Conference report

The role of steroids in the treatment of arthritis

The sixth annual day conference in the series 'Growing points in the treatment of rheumatic diseases' was held on 2 May 1985 at the Yorkshire Regional Health Authority, Harrogate. The organisers were Dr H A Bird and Professor V Wright, and an audience of almost 70 discussed the many ways in which steroids should or should not be used in the management of different sorts of arthritis.

Dr A Harvey (Leeds) presented a literature review on the many different ways in which steroids might ameliorate inflammation. Discussion centred on whether all steroids work in the same way and whether different duration of action is a function of chemical structure or pharmacokinetic properties. Side effects might be mediated through different pathways to the therapeutic effect. Dr Blower (Manchester) then described her methods for measuring polypeptide synthesis in vitro in polymorphonuclear leucocytes. The synthesis of at least seven polypeptides was increased in the presence of dexamethasone. Incorporation of radiolabelled methionine was, however, reduced in cells from patients with active rheumatoid arthritis compared with normals.

The conference failed to agree on the mode of action of corticosteroids, and the discussion then moved to side effects. Alteration in hypothalamic-pituitary-adrenal axis function in patients receiving long term intra-articular corticosteroids was described by Dr Reid (Aberdeen). This route of administration, analogous to slow release to the systemic circulation from a depot preparation, caused suppression of the axis for periods of up to six weeks after intra-articular therapy. This side effect should not be forgotten, and discussion suggested this might be more of a problem than the risk of Charcot's arthropathy after successive injections. In his second paper Dr Reid described his most recent studies on bone mass, with neutron activation analysis, when corticosteroid-treated patients with rheumatoid arthritis, asthma, and polymyalgia rheumatica were compared with asthma patients not receiving steroids as a control group. The total body calcium was significantly less in rheumatoid patients compared with those with polymyalgia or asthma, on or off steroids. This reduction in bone mass in rheumatoid patients was

proportional to the dose of steroid used. Dr Teitsson (Glasgow) then described his collection of patients with avascular necrosis of the hip. This condition occurred in a wide variety of conditions, rheumatic and non-rheumatic. Nine of a series of 22 patients who developed this condition had been taking steroids. When the five patients in the series with rheumatoid disease were examined more closely, three of the five were found to have recently received pulse intravenous methylprednisolone therapy.

Dr Byron (Oxford) then presented a provocative paper suggesting a 'second-line' action for steroid therapy. Prednisolone needed to be prescribed in a dose greater than 15 mg/day to maintain an anti-inflammatory effect, but the effect of lower doses of steroid on rheumatoid disease outcome was untested. The combined Nuffield Foundation and MRC trial showed erosions in 60% of patients on analgesics only, compared with 20% of patients taking a mean daily dose of 11 mg prednisolone. A multicentre study to determine whether prednisolone had 'second-line' action was necessary, and a total recruitment of 180 patients would be required to provide a confident answer. Dr Byron had found that 24% of rheumatoid patients attending a routine outpatient clinic were taking prednisolone (mean dose 5.6 mg daily). Several rheumatologists claimed that they started only one or two rheumatoid patients on systemic prednisolone each year, but discussion suggested that in at least three major centres as many as 25% of all rheumatoid patients were taking the drug; the preaching differed considerably from the practice. There was discussion on whether patients who might be placed on 7.5 mg prednisolone a day would develop an emotional and physical dependence upon the drug that might have ethical implications.

The afternoon session concentrated more on clinical outcome. Professor Stimson (Strathclyde) described a new corticosteroid (Org 6632) with a novel immunoregulatory profile. This halogenated glucocorticoid displayed only 20% of conventional dexamethasone activity. However, the compound was unique in enhancing antibody production in mice to both T cell dependent and independent antigens in an antigen-specific manner. Administration

tion of a single low dose caused an increase in circulating rheumatoid factor, a feature unique amongst testing of up to 40 other compounds. Dr Pullar (Glasgow) described 28 patients with rheumatoid arthritis who had received corticosteroids for at least five years. Evidence of active arthritis and advancing radiological damage was present in the group (median dose 4 mg/day) in spite of continued steroid therapy. Twelve out of 22 patients who received a short Synacthen test showed a deficient response. Surprisingly few patients chose to attend more frequently to receive help in the steroid weaning process. As steroids were reduced, the Ritchie articular index rose significantly. A multicentre comparison of three doses of intravenous methylprednisolone in the treatment of active rheumatoid arthritis was then presented by Dr Colaco (Middlesex Hospital, London) on behalf of a large group of other investigators. Three doses (40, 500, and 1000 mg), each given by slow intravenous infusion over a 24-hour inpatient stay, were compared. Results were presented on 69 patients. The single pulse of 1000 mg proved the most effective, producing sustained clinical response for six weeks. Aseptic bone necrosis had occurred in three patients (two on 1000 mg and one on 40 mg). This study was complemented by Dr Neumann (Leeds), who described pulsed methylprednisolone in rheumatoid arthritis, given either alone or in combination with sulphasalazine or D-penicillamine. A dramatic clinical improvement had also been observed with the use of methylprednisolone alone, but it was the impression of the Leeds group that this was relatively short lived. It was logical to start either sulphasalazine or D-penicillamine simultaneously, and the presence of Solu-Medrone appeared to accelerate the conventional response to either of these drugs but did not appear to potentiate it. No

examples of aseptic necrosis of the hip had been seen.

Dr Hunter (Glasgow) described a multicentre double blind study of Org 6216 (Rimexolone) used as a single intra-articular injection to the rheumatoid knee joint at doses of 10, 20, or 40 mg. The 40 mg injection was the best tolerated and produced a symptomatic improvement lasting 12 weeks. The drug was non-fluorinated and had a low solubility.

In the final session discussion moved to polymyalgia rheumatica, a disease in which all were agreed that steroids were invaluable. Dr Bird (Leeds) reviewed the serial evaluation of acute phase reactants as patients with polymyalgia were started on steroids and were weaned off the drug. No single acute phase reactant (or even a group of them) allowed reliable prediction of those patients who could be successfully weaned from steroids without risk of remission. When patients started the drug the C-reactive protein changed first, then the erythrocyte sedimentation rate, and lastly, the viscosity. Dr Taggart (Belfast) then argued that patients with polymyalgia seemed to develop fewer steroid side effects than age matched patients with rheumatoid arthritis. The study on bone mass presented earlier had tended to confirm this clinical impression. The pharmacokinetics of prednisolone had therefore been compared in patients with polymyalgia, rheumatoid arthritis, and asthma, all receiving comparable doses of steroids. Although the polymyalgia patients were inevitably older, there was no significant difference in steroid handling between the three groups. The clinical impression could not be explained by altered pharmacokinetics.

It is hoped to hold the next meeting in this series in Harrogate on the first Thursday in May 1986.

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