ADRENALIN-LIKE SUBSTANCES IN MYASTHENIA

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The neuro-humoral theory of nerve excitation is largely responsible for the discovery of the pathogenesis of myasthenia. The elucidation of the role of acetylcholine in the process of excitation has led to a greater understanding of the intimate mechanisms of the motor disorders in myasthenia. On this basis considerable success has been achieved in the development of pathogenetically justified treatment, directed at regulation of the disturbed acetylcholine metabolism by means of the use of the so-called anticholinesterase preparations.

Numerous investigations on this problem have been devoted mainly to an exploration of the various possible causes of the acetylcholine deficiency: to its destruction, its inadequate synthesis, and to the blockade by curare-like substances, i.e., to factors leading eventually to a state of so-called "functional asynapsia" [3]. Investigations of this sort are characterized by some degree of one-sidedness. For a comprehensive investigation of the problem it is necessary to account for the role of another hormonal factor which is of essential importance in the normal processes of neuromuscular excitation, namely the role of adrenalin and of adrenalin-like substances. An explanation of the role of these factors in the mechanism of the disorders and of the restoration of function in myasthenia is all the more necessary since the activity of the cholinergic and adrenergic systems in the processes of neuromuscular activity in a number of cases is not antagonistic but synergistic.

In connection with these problems, the aim of our investigation was to study the changes in adrenalin and adrenalin-like substances in myasthenia in association with the use of drugs causing clinical improvement of myasthenic patients. Such factors include anticholinesterase preparations (proserin — prostigmin methylsulfate) and the adrenocorticotropic hormone (ACTH), and x-ray irradiation of the thymus gland.

EXPERIMENTAL METHOD

The adrenalin and adrenalin-like substances of the venous blood were determined by the method of Shaw [9] as modified by Utevskii and Butom [6]. The final staining was estimated colorimetrically on a type SF 4 spectrophotometer at a wavelength of 630 nm. In this way the following fractions of adrenalin-like substances in the blood of normal persons and of patients with myasthenia

<table>
<thead>
<tr>
<th>Name of group</th>
<th>No. of cases</th>
<th>RAS</th>
<th>TA</th>
<th>CSP</th>
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<tr>
<td>Normal</td>
<td>24</td>
<td>7.8</td>
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Symbols: M — arithmetic mean; m — mean square error of the arithmetic mean.

TABLE 1

Adrenalin-Like Substances in the Blood of Normal Persons and of Patients with Myasthenia

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Total adrenalin (in %)

Number of cases

1 2 3 4 5 6 7

1 2 3 4 5 6 7 8 9 10 11 12 13 14

Total adrenalin content in the normal subject and in myasthenia;

--- normal; - - - - myasthenia.

substances were determined: 1) in acid medium - the reduced adrenalin-like substances (RAS); 2) the content of dehydroadrenalin-like substances, by the difference between the content of RAS in the presence and absence of ascorbic acid; the total content of both fractions is referred to as "total adrenalin" (TA). The ratio between the values obtained by treatment with alkali and acid is an expression of the "coefficient of specificity" (CSP), which enables the relative content of adrenalin and of as yet unidentified adrenalin-like substances (chromogens) in the RAS fraction, a component of which is noradrenalin, to be judged. When the CSP > 2 it is considered that the RAS contains only adrenalin, and when the CSP < 1 adrenalin is absent. When 1 < CSP < 2 it is considered that the RAS is a mixture of adrenalin and of as yet unidentified adrenalin-like substances. In this paper the values of the RAS, TA and CSP are given in tables. Observations were made on 24 apparently healthy persons and on 23 patients with myasthenia before the commencement of treatment, in a state of myasthenic exhaustion.

EXPERIMENTAL RESULTS

The results of statistical analysis of the experimental findings are shown in Table 1.

Analysis of the figures in Table 1 shows that in myasthenia there is a tendency for the RAS content of the blood to fall. Under these circumstances the value of the CSP shows that both in the normal subject and in patients with myasthenia free adrenalin does not appear in the blood and only chromogens may be detected (CSP < 1). The tendency for the adrenalin-like substances to fall in myasthenia is also shown by the Gaussian distribution curves of the total adrenalin content in the normal subject and in myasthenia (see Figure). Some reduction in the content of adrenalin-like substances in the blood of patients with myasthenia we regard as the result of the acetylcholine deficiency in myasthenia.

The study of the movements of the content of adrenalin-like substances in the blood of 21 patients (35 observations) before and 45 minutes after the subcutaneous injection of 2 ml of a 0.05% solution of proserin (when a sudden improvement in the clinical condition of the patients took place) showed that in the majority of cases (29 out of 35) there was an increase in the total content of adrenalin-like substances, mainly due to the unoxidized fractions. Under these conditions the CSP of these simple changes was not ascertained. In different patients the increase in the adrenalin-like substances differed (from 0.3 to 4 γ%) and varied in the same patient during repeated examinations, but as a rule there was a clear tendency towards an increase in the adrenalin-like substances.

In Table 2 are shown the results of a study of the effect of proserin on the content of adrenalin-like substances in the blood—the arithmetic mean values of the RAS, TA and CSP, their mean square errors and coefficients of significance.

It can be seen from Table 2 that after the injection of proserin into the patient there is observed an increase in the RAS and TA, and the differences observed are statistically significant, t ≥ 3.

We also observed similar changes in the content of adrenalin-like substances in the CSF in three patients under observation 10 minutes after the subcutaneous injection of proserin (Table 3).