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LETTER TO THE EDITOR

EFFECT OF VINCA ALKALOIDS ON INTESTINAL ABSORPTION OF GLUCOSE

Sir,

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Vinca alkaloids are well known for their antimitotic and antitumor activities. It inhibits transcription and translation (1, 2, 3). Vinca alkaloids cause specific mitotic arrest of cells. The drugs derived from these alkaloids are: Vinblastine and vincrystine. These drugs have been extensively used for studying the nature of cell arrest and the associated changes in various clinical (neoplastic conditions) and experimental studies.

In our study 84 female albino rats were used. The rats were starved prior to the experiment for about 12 to 14 hrs. The dosing of the rats was done using vinblastine sulphate solutions in normal saline. The solutions were injected intraperitoneally (1 mg/kg body weight). The dosage schedule followed reports of Sharma and Nagachoudhury (4) in such a way that desired arrest of mitosis could be achieved, without producing obvious toxic effects on gut mucosa. To achieve the desired level the doses drug were repeated four hourly and the readings were taken after 4–5 hrs of the last treatment.

The animals were allowed to undergo a period of absorption after injection of test solutions. The absorption study was done after anaesthetizing the animals with sodium pentothal (40 mg/kg body weight). The abdomen was then incised along midline and intestine was washed thoroughly with saline at 37°C. The test solutions containing 300 mM D-glucose (solutions in normal saline) were injected by a fine syringe at 37°C. The animals were than allowed to undergo an absorptive period of 10 minutes being maintained at approximately 37°C. The loops were then excised by sacrificing the animal and washed with warm normal saline. The solution thus obtained was analyzed for D-glucose. To estimate the amount absorbed by the animal, the difference between the injected solution values and recovered solution was calculated. For measuring the amount of the D-glucose, the intestinal tissue was dried at 110°C for about 14–16 hours. Then D-glucose was estimated by glucose oxidase-peroxidase method (5).

The results obtained at the end of twelfth hour revealed a significant reduction in glucose absorption from the distal jejunum, proximal ileum and distal ileum (Table I). Thus a transport rate for glucose was significantly affected by administrating vinca alkaloids. Beer (6) suggested that vinblastine inhibits energy producing

TABLE I: Effect of Viblastine on intestinal absorption of D-glucose (μ moles/gm dry wt./hr.) in adult rats *in vivo*.

	Sac 1 (Proximal jejunum)	*Sac 2 (Distal jejunum)*	*Sac 3 (Proximal ileum)*	*Sac 4 (Distal ileum)*	*Total absorption from all the rats*
Control	3105±84 (5)	3767±133 (5)	3388±77 (5)	2980±132 (5)	3310±79 (5)
Vinblastine 1 dose	3403±122* (3)	4010±79* (3)	3571±30* (3)	2851±176* (3)	3539±30* (3)
Vinblastine 2 doses	3298±34* (3)	4010±330* (3)	3147±36* (3)	2963±76* (3)	3355±123* (3)
Vinblastine 3 doses	3185±40* (3)	2563±195** (3)	2481±97*** (3)	1858±77*** (3)	2521±75*** (3)

*P = N.S. **P<0.01 ***P<0.001
Figures in brackets show number of experiments.
Vinblastine was given 1 mg/kg body wt/dose intraperitoneally.

mechanisms in small intestinal cells which are essential for active uptake/transport processes.

Vinca alkaloids are mitotic inhibitors, bind to microtubular protein-tubulin and cause bone disruption of mitotic spindle. The chromosomes fail to move apart during mitosis: metaphase arrest occurs. They are cell cycle specific and act in the mitotic phase (7).

The vinca alkaloids have become clinically useful since the discovery of their antitumour properties in 1959. Initially, extracts of the periwinkle plant (Catharanthus roseus) were investigated because of putative hypoglycemic properties, but were noted to cause marrow suppression in rats and antileukemic effects *in vitro*. Vinblastine binds to the microtubular proteins of the mitotic spindle, leading to crystallization of the microtubule and mitotic arrest or cell death. Vinblastine has some immunosuppressant effect also. The vinca alkaloids are considered to be cell cycle phase-specific (8, 9, 10, 11).

The present work involved basically the effect of vinca alkaloids on the transport kinetics of D-glucose. The decrease in absorption of glucose from small intestine of vinblastine treated rats in the present study is definitely arising out of a modification of the cell membrane, presumably affecting the affinity sites of the glucose binding on the membrane.

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