EFFECTS OF DEXAMETHASONE, PREDNISOLONE AND CORTISOL ON THE MAST CELLS AND TISSUE EOSINOPHILS IN RAT GASTRIC MUCOSA

By

Toimi Räsänen

ABSTRACT

Intact rats were injected intramuscularly at 8-hourly intervals with equal amounts, 6×1.0 mg, of dexamethasone (16α-methyl-9α-fluoro-prednisolone) as phosphate, prednisolone (11β,17,21-trihydroxy-pregna-1,4-diene-3,20-dione) and cortisol (11β,17,21-trihydroxy-pregn-4-ene-3,20-dione) both as succinates, all three in water soluble form. The rats were decapitated 4 hours after the last injection and the mucosal mast cells and tissue eosinophilic cells in the body mucosa of the glandular stomach counted. Calculation of the mast cell degranulation and the destruction of tissue eosinophils during the experiment gave the following degranulation coefficients for the degranulation of gastric mucosal mast cells: 0.541 for dexamethasone, 0.177 for prednisolone and 0.088 for cortisol. The corresponding destruction coefficients for the loss of tissue eosinophilia were 0.858, 0.156 and 0.124.

It is suggested that the degranulation and destruction coefficients obtained in the investigation are correlated with the catabolic biological activity of the glucocorticoids.

The number of mucosal mast cells in the mucosa of the rat stomach is fairly rapidly influenced by glucocorticoids, and the number of degranulated mast cells is correlated with the amount of glucocorticoid used (Räsänen 1961). The mast cells of connective tissue are not nearly as sensitive to the effect of glucocorticoids (Räsänen 1960 b). Mucosal mast cells differ from the mast cells of connective tissue morphologically as well as in their enzymatic structure.

Supported by the Sigrid Jusélius Foundation.
Moreover, histamine is not released by diamines from the gastric mucosa as it is from other tissues (Mota & Dias Da Silva 1960).

The number of tissue eosinophils in the lamina propria of gastric mucosa seems to be dependent on the activity of the reticuloendothelial system while subjected to the effect of hormonal factors (Wegelius & Teir 1958). Blood eosinophilia also seems to depend quantitatively on the amount of ACTH (Speirs et al. 1953) or on the amount of glucocorticoids present (Coste et al. 1951).

It has been shown that different glucocorticoids in the same dosage exert a very different catabolic effect on the metabolism of the organism. Among the hormone used in the present work such an effect is most marked with dexamethasone and least with cortisol. The effect of equal amounts of dexamethasone, prednisolone and cortisol on the mast cells and tissue eosinophils of the lamina propria of the rat stomach are compared.

**METHOD**

Male rats of Wistar strain, aged 4 months were injected intramuscularly at 8-hourly intervals with $6 \times 1.0$ mg of the following corticoids. The injections were given to 10 rats in each group.

1. Dexamethasone (Decadron phosphate, Merck). The mean weight of the rats was 178.8 g (range 158–198);
2. Prednisolone (Di-Adreson-F, Organon). The mean weight of the rats was 187.8 g (range 148–214);
3. Cortisol (Solu-Cortef, Upjohn). The mean weight of the rats was 181.8 g (range 136–204);
4. The controls, mean weight 179.2 g (range 168–212), received $6 \times 0.5$ ml of normal saline.

The dose was calculated to make up the equivalent of 1.0 mg of the hormone, whatever the structure of the acid radical.

The rats were starved for 8 hours before the last injection and then kept in cages with wire netting floors to prevent them from eating their excrement. The last injection was given at 0830–0930 hours and the animals were decapitated 4 hours later. The stomach was then exposed immediately, and bisected longitudinally. One part was fixed in 4 per cent fresh basic lead acetate and the other part in Bouin’s fluid. After embedding in paraffin, the former samples were cut in 10 $\mu$ sections and stained with 1 per cent aqueous solution and toluidine blue; the latter were cut in 4 $\mu$ sections and stained with haemalaun-eosin. The cut surface was at right angles to the surface of the mucosa. The mucosal mast cells were counted in the superficial layer of the body mucosa of the samples stained with toluidine blue. In the samples stained with haemalaun-eosin, the tissue eosinophils were counted in the corresponding site in the basal part of the lamina propria. The method has been explained in detail previously (Räsänen 1960 a, b).

The cells were counted per mm$^2$ of tissue. Fisher’s t-test was used in the statistical treatment of the results. Degranulation or destruction coefficient illustrating the rate of mast cell degranulation and of tissue eosinophil destruction was also calculated.

