Effect of Cytidine Diphosphate Choline on Growth Hormone and Prolactin Secretion in Man

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Synopsis

The effect of intravenous infusion of cytidine diphosphate choline (CDP-choline) on the serum levels of growth hormone (GH) and prolactin (PRL) was studied in six normal adult male subjects. Serum GH levels increased and reached a maximum at 60-90 min after the initiation of infusion in all subjects examined. The mean peak value of GH in six subjects was 10.0±2.1 (mean±SE) ng/ml, which was significantly higher than the basal level (p<0.01). In four subjects, serum PRL levels decreased from 10-24 ng/ml to less than 7.2 ng/ml at 60-120 min, while in the other two no significant change was observed. These results indicate that CDP-choline affects GH and PRL secretion from the anterior pituitary.

The regulatory mechanism of growth hormone (GH) secretion from the anterior pituitary is closely related to the brain catecholamine metabolism. 1-DOPA, a precursor of dopamine, which has been in clinical use for the treatment of Parkinson's disease, stimulates GH secretion (Boyd et al., 1970; Kansal et al., 1972) and inhibits prolactin (PRL) release (Friesen et al., 1972; Kleinberg et al., 1971) from the pituitary. These effects appear to be regulated by the dopaminergic mechanism in the hypothalamus.

Cytidine diphosphate choline (CDP-choline), the structural formula of which is shown in Fig. 1, was developed as a drug to treat the patients with consciousness disturbed and was found to have some effect on Parkinson's disease. Data for 136 patients with Parkinson's disease treated at 20 medical institutions in Japan showed that CDP-choline combined with tryhexyphenidyl hydrochloride (THP) significantly improved the symptoms compared to the control given THP only. (Tsubaki et al., 1974). No significant difference in effectiveness was noted between the group treated with the combination of CDP-choline and 1-DOPA and that treated with 1-DOPA only (Tsubaki et al., 1974). In addition, evidence has been accumulated that CDP-choline is concerned with the dopamine metabolism in the brain (Kinoshita et al., 1974; Manaka et al., 1974). We postulate that CDP-choline affects the secretion of anterior pituitary hormone. This communication evaluates the effect of this drug on the serum levels of GH and PRL in normal men.

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Fig. 1. Structural formula of CDP-choline.
Materials and Methods

Six normal adult male subjects aged 18-42 were allowed to rest quietly in bed following an overnight fast. After a baseline sample was obtained, 1 g of CDP-choline in 300 ml of physiological saline was infused intravenously over a period of 30 min. Blood specimens were withdrawn from an antecubital vein at intervals of 30 min after the initiation of infusion. No adverse effect was observed during and after the infusion of CDP-choline. The control studies were performed on the same subjects with saline infusion. All studies were started between 0830 and 0930 hr. The serum levels of GH and PRL were determined by the established double antibody radioimmunoassay technique using Dainabot Radioisotope Kit and CEA-IRE-SORIN Kit, respectively. The minimal level detectable was 0.5 ng/ml for GH and 1.25 ng/ml for PRL.

Results

Effects of CDP-choline on the serum levels of GH and PRL are shown in Fig. 2. In five out of the six subjects, the serum GH levels increased from less than 3.3 ng/ml to the maximum ranging from 6.6 to 17.0 ng/ml at 60-90 min after the onset of infusion. In the sixth subject, the GH levels slightly increased from 1.3 to 2.4 ng/ml. The mean GH level of the six subjects at 60 min was 8.6 ± 2.0 (mean ± SE) ng/ml. This elevation of the serum GH level was statistically significant when compared with the control studies in which saline was infused (p<0.01).

In four subjects, the serum PRL levels decreased from 10-24 ng/ml to less than 7.2 ng/ml at 60-90 min after the infusion, but in the other two no significant change was seen. The mean PRL of the six subjects at 90 min was 5.4 ± 0.7 ng/ml, which was significantly lower than the control studies with saline infusion (p<0.01) and different from the basal level (p<0.05).

Discussion

Recently, it has been recognized that the release of GH and PRL from the anterior pituitary is regulated by the dopaminergic system which, when activated, causes secretion of GH and inhibits PRL release from the pituitary. Also some drugs related to the catecholamine metabolism are known to affect GH and PRL secretion. In man, L-DOPA, a precursor of dopamine, stimulates GH (Boyd et al., 1970; Kansal et al., 1972) and inhibits PRL (Friesen et al., 1972; Kleinberg et al., 1971) secretion, while chlorpromazine, an antagonist of the dopaminergic system, inhibits GH and stimulates PRL secretion (Friesen et al., 1972; Sherman et al., 1971). Fusaric acid, an inhibitor of dopamine
hydroxylase which catalyzes the conversion of dopamine to norepinephrine, causes the elevation of the plasma GH concentration in normal men (Hidaka et al., 1973). Our present experiments indicate that CDP-choline also stimulates GH and inhibits PRL release.

CDP-choline affects the central nervous system by improving the phospholipid metabolism (Kornberg and Pricer, 1952; Kennedy and Weiss, 1956) and participating in the dopamine metabolism (Kinoshita et al., 1974; Manaka et al., 1974). The intraperitoneal injection of CDP-choline in mice caused a marked increase in brain dopamine content (Kinoshita et al., 1974). Manaka et al., showed that CDP-choline inhibited the diminution of the brain dopamine content due to brain destruction (Manaka et al., 1974). They observed that destruction of cat substantia nigra caused depletion of dopamine content in the caudate nucleus, while in cats treated with CDP-choline such a depletion was completely inhibited. These results suggest that CDP-choline might promote dopamine production in the central nervous system.

Our present data indicate that CDP-choline affects GH and PRL secretion from the anterior pituitary. These effects are possibly due to the activation of the dopaminergic system by the drug, but the precise mechanism remains obscure.

References