SUPPLEMENTARY VITAMINS IN EXPERIMENTAL PORPHYRIA

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Acute intermittent porphyria is an inherited metabolic disorder presenting a varied symptomatology, commonly abdominal pain and an ascending paralysis. Chemically, the disorder is characterized by an accumulation of porphyrins and porphyrin precursors in the liver and an elevated excretion of these compounds, principally porphobilinogen, in the urine (Sachs, 1931, and Westall, 1952). Duesberg (1932) reported an elevated porphyrin excretion in a patient receiving allylisopropylacetylcarbamide [Sedormid]. This observation suggested to Schmid and Schwartz (1952) a means of experimentally producing porphyria. In recent years other investigators have used Sedormid, or a water soluble analogue, allylisopropylacetamide, abbreviated as AIA, to induce an experimental porphyria of the acute intermittent type in rabbits, rats and chick embryos (Benard, et al., 1953, and Labbe, et al., 1954). However, it is possible that in the genetically determined human type of acute intermittent porphyria, the biochemical mechanism responsible for porphobilinogenuria may not be the same as that produced by a chemical such as Sedormid or AIA. The genetic abnormality would be expected to have a single locus of effect (Giraud, et al., 1960), whereas the chemically induced malfunction possibly has a multiple locus.

It was noted that during the period of experimental porphyria induction in albino rats, they became very lethargic, and their consumption of food and water, offered *ad libitum*, dropped to zero. Remembering that AIA is structurally related to the barbiturate family, and during these experiments was administered twice daily for three consecutive days, this is not surprising. Therefore we investigated malnutrition in experimental animals as a possible complicating factor in drug induced porphyria experiments.

Methods and Materials

Four groups of male Wistar rats were used in this study, with five animals in each group. Porphyria was induced and maintained by the subcutaneous injection, twice daily for three consecutive days, of 25 mgm of AIA in 1 cc of warm, isotonic saline.

The first group was given AIA and fed by stomach tube once daily with 3.5 cc of an aqueous solution containing 4 g of glucose, 10 mgm of thiamine, 5 mgm of riboflavin, 30 mgm of niacin, 30 mgm of pyridoxine and 30 mgm of vitamin C. A second group was given AIA, and fed by stomach tube once daily with 3.5 cc of an aqueous solution con-

taining only the B and C vitamins. The third group were deprived of all food and water except the glucose and B and C vitamin solution fed to group one, also delivered by stomach tube. Finally, the fourth group was untreated, and starved for the duration of the experiment.

The animals were weighed before starting the experiment, and daily during the experiment. Following three days of treatment, the animals were sacrificed by cervical separation. The livers were removed after the method of Rokitansky, blotted upon filter paper, and weighed. These data are summarized in Table 1.

Observations

The average weight loss of the starved animals was the same, and the percent weight loss almost the same as that of the porphyric rats force fed a vitamin B supplement. However, the livers of the rats of both porphyric groups showed over a two-fold increase in weight over those of the normal starved group, and almost the same increase over the livers of the normal starved group force fed with glucose and vitamins. The porphyric animals that were force fed glucose and vitamins suffered the least loss of weight, and the normal animals fed the identical ration a 1.4% greater loss. The starved animals lost more weight than the normal animals that were fed, with a large increment of this loss reflected in the sacrifice of liver carbohydrate stores. The porphyric rats, which were fed upon vitamins only, lost more weight than all of the other groups and exhibited the greatest hepatic enlargement.

Discussion

When the liver is healthy, porphyrins are excreted harmlessly into the bile; when diseased, they are retained in the blood and symptoms are produced (Sherlock, 1955). Inasmuch as animals treated with AIA become lethargic and do not feed, it was postulated that malnutrition might be one of the factors contributing to the hepatic enlargement re-

Table 1.—Summarization of the Weight of Livers and Changes in Body Weight of the Four Groups of Rats.

	AIA-Treated		Non-Treated	
	Glucose vitamins	*Vitamins*	*Glucose vitamins*	*Starved*
Average starting weight of each group	290 gms	287 gms	295 gms	293 gms
Average finishing weight of each group.....	243 gms	232 gms	243 gms	238 gms
Average weight loss for each group	47 gms	55 gms	52 gms	55 gms
Percent weight loss for each group ...	16.2%	19.0%	17.6%	18.9%
Average liver weight for each group ...	13 gms	13.3 gms	8 gms	6.2 gms

sponse to the drug. Vitamins of the B complex enter into several of the enzyme systems present in the liver; ascorbic acid is necessary for the formation of intercellular substances. Hence it was postulated that an adequate supply of these metabolic catalysts, coupled with sufficient glucose to supply the immediate caloric requirements of the starving animal, would protect the liver from the increase in size commensurate with experimental porphyria.

The results indicate that the vitamin and glucose therapy had a beneficial effect upon the body's general economy. These animals lost less weight than any other group. The starved animals lost less weight than all others, the glucose and vitamin feeding protecting the normal group. However, energy and vitamins are obviously insufficient to prevent some loss, and it is thought that a protein should have been added to the diet.

The porphyric rats fed on vitamins alone suffered the greatest loss of weight as well as having the most enlarged livers, while the AIA treated animals fed upon sugar and vitamins exhibited greatly enlarged livers. It is thought that the hepatic effects of experimentally induced porphyria will not be ameliorated by fortifying the diet with B complex and C vitamins, and using glucose to supply the calculated energy requirements of the animal.

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