Effect of Reserpine and Chlorpromazine on Some Cold Stress-Induced Biochemical Alterations

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The effects of reserpine and chlorpromazine on cold stress-induced changes in adrenal ascorbic acid of rats and blood glucose, serum cholesterol, and serum sodium levels of rabbits were studied. While pretreatment with chlorpromazine minimized many of these stress-induced alterations, reserpine pretreatment aggravated them. Reserpine was found to be effective in preventing the stress-induced reduction of serum cholesterol level. Pretreatment with chlorpromazine minimized the adrenal ascorbic acid depletion due to cold stress. It also significantly prevented rise in blood sugar and fall in serum sodium produced by cold stress.

STRESS stimulates the hypothalamo-adrenal axis and produces a number of functional and biochemical alterations. It is a well known fact that most types of stresses have associated psychic components, and a number of stress-induced changes are mediated through the hypothalamus. Tranquilizers, by calming the mind, could possibly reduce the psychic component of stress and thus minimize the stress-induced alterations. A survey of the past literature shows that only few sporadic studies have been made so far to study the effect of tranquilizers on stress-induced biochemical changes (1–4). Though a considerable amount of work has been done to study the changes in the adrenal ascorbic acid and blood glucose levels during stress, difference of opinion exists regarding the effectiveness of tranquilizers to counteract these changes (1–3, 5, 6), and the present study is aimed at clarifying the divergent views expressed by different workers in this regard. No previous attempt has been made to study the influence of tranquilizers on stress-induced changes in the circulating ions and cholesterol, and therefore, this virgin field of exploration was selected with the hope that with such lucid exposition of the beginning stages of altered metabolism, an insight into the diverse disturbances caused by stress could be attained which will hasten the development of appropriate therapeutic agents for the prevention or amelioration of some of the stress-induced abnormalities.

MATERIAL AND METHODS

Albino rats (125 to 175 Gm.) and rabbits (1.25 to 1.75 Kg.) were subjected to cold stress by keeping them at an environmental temperature of 2° ± 1° for 1 hr. In order to keep the animals in identical conditions the day before the experiment (12 hr. before experimentation) they were isolated, during which period no food was given. The effects of drugs and stress were determined on rat adrenal ascorbic acid and rabbit blood glucose, serum cholesterol, and sodium. The levels were studied in normal controls, after stress, after tranquilizers, and after producing stress in animals pretreated with tranquilizers. Reserpine and chlorpromazine were administered in doses of 1 mg./Kg. intraperitoneally in rats. In rabbits these drugs were administered intramuscularly in a dose of 0.3 mg./Kg. and 3 mg./Kg., respectively. The animals were subjected to stress 45 min. after chlorpromazine and 4 hr. after reserpine pretreatments. The rats were decapitated and the rabbit's blood was collected immediately after stress or after an equivalent interval following the drug administration in those animals not subjected to stress, for the biochemical studies.

Adrenal ascorbic acid was extracted in 4% trichloroacetic acid and estimated by the method of Roe and Kuether (7). Blood glucose was estimated by Somogyi-Nelson's method (8, 9), serum cholesterol by Bloor's method, as given in the handbook of "Lumetron Photoelectric Colorimeter," model 400-A, p. 536, and serum sodium by using a flame photometer (10).

RESULTS

The findings are summarized in Fig. 1, which shows control levels and alterations in various biochemical parameters after drug, after stress, and after drug plus stress.

The depletion of adrenal ascorbic acid after stress was increased in reserpine-pretreated animals and decreased in chlorpromazine-pretreated animals. While reserpine produced a significant depletion in the control adrenal ascorbic acid level, the change due to chlorpromazine treatment was insignificant. Significant hyperglycemia was seen after cold stress and also after reserpine and chlorpromazine treatment. Stress-induced hyperglycemia was less in chlorpromazine and exaggerated in reserpine-pretreated animals. Stress produced a fall in serum cholesterol level. Reserpine pretreatment reduced this fall, but pretreatment with chlorpromazine was ineffective in this respect. Neither drug altered the prestress control cholesterol level. A moderate reduction in serum sodium level occurred after stress. Pretreatment with reserpine aggravated this stress-induced alteration while pretreatment with chlorpromazine minimized it. The prestress control sodium level was unaltered after reserpine or chlorpromazine.

DISCUSSION

Acute cold stress produces a fall in adrenal ascorbic acid, serum cholesterol, and serum sodium levels and a rise in blood glucose level. Most actions of reserpine are stress-like and a number of stress-induced alterations are aggravated by its pretreatment. Stress-like effects of reserpine have been reported by others (11–13). It may be a nonspecific action or an action mediated *via* hypothalamus as proposed by Maickel *et al.* (12). Most effects of chlorpromazine pretreatment on stress are just opposite to those seen after reserpine.

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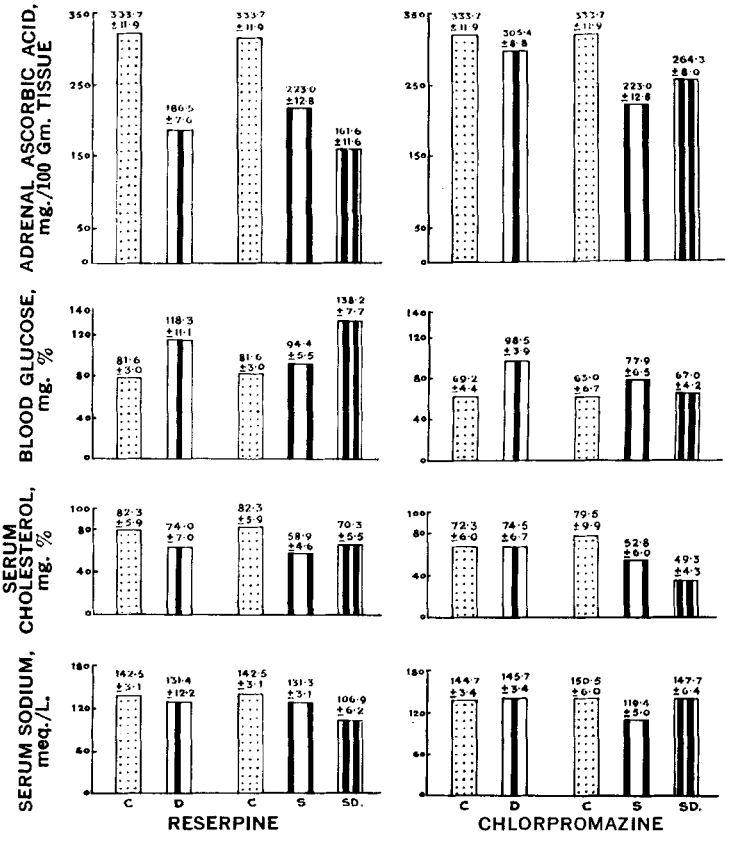

Fig. 1.—Effect of reserpine and chlorpromazine on cold stress-induced biochemical alterations. Key: C, control; D, drug alone; S, stress alone; SD, stress after drug pretreatment. The number of animals used for the adrenal ascorbic acid estimation was 36 (control), 15 (cold stress alone), and 8 each in other groups; while in the case of all other experiments the number of animals was 8 in each group. In some of these experiments control of animals was taken more than once. For easy comprehension, the control values have been shown along with corresponding observation. The figures denote mean values ± standard error in each group.

These opposing actions of reserpine and chlorpromazine point to their different mechanisms of action. There could be some relationship of this difference to their different actions on ergotropic and trophotropic systems of Hess (14), as reported by Brodie *et al.* (15). Work on these lines is in progress.

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