Ankylosing Spondylitis

The response to indomethacin in the 32 patients with ankylosing spondylitis was good in 16, fair in six, poor in one, and nil in nine. In 19 patients the treatment of choice was indomethacin, and in nine it was phenylbutazone or oxyphenbutazone; four patients considered them to be of equal value.

Osteoarthritis

The response to indomethacin in the 52 patients with osteoarthritis was good in 30, fair in four, poor in seven, and nil in 11. It was possible to compare indomethacin with the pyrazoles in 39 patients. Indomethacin was the drug of choice in 15 and phenylbutazone or oxyphenbutazone in 13; 11 found them equally satisfactory.

SIDE-EFFECTS

Side-effects occurred in 104 of the 202 patients treated with indomethacin (51.48%); this consisted of 67 out of 101 (66.3%) on indomethacin tablets, and 37 out of 101 on capsules (36.6%).

The following complaints were noted, the incidence being recorded in brackets: headache (46), giddiness (25), dyspepsia (16), muzziness (16), nausea (12), vomiting (5), rash (4), diarrhea (4), felt odd (2), sleepy (2), heavy legs (2), drunk (1), faint (1), mouth ulceration (1), unpleasant taste (1), depression (1), lassitude and nightmares (1), swollen tongue (1), costive (1), and shakiness (1).

In 88 patients side-effects occurred within seven days of starting indomethacin, in nine patients within seven to 14 days, and in two patients between 14 and 21 days. Side-effects occurred after three weeks in five patients only.

Dyspepsia occurred in 16 of the 202 patients (7.92%). In contrast, of the 170 patients who received a pyrazole agent 40 had dyspepsia (23.5%). In no patient was there overt evidence of gastro-intestinal haemorrhage, and none developed perforation. One patient with rheumatoid arthritis and one with osteoarthritis of the hip had slow gastro-intestinal blood loss, the administration of indomethacin being associated with a fall in the haemoglobin by 20–40% within a month.

Barium studies were available for 16 patients, all of whom had dyspepsia on phenylbutazone or oxyphenbutazone and eight on indomethacin. A duodenal ulcer was detected in seven patients, all intolerant of pyrazoles; indomethacin was tolerated by four of these patients and caused dyspepsia in three; these seven have received 995 patient days of treatment with indomethacin to date. In five patients with demonstrable gastric ulcers—one with a hiatus hernia also—all intolerant of phenylbutazone, indomethacin was associated with dyspepsia in one, being well tolerated in four patients; this group has received 571 patient days of treatment to date without serious gastro-intestinal complications. In three patients no abnormality was detected on barium-meal examination. All three were intolerant of phenylbutazone; indomethacin was associated with dyspepsia in two patients, and in one may have been the cause of anaemia by slow continuous blood loss. One patient, with both a hiatus hernia and gall-stones, suffered from dyspepsia on indomethacin, phenylbutazone, salicylates, and placebo.

DISCUSSION

It is increasingly apparent that the therapeutic effect of indomethacin has many similarities to that of phenylbutazone, irrespective of the mode of action. Though painful symptoms are relieved by phenylbutazone, the action being remarkably even throughout the 24 hours, reduction of joint swelling occurs in only occasional cases of rheumatoid arthritis. The regular, predictable reduction of joint size with the corticosteroids, offset by the untoward affects of prolonged therapy, suggested that the advent of a new non-steroid preparation with this property would be a considerable advance. Of the many preparations tried in the last 17 years at the Westminster Hospital (F.D.H.) indomethacin has been the first non-steroid drug to produce a measurable reduction in joint size in selected cases of active rheumatoid arthritis. The spectrum of side-effects on indomethacin overlaps phenylbutazone slightly with respect to the gastro-intestinal tract but is otherwise quite different. It is possible that the response to indomethacin is not as consistent as that obtained from phenylbutazone over the 24 hours; in this series the overall response was slightly less than 60%.

The double-blind trial confirmed that, under defined conditions, there was no significant difference between indomethacin, 75 mg. daily, and phenylbutazone, 300 mg. daily, in the relief of pain and stiffness in rheumatoid arthritis. Though the alteration of joint size on the two drugs was not statistically significant, the