

Influence of D-Sorbitol on Absorption of Vitamin B₁₂ by Patients with Pernicious Anemia and Achlorhydria

BACON CHOW, PH.D.,* STANLEY TAUBER, M.D.,† IRVING WOLDOW, M.D.,‡ SAMUEL YEH, M.D.,§ AND BRUNO RANKE, DR. RER. NAT.¶

RECENTLY, Chow *et al.*¹ reported on an elixir containing vitamin B₁₂ that produced serum vitamin B₁₂ levels in healthy young and aged people that were significantly higher than could be obtained with larger oral doses of vitamin B₁₂ alone. In the same paper they reported that the elixir did not seem to be effective in treating patients for pernicious anemia.

Later studies by Chow and others^{2,3} established that the absorption-enhancing factor in the elixir was D-sorbitol, a substance which is not derived from intrinsic factor. The studies also indicated that when enough D-sorbitol is administered with vitamin B₁₂ there is a statistically significant increase in absorption of the vitamin by pregnant women and old people.⁴ Other investigators demonstrated this unusual property of D-sorbitol in normal subjects⁵ and in laboratory animals.⁶⁻⁹

Although D-sorbitol did not improve absorption of vitamin B₁₂ by patients with pernicious anemia, its established ability to improve absorption in other types of patients led us to test it once again in patients with pernicious anemia on the chance that our original finding might be in error. The effect of sorbitol on the

absorption of vitamin B₁₂ by subjects with achlorhydria was also studied.

MATERIALS AND METHODS

Patients with Pernicious Anemia

Twelve patients with pernicious anemia in remission participated in the study. The diagnoses of pernicious anemia were made by bone-marrow tests and by determining the amount of vitamin B₁₂ excreted in the urine.

In the urinary excretion test, 2 µg of radioactive vitamin B₁₂ labeled with Co⁶⁰ (specific activity, 180 µc/mg) was administered to the patient in 30 ml of water with which the container was rinsed. Two hours later, the patient was given an intramuscular injection of 1000 µg of unlabeled vitamin B₁₂. Urine was then collected from the patient for 24 hours. After measuring the volume of urine, one half was evaporated on a steam bath until less than 50 ml remained. The amount of radioactivity in this residue was measured by a scintillation counter. Three or more months later, the test was repeated, using 10 ml of a 60 per cent aqueous solution of D-sorbitol in place of 10 ml of water.

Subjects with Achlorhydria

A total of 19 subjects with achlorhydria which was diagnosed by gastric juice analysis and/or by Diagnex¶ feeding were randomly divided into two groups. Group A (10 patients) received 50 µg of radioactive vitamin B₁₂ alone, and Group B (9 patients) received the

¶ Kindly supplied to us by E. R. Squibb & Sons, Inc.; equal to quinine resin.

From the Department of Biochemistry, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, Maryland.

* Department of Biochemistry, Johns Hopkins University; † Assistant in Medicine and Department of Research, Albert Einstein Medical Center, Philadelphia, Pennsylvania. ‡ Department of Hematology, Albert Einstein Medical Center, Northern Division, Philadelphia, Pennsylvania. § Department of Biochemistry, Johns Hopkins University; ¶ Present address: Universitäts-Krankenhaus Eppendorf, Hamburg, Germany.

same amount of vitamin B₁₂ together with 10 ml of a 60 per cent aqueous solution of D-sorbitol. These studies were conducted on four separate occasions (identified as studies 1-4), with the number of subjects in each group shown in Table II. Two hours later all subjects were injected with 1000 μ g of unlabeled vitamin B₁₂ and their urine samples were collected for 24 hours for radioactivity measurement.

RESULTS

Patients with Pernicious Anemia

Our studies with the urinary excretion test in more than 100 healthy subjects show that the average normal excretion is 11.0 per cent of the test dose of vitamin B₁₂. As shown in Table I, in the first test all patients excreted less than 1.5 per cent of the dose of vitamin B₁₂, thus confirming the diagnoses of pernicious anemia. The test with D-sorbitol demonstrated that a 60 per cent aqueous solution of D-sorbitol had no effect on the absorption of orally administered vitamin B₁₂ by patients with pernicious anemia; D-sorbitol increased absorption in only 1 of the 12 patients tested (patient 5 in Table I).

Subjects with Achlorhydria

The data on the urinary excretion of subjects

TABLE I
Effect of D-Sorbitol on the Urinary Excretion of Orally Fed Radioactive Vitamin B₁₂ by Patients with Pernicious Anemia^a

Patient	Vitamin B ₁₂ + water	Vitamin B ₁₂ + sorbitol
1	0.1	0.7
2	0.5 ^b	0.5
3	0.5 ^b	0.5
4	0.1	0.1
5	1.5	5.0 ^c
6	0.1	0.1
7	0.5	1.0
8	0.6	1.5
9	—	1.2
10	—	1.4
11	—	0.5
12	—	1.4

^a All results are expressed as per cent of the 2 μ g of radiovitamin B₁₂ given orally.

