THE EFFECT OF CORTISONE UPON TYPHOID INTOXICATION IN RABBITS

Z. A. Popenenkova

From the Division of Experimental Chemotherapy of the Institute of Pharmacology and Chemotherapy (Director - Active Member Acad. Med. Sci. USSR V. V. Zakusov) Acad. Med. Sci. USSR, Moscow

(Received February 18, 1957. Presented by Active Member Acad. Med. Sci. USSR V.V. Zakusov)

During infectious illnesses medicines not possessing antibacterial actions are used at times as, for example, antihistamines and hormones, the goal sought being the alleviation of the manifestations of intoxication or the blockade of tissue pathological reactions.

From the literature, it is known that cortisone exacerbates the clinical course of tuberculosis [9, 15], spir- ochetoses [16], mycoses [20] and many other infections. We established that cortisone speeds the clinical course of rabbit pneumococcal infections, hastening their death [4]. The question arises as to the reason for this negative influence of the cortisone upon so many infections: is it that it depresses those factors which act as barriers to the multiplication of the infectious agents within the organism or is it that it suppresses those mechanisms which prevent the intensification of developing intoxications?

Z.A. Ermganova showed that cortisone suppresses the ability of the endothelial-macrophagic system to have its cells destroy the engulfed bacteria [8]. This fact may be one of the reasons why cortisone hastens the course of the infection and hastens the dissemination of the bacteria. Alongside with this observation, some authors have observed that cortisone lowers the febrile response in patients with typhoid fever and in animals in response to typhoid vaccine [13]. V.L. Goncharova showed that cortisone diminishes the percentage of deaths in mice and prevents the death of rats during the course of typhoid intoxication [1]. The author attributes this fact to increased resistance to the bacterial intoxication on the part of the organism receiving cortisone.

Having been convinced that cortisone intensifies the severity of rabbit pneumococcal infection [4], we set ourselves the goal of determining the effectiveness of the preparation in a pathological situation where there was only the factor of intoxication, the living microbial agent having been excluded. For this purpose we used the method of producing typhoidal intoxication in rabbits.

EXPERIMENTAL METHODS

The experiments were performed on 28 rabbits weighing an average of 2.2 kg, the animals being divided into four equal groups. The first group received only typhoid vaccine, the second was given cortisone and typhoid vaccine, the third group was given cortisone only and the fourth group received physiological saline. The animals in the first two groups received in the ear veins a slow injection of warmed typhoid vaccine prepared from laboratory strain B. Typhoides abdominis #4446, the dose being 25 billion microbes per 1 kg body weight. Biddle, Sawyer & Co. cortisone acetate was used. The cortisone was given intramuscularly as 5 mg per 1 kg body weight, this dose being repeated twice daily until the death of the animal. The first injection was given 30 minutes prior to the injection of the typhoid vaccine. The physiological saline was given in the amount of 0.1 cc and administered in the same sequence as cortisone.

Blood sugars in the rabbits were done by the method of Hagedorn-Jensen; adrenalin in the blood and adrenals by the Utevsky method; while ascorbic acid-content of blood and adrenals was determined by titration with 0.02% solution of 2, 6-dichlorphenolindophenol.
The blood for the determinations was taken from the ear vein of the fasting animal prior to injection of cortisone or typhoid vaccine, 24 hours after the injection of the vaccine if the animal was still alive and also at the moment of death. Two rabbits in the first group and 3 in the second which were in very poor condition were killed by means of air emboli. The rabbits of the 3d and 4th group were killed by means of air emboli in the same time intervals at which the animals of the 2d group died.

Immediately on the death of the animal, the adrenals of the animal were taken out and weighed, after which they were ground in quartz sand and prepared for further studies by having the proteins extracted with the aid of 10% solutions of trichloroacetic acid.

**EXPERIMENTAL RESULTS**

The experiments of this investigation indicate that cortisone delays rabbit deaths resulting from typhoid intoxication an average of 38 hours (Table 1). It follows that cortisone did not suppress the mechanisms producing resistance to typhoid intoxication.

**TABLE I**

Survival Rate of Animals Subjected to Typhoid Intoxication and Both Treated and Untreated with Cortisone

<table>
<thead>
<tr>
<th>Preparation introduced</th>
<th>Total number of rabbits</th>
<th>Number of rabbits</th>
<th>sacrificing after dying after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typhoid vaccine</td>
<td>7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Cortisone and typhoid vaccine</td>
<td>7</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

The normal blood sugar in rabbits is 108-117 mg %. In the first group the blood sugar level in the first 24 hours of observation remained normal. In the rabbits of this group, dying at later times, there was noted a hyperglycemia, the concentration of the sugar rising 2-24/2 times over the base figures reaching 267 mg %, 218 mg %.

When cortisone was administered, hyperglycemia was observed within a day of introduction of the typhoid vaccine. Only in 2 rabbits of the second group (in one, at the moment of death) did the sugar concentration in the blood not rise within the first day. Subsequently, all the rabbits developed hyperglycemia. Compared with base level, blood sugars rose 11/2-2 fold. Giving cortisone to healthy rabbits caused blood sugars to rise 11/2-2 times as compared with beginning readings. It follows that cortisone did not substantially affect blood sugar levels produced by typhoid intoxication as it produced hyperglycemia also in healthy rabbits.

The normal rabbit blood adrenalin concentration averages 0.027 mg %, fluctuating between 0.011 and 0.036 mg %. In the first day of observation, the rabbits of the first group maintained an adrenalin level within normal limits averaging 0.026 mg %. Rabbits of this group sacrificed in the second day or later had a 2-24/2 fold adrenalin rise averaging between 0.063 and 0.047 mg % and being in agreement with similar data for the fourth animal group. In this fourth group of rabbits all indicators remain unaltered during the course of the experiment.

In rabbits of the second group hyperadrenalinemia was observed within the first day averaging 0.049 mg %. In the second day the adrenalin concentration in the blood attained still greater figures averaging 0.063 mg %; this level was also above normal averaging 0.044 mg % in rabbits dying at later times. Cortisone injected into healthy rabbits did not produce appreciable changes in the adrenalin content of the blood.