433

Acta endocr. 41, 3

28
This procedure should actually require a proportional analysis; however, one injection interval, i.e., 8 hours, was selected for the sake of simplicity. The following equation was used:

\[ y = y_0 \cdot e^{-kt}, \]

in which \( y \) = cells/mm\(^2\) of tissue, \( y_0 \) = initial value for the controls, \( t \) = time interval, \( k \) = degranulation or destruction coefficient = destroyed proportion/time interval.

**RESULTS**

The results of the cell counts are given in Fig. 1.

Degranulation on mucosal mast cells and destruction of tissue eosinophilia obviously occur in gastric mucosa during the glucocorticoid effect. The significance levels of the differences between the different groups were high (\( P < 0.001 \)) for all the substances except between the prednisolone and cortisol groups (\( P < 0.05 \) for mast cell counts). These two groups do not differ significantly from each other with regard to tissue eosinophilia.

Gastric mucosal mast cells are degranulated almost completely and tissue eosinophilia disappears with dexamethasone. Cortisol had a very slight effect on these cells.

The following degranulation and destruction coefficients were obtained:

<table>
<thead>
<tr>
<th>Mast cells</th>
<th>Tissue eosinophils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone: 0.541</td>
<td>0.858</td>
</tr>
<tr>
<td>Prednisolone: 0.177</td>
<td>0.156</td>
</tr>
<tr>
<td>Cortisol: 0.088</td>
<td>0.124</td>
</tr>
</tbody>
</table>

The ratios of the mast cell degranulation coefficients are 6.1:2.0:1.0; the ratios of the destruction coefficients of tissue eosinophilia are 6.9:1.3:1.0, when 1 is taken as a coefficient of cortisol.

The mast cells of the gastric mucosa apparently were not destroyed during the glucocorticoid effect, although they lost the metachromatically staining

\[ \text{Fig 1.} \]

The number of mucosal mast cells and tissue eosinophils in rat gastric body mucosa per sq mm of tissue after dexamethasone, prednisolone and hydrocortisone application, and in controls.
part of their granules. Orthochromatically staining granules and vacuoles were seen in partly degranulated mast cells. The nuclei of degranulating mast cells showed no signs of destruction; metachromatic staining was observed in the nuclei of some mucosal mast cells.

The tissue eosinophils in the lamina propria of the gastric mucosa seemed to lose their granules during the glucocorticoid effect. The granules dissolved as a diffuse substance in the protoplasm, which stains eosinophilically. The nuclei displayed fragmentation into small particles which were reduced in number as the destruction of the cell progressed.

**DISCUSSION**

It has been shown previously, that dexamethasone is about 5 times as effective as prednisolone in inhibiting the histamine and serotonin induced asthma of guinea pigs (Zicha et al. 1960). Prednisolone, on the other hand, is 3–4 times as effective as cortisol in inhibiting inflammation (Bunim et al. 1955). The degranulating effect of dexamethasone, prednisolone and cortisol on mucosal mast cells of the stomach and the destructive effect of the corticoids on tissue eosinophilia are of the same order.

It is probable that glucocorticoids have a destructive action on eosinophilic leukocytes in the reticuloendothelial system (Esselier et al. 1954). Their number in the blood seems to depend on the amount of glucocorticoid used (Coste et al. 1951), as has been shown for the lamina propria of gastric mucosa (Räsänen 1961). The present investigation shows that the degree of tissue eosinophilia is dependent on the biological activity of glucocorticoid.

Blood eosinopenia has been produced by numerous protein and carbohydrate metabolites in both intact and adrenalectomised rats (Aschkenasy 1959). Glucocorticoid-stimulated metabolites in the gastric mucosa may account for the ensuing eosinopenia.

The large depot of histamine in the mucosa of the gastrointestinal canal, however, cannot be disregarded in these circumstances; glucocorticoids may mobilise i.a. histamine which has been found to have a destructive effect on eosinophilic leukocytes (Archer 1960 b). Eosinophil cell suspension is an excellent antihistaminic (Archer 1960 a).

Degranulation- and destruction coefficients indicate to some extent, the loss of the remaining cells per unit of time, which in this investigation was the time elapsing between two injections. In a previous study a logarithmic relation was found between degranulation or destruction and the amount of prednisolone injected into rats (Räsänen 1961). Comparison of the previous results with the present ones using this coefficient shows that a dose of prednisolone of $9 \times 1.0\, \text{mg}$ had about the same effect on the mast cells as on the eosino-
philic cells of the gastric mucosa. On the other hand, the effect of $6 \times 1.0$ mg of dexamethasone in the present experiment is about 2-4 times as great as that of $9 \times 10.0$ mg of prednisolone. Thus, the effect of dexamethasone on mast cells and eosinophils of the gastric mucosa is about 20-40 times at great as that of prednisolone.

REFERENCES

Räsänen T.: Gastroenterology 38 (1960 b) 70.

Received on April 11th, 1962.