

Effect of Sorbitol on Iron Absorption in Man

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SEVERAL authors^{1,2} have observed that sorbitol increases the intestinal absorption of vitamin B₁₂ both in man and in animals. A similar effect for iron has been demonstrated in the rat³ and, although it has been studied in man,⁴ the method used does not seem adequate. Studies by means of the Fe⁵⁹ utilization test on the action of sorbitol in human iron absorption are presented in this paper.

MATERIAL AND METHODS

All subjects were adults, nine normal volunteers and three patients§ with iron deficiency classified on the basis of their serum iron and unsaturated iron-binding capacity. Two of the latter patients were slightly anemic^{||} (Table I); none received supplementary iron throughout the observation period. The serum iron was determined using the method of Peters et al.⁵ and the unsaturated iron-binding capacity by that of Finch and Rath.⁶

Two iron preparations were tested. One was a ferrous sulfate solution containing 6.66 mg. of iron per ml. The other solution had the same concentration of ferrous sulfate but also included 11.66 mg. of sorbitol per mg. of iron. No other iron preparations were used during either the observation period preceding the study or the study itself.

The Fe⁵⁹ utilization tests performed in each subject were identical; the only variable being the presence or absence of sorbitol in the iron solution. For each of two fourteen-day trial periods, 0.5 mg. of

iron per kg. of body weight, labeled with 10 to 12 μ c. of Fe⁵⁹SO₄; were administered at 11 A.M. In the men, there were twenty-eight days between the first and second trials; but in the women, trials were not started until two to three days after menses had stopped. Some subjects received the ferrous sulfate with sorbitol first, while in others the solution without sorbitol was the first preparation tested.

Duplicate 5 ml. samples of whole blood were obtained seven, ten and fourteen days after the administration of iron and the radioactivity of each was measured in a well scintillator counter.

The Fe⁵⁹ used for hemoglobin synthesis, expressed as per cent of total given dose, was obtained multiplying the per cent of given dose found in 1 ml. of red blood cells by the red cell volume calculated according to the normal mean values of Rodriguez Moyano et al.⁷: 30.66 ml. per kg. for men and 22.47 for women. In anemic patients, the red cell volume was arbitrarily corrected by factor:

$$\frac{\text{Observed hematocrit}}{\text{Mean normal hematocrit}^7}$$

RESULTS

Table I shows the amount of Fe⁵⁹, in per cent of given dose, found in the erythrocytes on days seven, ten and fourteen, as well as the averages of the hematologic values found. No significant changes in the venous hematocrit occurred throughout the study.

In Table II, maximal values obtained in each study, regardless of the day, are shown in the first two columns. In the third column they are compared as a ratio; values above 1.00 indicate better iron absorption with the sorbitol preparation and below 1.00, the opposite.

Ten of the twelve patients absorbed from 35 to 137 per cent more iron when the solution given contained sorbitol. Only two patients (Cases 1 and 12) showed diminished iron absorption (0.66 and 0.75 ratios, respectively).

Normal subjects absorbed an average of 8.41 per cent of iron from the sorbitol prepara-

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This study was supported by the Smith Kline & French Laboratories.

§ Two patients (Cases 10 and 11) had a past history of bleeding and one (Case 12) had frequently donated blood.

|| Normal mean hemoglobin values in residents of Mexico City are 17.8 (standard deviation (S.D.) = 1.51) gm. per 100 ml. for men and 15.2 (S.D. = 0.97) gm. per 100 ml. for women.¹⁵

TABLE I
Comparative Fe⁵⁹ Utilization Tests with and without Sorbitol

Case No.	Sex	Hemoglobin (gm./100 ml.)	Hematocrit (%)	Serum Iron (μg./100 ml.)	Unsaturated Iron-Binding Capacity (μg./100 ml.)	Red Cell Volume (ml.)	Fe ⁵⁹ in Hemoglobin (% of given dose)					
							Without Sorbitol			With Sorbitol		
							Day 7	Day 10	Day 14	Day 7	Day 10	Day 14
<i>Normal Subjects</i>												
1	M	16.7	49	76	300	2146	...	3.57	4.12	...	2.71	2.72
2	M	17.2	53	132	...	1717	0.54	1.39	2.30	...	3.10	2.92
3	F	14.7	47	100	150	1287	7.06	8.10	7.70	13.57	14.67	15.26
4	M	15.3	45	88	250	2453	...	5.08	4.35	8.54	9.51	10.11
5	M	17.6	51	67	170	2039	2.58	2.62	2.81	4.01	4.58	5.64
6	M	16.3	49	134	200	1901	...	4.86	5.40	10.18	10.97	11.32
7	M	16.9	50	104	200	2054	1.92	2.48	2.21	4.92	4.58	5.73
8	M	19.0	58	180	150	2146	4.60	...	5.05	10.76	11.92	11.31
9	M	15.7	47	167	120	2146	...	3.93	4.18	...	9.90	9.54
<i>Patients with Iron Deficiency</i>												
10	F	10.2	34	35	420	890	26.63	...	29.56	45.51	44.15	46.03
11	M	13.9	44	44	320	1447	4.66	5.45	6.16	8.81	8.77	8.69
12	M	16.4	50	34	360	2269	22.54	24.62	27.33	...	20.02	20.35

NOTE: Subjects ranged in age from eighteen to thirty-eight years and in body weight from 46 to 80 kg.

tion and 4.39 per cent from the control solution. Average absorption values in iron deficient subjects were 25.73 and 21.02 per cent, respectively.

