uptake values. The data for treated knees (Table 3) indicate that the mean ^{99m}Tc knee uptake was still significantly different from the pretreatment value on day 14. Table 4 shows that the ^{99m}Tc uptake in the untreated knees did not vary significantly with time.

There was a day-to-day variation in the knee temperatures which masked the effect of the hydrocortisone therapy. However, when the temperature difference between each subject's knees was taken,

Table 1 Subjective pain score

Day	0	3	7	14
No. of knees	12	12	12	12
Mean	6.2	3.1	3.0	3.8
SD	± 1.9	± 2.6	± 3.2	± 3.3
P	—	≤ 0.01	≤ 0.01	NS

Table 2 Index of joint inflammation

Day	0	3	7	14
No. of knees	12	12	12	12
Mean	4.5	2.0	2.3	2.7
SD	± 3.4	± 3.1	± 3.1	± 2.6
P	—	≤ 0.01	≤ 0.05	NS

Table 3 Normalised ^{99m}Tc knee uptake (NTU) in treated knees

Day	0	3	7	14
No. of knees	12	11	12	12
Mean	33.4	27.0	29.7	30.5
SD	± 9.1	± 7.0	± 7.3	± 9.1
P	—	≤ 0.01	≤ 0.01	≤ 0.05

Table 4 Normalised ^{99m}Tc knee uptake (NTU) in untreated knees

Day	0	3	7	14
No. of knees	9	8	9	9
Mean	24.7	23.7	25.9	25.2
SD	± 5.8	± 4.2	± 5.6	± 5.6
P	—	NS	NS	NS

this variation was minimised. Therefore, the results presented are temperature differences between treated and untreated knees. The mean temperature differences obtained using the computer-linked Bofors camera are referred to as the computed temperature differences, while the direct measurements of skin temperature are referred to as the thermistor temperature differences.

Table 5 shows that the mean computed temperature difference was significantly lower than the pretreatment value on day 3 only ($P=0.05$). It is apparent from Table 6 that the thermistor temperature difference followed the same pattern. The fact that the mean temperature difference as measured by the thermistor was considerably larger than the mean differences using the Bofors camera is due to the fact that the latter technique averages the temperature over an area which contains the relatively cool patella as a major component.

In addition to studying the variation of the group means of the parameters with time, correlations between parameters were sought. Fig. 1 shows the good correlation between the subjective pain score and the index of joint inflammation obtained by

Table 5 Computed temperature difference

Day	0	3	7	14
No. of knees	9	6	7	9
Mean	1.17	0.27	0.07	0.60
SD	± 1.25	± 0.67	± 0.69	± 0.54
P	—	0.05	NS	NS

Table 6 Thermistor temperature difference

Day	0	3	7	14
No. of knees	9	9	9	9
Mean	2.27	0.02	0.37	0.94
SD	± 2.48	± 2.20	± 1.25	± 1.24
P	—	0.05	NS	NS

clinical assessment. The regression equation for this correlation is $\text{Pain} = 1.17 (\text{Index}) + 0.635$ ($n=48$, $r=0.751$, $P \leq 0.01$).

The correlations for the normalised ^{99m}Tc uptake (NTU) with joint inflammation index and subjective pain score are shown in Figs. 2 and 3 respectively. The regression equation for NTU on joint inflammation index is $\text{NTU} = 1.91 (\text{Index}) + 24.6$ ($n=47$, $r=0.453$, $P \leq 0.01$); while that for NTU on subjective pain score is $\text{NTU} = 1.05 (\text{Pain}) + 26$ ($n=47$, $r=0.380$, $P \leq 0.05$). The self consistency of the data is illustrated by the fact that in the above equations the asymptomatic NTU value is, $\text{NTU} = 24.6$ for $\text{Index} = 0$, and $\text{NTU} = 26.0$ for $\text{Pain} = 0$, while the overall mean NTU for the untreated knee groups is $\text{NTU} = 24.9$.

Fig. 4 shows the excellent correlation between the computed temperature difference and the thermistor temperature difference. The regression equation is: $\text{Computed Temperature Difference} = 0.46 (\text{Thermistor Temp Diff}) + 0.078$ ($n=38$, $r=0.84$, $P \leq 0.01$).

Other pairs of parameters which were tested unsuccessfully for correlation were computed temperature difference versus pain score, computed temperature difference versus joint inflammation index, thermistor temperature difference versus pain score, thermistor temperature difference versus joint inflammation index, NTU versus computed temperature difference and NTU versus thermistor temperature difference.

Fig. 1 Correlation between subjective pain score and index of joint inflammation

Fig. 2 Correlation between normalised ^{99m}Tc knee uptake (NTU) and index of joint inflammation

Fig. 3 Correlation between normalised ^{99m}Tc knee uptake and subjective pain score

Fig. 4 Correlation between computed temperature difference and thermistor temperature difference

Discussion

The purpose of the study was to assess the various methods of measuring inflammation in the actively involved rheumatoid knee joint and not to test the efficacy of the steroid therapy. As expected, the therapy decreased the degree of inflammation in the treated knees and the group mean of every parameter showed this improvement although, as noted above, not all the changes were statistically significant.

The good correlation between the subjective pain score and the clinically assessed index of joint inflammation indicates that in general the patient's estimate of pain relief is a useful guide and that the physician following a strict format for scoring key clinical signs also provides a satisfactory measure of rheumatoid inflammation and response to treatment. With regard to the objective parameters, ^{99m}Tc uptake correlated significantly with both pain score and joint inflammation index. This suggests that the ^{99m}Tc uptake also provides a satisfactory measure of the response of rheumatoid inflammation to treatment. From our results it appears that subjective pain score and the joint inflammation index are the better indices for grading the degree of rheumatoid inflammation, while the ^{99m}Tc uptake is a more sensitive indicator of changes in the degree of inflammation.

With regard to the results of thermography, the mean temperature of the 10 cm square drawn on the knee is, to a close approximation, related to the 'thermographic index' proposed by Collins *et al.* (1971). Unlike these workers, considerable variations in this 'thermographic index' were observed between patients and with time in a single patient, although the mean value for our group of patients was similar to that obtained from their group. The need

to measure inter-knee temperature differences in order to obtain meaningful results eliminates the possibility of investigating patients with bilateral involvement, while the assessment of systemic drug therapy by such techniques even in patients with unilateral involvement would be open to criticism as the asymptomatic knee could not be considered as a normal control. It is notable that in this study the information obtained with the relatively cheap and technologically unsophisticated thermistor probe was not improved using the computer-linked infrared camera.

Finally, as expected, no one assessment parameter proved to be ideal for measuring inflammation, indeed without invasive identification and quantitation of inflamed tissue there is no way of estimating the absolute merit of the parameters considered. However, it appears that for routine assessment of the degree of inflammation the objective tests are no better than the cheaper and simpler estimates by patient and clinician. The role of the objective tests, in particular the ^{99m}Tc joint uptake measurement, is more likely to be in the area of drug assessment where stability, operator independence, and sensitivity to change in inflammation are more relevant.

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