A COMPARATIVE EVALUATION OF THE ANTIPERMEABILITY EFFECTS OF SOME RECENT CORTICOSTEROIDS

By

S. S. MISRA AND H.N. SAPRU

From the Department of Pharmacology, G.S.V.M. Medical College, Kanpur

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The effect of some recent corticosteroids on the permeability of synovial membrane of rabbits was studied. Seifter and Beader's method was employed. Hydrocortisone and prednisolone were found to decrease the permeability of synovial membrane while dexamethasone and triamcinolone increased it. The anti-inflammatory effect of these corticoids in relation to their effect on permeability of synovial membrane have been discussed.

Many corticosteroids have been produced since 1948 and their increasing use as antirheumatic drugs has resulted in attempts by various workers to explore the mechanism underlying their antirheumatic property. Effects of corticoids on permeability have, in part, been considered to be one of the factors in the antirheumatic action of these drugs. Bishop (1954) observed that cortisone and some other corticoids prevent the permeability of synovial membrane, produced by hyaluronidase, to India-ink. Hyaluronidase influences the permeability of synovial membrane by dissolving hyaluronic acid which is a constituent of the matrix. Cortisone may antagonise this action, thus preventing the synovial fluid from draining out, and may, thus, afford relief to the joints in rheumatoid arthritis due to the presence of adequate lubricating fluid. Ciocci and Cervini (1959), however, hold that the antirheumatic properties of cortisone and some corticoids are not in accord with their effect on permeability of synovial membrane which increased according to these authors. Cugurra (1955), observed that intra-articular and intramuscular injections of cortisone do not modify, in an important manner, the activity of hyaluronidase on synovial membrane. Freeman (1951) reported a definite antipermeability effect of cortisone and other corticoids on synovial membrane. The position, thus, is highly controversial in this regard. The present investigation was undertaken to unravel this controversy.

METHODS

Seifter and Beader's method (1955) was employed. Male rabbits weighing 2-4 kg. each were procured from the animal house of C.D.R.I., Lucknow,

and maintained under standard dietetic conditions. Tap water was given *adlibitum*. Each rabbit was used once in seven days and for not more than five times in all. Clinical grade of phenolsulphonpthalein (P.S.P.) was injected in synovial sac and its rate of excretion in urine served as an index of permeability of synovial membrane. A Folley's retention catheter lubricated with liquid paraffin was employed for collection of urine. 26 gauge 1" needles were employed for making injections in synovial sac. Four corticoids viz. hydrocortisone, prednisolone, dexamethasone and triamcinalone were selected for the present study.

The drugs were administered in the following dosage (i) hydrocortisone 12 mg. i. v., (ii) prednisolone 7 5 mg. i. v., (iii) dexamethasone 4 mg. i. v.. (iv) triamcinalone 8 mg. subcutaneously.

The intravenous injections were given in the marginal ear vein of rabbits. The insolubility of triamcinalone in inert solvents necessitated its administration by the subcutaneous route.

Two groups, each of four rabbits, were selected for experiments with each corticosteroid. In one group, the normal excretion of P.S.P. in urine was determined and in the second the animals were treated with a corticosteroid before injecting the dye. In each experiment the rabbit was anaesthetised with an intraperitoneal injection of 60 mg/kg of body weight of sodium pentobarbital and secured on an animal board on its back. 1.25 mg of P.S.P. in 0.25 ml of physiological salt solution (P.S.S.) were injected in the synovial sac, a Folley's catheter introduced in the urinary bladder and urine samples collected by flushing 5 ml of P.S.S. through irrigation tube. The urine samples were collected every half an hour. The dye was estimated in the urine by standard colorimetric technique. Injections of corticoids were made 30 min before injection of the dye.

RESULTS

The results are summarized in Table I. Hydrocortisone increased the rate of excretion of P.S.P. initially and the peak of the excretion of the dye reached earlier than in the normal rabbit. This was followed by a significant decrease in excretion of the dye, thus prolonging the total time for complete excretion.

In case of prednisolone-treated animals, an initial increase in the rate of excretion, less marked than in the case of hydrocortisone-treated animals, was observed. This was followed by a marked decrease in the rate of the dye excretion.

TABLE I

Rabbits	Mean % excretion after injection of dye			
	After 30 min	After 60 min	After 90 min	After 120 min
Normal	7	30.6	7.8	5.3
Hydrocortisone treated	22.9	8.2	7.3	4.0
Prednisolone treated	13.9	4.0	4.0	3.6
Dexamethasone treated	more than 40	more than 40	12.2	4.0
Triamcinalone treated	40	24.0	8	4

Dexamethasone-treated animals manifested a significant increase in the rate of excretion of the dye, early onset of the action of the drug and the percentage of the dye excreted during first half hour was nearly 6 times more than in the case of normal rabbits. The rate of excretion continued to remain more than the normal in all subsequent readings.

The observations in case of triamcinalone-treated animals showed a sustained increase in the rate of excretion of the dye with the peak of excretion more or less identical to that of dexamethasone-treated animals.

DISCUSSION

The results of the present investigation suggest that hydrocortisone on the whole decreases the permeability of synovial membrane. For the initial increase of excretion of the dye other factors like permeability of blood vessels etc may be responsible. The low percentage of the dye excreted in the subsequent observations indicates the decreased permeability of synovial membrane. The effect of prednisolone is similar but more pronounced than in the case of hydrocortisone. Dexamethasone, however, shows clearly the increased permeability of synovial membrane. Triamcinalone also shows a similar effect but the increased permeability is lesser than in the case of dexamethasone. There does not seem to be an agreement between the anti-inflammatory properties of these corticoids and their effect on the permeability of synovial membrane.

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