COMMENTS

There are two main objections to conclusions drawn from quantitative results obtained in the iron utilization test. One is that although the test is considered a fairly accurate index of absorption⁸⁻¹⁰ there are individual differences in the rate of utilization of absorbed iron. The other objection is to the use of a theoretic blood volume in calculating the total circulating radio iron.* Both objections are probably overcome by the fact that each subject tested served as his own control, and it seems unlikely that major changes in blood volume would have occurred during the relatively short

* Sorbitol is known as an osmotic diuretic but, to achieve this effect, it must be administered intravenously in relatively large doses. In this study, sorbitol was given orally in small quantities and seven to fourteen days before measuring red blood cell radioactivity; therefore it does not seem likely that there would be any measureable effect on hematocentration.

period that elapsed between each test; the likelihood that there would be significant changes in the subject's rate of iron utilization during this time also seems small.

Results obtained by others who have used ferrous sulfate are given in Table III. It is recognized, of course, that strict comparison is difficult because of differences in the dose; however, in our nine normal patients the mean absorption rate with the ferrous sulfate solution alone was 4.39 per cent, which seems comparable to the 3.90 per cent found by others. Certainly our mean value is lower than that obtained by Moore et al.¹⁴ in two single cases, but comparable to the mean of the cases studied by different authors. Furthermore, Moore et al. calculated the blood volume assuming a ratio of 80 ml. per kg. of body weight, derived from indirect estimations of the blood volume, whereas we used a ratio of 67 ml. per kg. for men and 60 ml. per kg. for women derived from our normal series of direct measurements of the blood volume.⁷

The mean absorption rate with the sorbitol-containing formula for the nine normal subjects was 8.41 per cent which is significantly

TABLE II
Comparative Maximal Values of Fe⁵⁹ Utilization Tests
of Table I

Case No.	Fe ⁵⁹ in Hemoglobin (% of given dose)		Iron and Sorbitol ratio
	Without Sorbitol	With Sorbitol	
<i>Normal Subjects</i>			
1*	4.12	2.72	0.66
2	2.30	3.10	1.35
3	8.10	15.26	1.88
4	5.08	10.11	1.99
5*	2.81	5.64	2.00
6*	5.40	11.32	2.10
7*	2.48	5.73	2.31
8*	5.05	11.92	2.36
9*	4.18	9.90	2.37
Average	4.39	8.41	1.89
"t" test	4.16 (p < 0.01)		
<i>Iron Deficient Subjects</i>			
10	29.56	46.03	1.56
11	6.16	8.81	1.43
12	27.33	20.35	0.75
Average	21.02	25.73	1.25

* First study with the sorbitol preparation.

higher (p < 0.01) than that of the ferrous sulfate alone. The high proportion of patients (in both normal subjects and iron deficient patients, ten of twelve) showing better iron absorption with the sorbitol-containing formula is also statistically significant (P < 0.02). These results strongly suggest that sorbitol increases iron absorption in man.

SUMMARY

Comparative Fe⁵⁹ iron utilization tests were carried out in nine normal and three iron-deficient subjects. The utilization of iron in each subject was determined after receiving a ferrous sulfate solution alone, and after receiving a ferrous sulfate solution, of the same concentration, to which sorbitol had been added.

Higher iron absorption from the sorbitol-

TABLE III
Other Authors' Results of Iron Utilization Tests Using
FeSO₄ (0.3 to 1 mg. of Iron/kg. of Body Weight)

Authors	Iron (mg./kg.)	Per Cent of Given Dose Found in Blood
Bothwell et al. ¹¹	0.3	1.10
Bothwell et al. ¹²	0.3	0.66 1.10 1.23 1.90 2.99 4.20 7.25 8.28
Alper et al. ¹³	0.5	0.70
Moore et al. ¹⁴	1.0 1.0	8.1 9.3
Average ± S.D. (12 cases)	0.43	3.90 ± 3.23
Our average ± S.D. (9 cases)	0.5	4.39 ± 1.71

containing solution was observed in ten of twelve patients, values being 1.35 to 2.37 times their own controls. The results strongly suggest that sorbitol improves iron absorption in man.

ACKNOWLEDGMENT

We are greatly indebted to Dr. Bacon F. Chow for suggesting the outline of this work and for his helpful criticism.

The ferrous sulfate used in this study was supplied by the Smith Kline & French Laboratories; the Fe⁵⁹ SO₄ was obtained from Abbott Laboratories and had a specific activity of 22.7 mc. per mg. of iron.

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