^b Approximate.

^c Only significant increase (low normal range).

TABLE II
Effect of D-Sorbitol on the Urinary Excretion of Orally Fed Radioactive Vitamin B₁₂ by Subjects with Achlorhydria^a

Study	Subject No.	Group A (vitamin B ₁₂ + water)	Group B (vitamin B ₁₂ + sorbitol)
1	1	1.61	2.38
	2	1.22	3.83
	3	2.14	3.17
2	4	0.51	1.91
	5	0.81	1.06
	6	1.66	2.34
3	7	1.73	1.35
	8	1.22	2.21
	9	0.56	^b
4	10	0.65	1.83
MEAN ^c		1.21 \pm 0.178	2.23 \pm 0.284

^a All results are expressed as per cent of the 50 μ g of radiovitamin B₁₂ given orally.

^b Only a small portion of the 24-hour urine specimen was collected and was, therefore, discarded.

^c Mean and standard error. The difference in the means of both groups is statistically significant ($p < 0.01$) calculated according to the Students' *t* test.

in Groups A and B are presented in Table II. They demonstrate that a 60 per cent aqueous solution of sorbitol enhances the absorption of orally administered vitamin B₁₂ by subjects with achlorhydria. The same effect was observed in four separate studies, and the difference in the urinary excretion of radioactivity is statistically significant.

DISCUSSION

The finding that D-sorbitol does not increase absorption of orally administered vitamin B₁₂ by patients with pernicious anemia agrees with the findings of Ellenbogen and his associates¹⁰ and confirms our original observation.

The lack of efficacy clearly differentiates D-sorbitol from intrinsic factor, which by definition must increase absorption of vitamin B₁₂ in patients with pernicious anemia. Since D-sorbitol can be effective in increasing absorption of vitamin B₁₂ in patients where there is no demonstrable lack of intrinsic factor, or even in subjects with achlorhydria, it appears that there are a number of different mechanisms by which vitamin B₁₂ is absorbed from the gastrointestinal tract.

SUMMARY AND CONCLUSIONS

D-sorbitol, a substance which is not derived from intrinsic factor, has been found to increase the absorption of orally administered vitamin B₁₂ by certain patients who presumably possess intrinsic factor. As seen in this study, however, D-sorbitol did not increase the absorption of vitamin B₁₂ by patients with pernicious anemia, but it did enhance the absorption in subjects with achlorhydria. Thus, these findings together with others^{2,3} demonstrate that D-sorbitol can aid to some extent the absorption of vitamin B₁₂ by all types of subjects studied except those with pernicious anemia.

REFERENCES

1. CHOW, B. F., HORONICK, A., and OKUDA, K.: Effect of an elixir on the absorption of vitamin B₁₂ by healthy young and old subjects. *AM. J. CLIN. NUTRITION* 4: 434, 1956.
2. CHOW, B. F., MEIER, P., and FREE, S. M., JR.: Absorption of vitamin B₁₂ enhanced by D-sorbitol. *AM. J. CLIN. NUTRITION* 6: 30, 1958.
3. CHOW, B. F., PRYSTOWSKY, H., HELLEGERS, A. E., and WONG, V.: Vitamin B₁₂ studies: Absorption in human pregnancy enhanced by D-sorbitol. *Am. J. Obst. & Gynec.* 76: 91, 1958.
4. CHOW, B. F., *et al.*: To be published.
5. CORNMAN, E.: Elevation of plasma B₁₂ levels after oral administration of vitamin B₁₂ and a "non-intrinsic factor" additive to humans. Presented at New York Academy of Medicine Symposium on Vitamin B₁₂, February, 1958.
6. GREENBERG, S. M., HERNDON, J. F., RICE, E. G., PARMELEE, E. T., GULESICH, J. J., and VAN LOON, E. J.: Enhancement of vitamin B₁₂ absorption by substances other than intrinsic factor. *Nature, London* 180: 1401, 1957.
7. RICE, E. G., HERNDON, J. F., VAN LOON, E. J., and GREENBERG, S. M.: Enhancement of vitamin B₁₂ absorption by D-sorbitol as measured by maternal and fetal tissue levels in pregnant rats. *Am. J. Physiol.* 193: 513, 1958.
8. MORGAN, T. B. and YUDKIN, J.: The vitamin-sparing action of sorbitol. *Nature, London* 180: 543, 1957.
9. LATNER, A. L.: Intrinsic factor and vitamin B₁₂ absorption. *Brit. M. J.* 2: 278, 1958.
10. ELLENBOGEN, L.: Effect of sorbitol on vitamin B₁₂ absorption in pernicious anemia patients. Presented at a Vitamin B₁₂ Symposium, Society for the Study of Blood, New York City, April, 1958.