J. of Obst. & Gyn. of India Vol. 51, No. 1: Jan/Feb 2001 Pg 92-93

Urinary Excretion of Porphyrins and Porphyrin Precursors by Iron Deficient Anemic Women

D. C. Sharma & Rati Mathur

Department of Biochemistry, S. M. S. Medical College, Jaipur – 302 004

Summary

The urinary excretion of porphyrins (uroporphyrin and coproporphyrin) and porphyrin precursors (delta-aminolevulinic acid and porphobilinogen) was determined in 25 non-anemic and 26 iron-deficient severely anemic non-pregnant women. The excretion of delta-aminolevulinic acid was almost halved in iron deficiency anemia, suggesting regulation of porphyrin synthesis at this step.

Introduction

Iron deficiency and consequent anemia is the second most common affliction in the world. Its incidence is much greater in India especially in women (Sharma et al. 1993). Iron and porphyrin metabolism are intimately related in the formation of hemoglobin. Therefore, it is natural to expect that deficiency of iron would affect the synthesis of porphyrins otherwise toxic porphyrins would accumulate.

The urinary excretion of porphyrins and their precursors was investigated in the past by a few workers and the results were quite contradictory. Thus Prato et al (1968) found significantly lower excretion of coproporphyrins in iron deficiency anemia but Chalevelakis et al (1977) reported non-significant changes in the excretion of uroporphyrins and coproporphyrins.

As regards porphyrin precursors, Heilmeyer (1964) reported an increase in delta-aminolevulinic acid (ALA) and a decrease in porphobilinogen (PBG) excretion in urine of iron-deficient subjects. Heilmeyer (1964) even found these changes reverting to normal when iron deficiency was abolished. However, Prato et al (1968) found non-significant changes, while Kaneko (1970) and Chalevelakis et al (1977) reported decreased urinary excretion of ALA in iron deficiency anemia.

Thus it is obvious that the published reports regarding urinary excretion of porphyrins and their precursors are quite contradictory and there is no information about this aspect in the Indian women. Therefore, the present study was undertaken.

Material and Methods

Subjects of iron deficiency were selected from out patient department of Mahila Chikitsalaya and Zanana Hospital of Jaipur. The criteria of selection was freedom from infection and febrile disease and their hemoglobin level. The women having hemoglobin below 12 g% were considered anemic and an attempt was made to selec

women with hemoglobin as low as possible. The subjects of non-anemic control group were selected from among medical students, neighbours and college and hospital staff. Only those purportedly healthy females were selected whose hemoglobin was above 12 g%.

Ten ml. of blood was drawn in the morning. Heparinised blood was used for determining hemoglobin, hematocrit, red cell and reticulocyte counts and for preparing peripheral blood film (Dacie and Lewis, 1994). Serum was used for determining serum iron (SI) and total iron binding capacity (TIBC) (Tietz, 1976) on an auto analyzer (Merck, Selectra).

Uroporphyrin and coproporphyrin were determined as done by Askevold (1951) and ALA and PBG as described by Varley (1974).

Results and Discussion

Table I shows hematologic values of non-anemic women and indicates the existence of severe anemia in anemic group women. That the cause of this anemia was iron deficiency was indicated by serum iron and percent saturation values (Table II) and the presence of hypochromic microcytic erythrocytes in peripheral blood films.

Table I
Haematologic Values

Parameter	Non-anemic group (25)	Anemic group (26)
Hb (g%)	12.3 ± 0.37	7.3 ± 1.05
TRBC (x10⁶ cu mm	3.88 ± 0.53	
PCV (%)	34.8 ± 2.7	22.7 ± 3.4
MCV (fl)	90.4 ± 7.9	78.5 ± 11.5
MCH (pg)	32.3 ± 3.5	24.5 ± 2.6
MCHC (%)	35.5 ± 1.9	32.1 ± 2.2

All values are mean ± S.D.
All values are significantly different statistically ($p < 0.001$).

Table II
Iron Values

Parameter	Non-anemic group (25)	Anemic group (26)
SI (mg/dl)	105.2 ± 12.5	54.2 ± 12.6
TRBC (mg/dl)	340.0 ± 35.1	378.7 ± 38.9
PS (%)	29.4 ± 4.4	14.5 ± 4.4

All values are mean ± SD.
All values are significantly different statistically ($p < 0.001$).

The excretion of porphyrin precursors and porphyrins in non-anemic and anemic women is shown in the Table III. ALA excretion was found to be almost halved in the iron deficient group, which was found to be highly significant statistically ($p<0.001$). The urinary excretion of PBG and both the porphyrins was not significantly altered.

Table III
Urinary Excretion of Porphyrins and their Precursors

Parameter	Non-anemic group (25)	Anemic group (26)
ALA (mg/day)	5.9 ± 1.2	3.1 ± 1.2**
PBG (mg/day)	1.5 ± 0.7	1.4 ± 0.6*
Uroporphyrins (mg/day)	22.2 ± 9.3	23.0 ± 10.0*
Coproporphyrins (mg/day)	100.7 ± 26.8	114.7 ± 38.9*

All values are mean ± S.D.
* Statistically insignificant ($p>0.10$)
** Statistically significant ($p<0.001$).

The increased urinary excretion of ALA was also found by Kaneko (1970) and Chalevelakis et al (1977) but not by Prato et al (1968) and Heilmeyer (1964). Similarly our finding of non-significant changes in porphyrin excretion is in agreement to Chalevelakis et al (1977) but in disagreement with Prato et al (1968). The reported variations in the excretion of porphyrins and porphyrin precursors may be due to differences in the techniques employed, severity of iron deficiency and anemia and possibility of incomplete collection of urine.

The decreased ALA excretion in urine in iron deficiency was explained by demonstration of inhibitory effect of accumulated protoporphyrin on the conversion of ALA to PBG (Heilmeyer, 1964). Recently it has been shown that iron regulates the synthesis of the enzyme, ALA synthase; iron deficiency results into decreased synthesis of ALA synthase and hence ALA (Elliot and Elliott, 1997). The regulation of porphyrin synthesis at its earlier steps (ALA synthesis) may be advantageous in preventing accumulation of highly toxic porphyrins in the body.

References

1. Askevold R. Scand. J. Clin. Lab. Invest. 3: 318; 1951.
2. Chalevelakis, G., Lyberatos, C., Manopoulos, D., Pyrovolakis, J. and Gardikas, C. Acta Haematol. 57: 305, 1977.
3. Dacie, JV and Lewis, SM. Practical haematology, 8th ed., Edinburgh, Churchill Livingstone, p. 49, 1994.
4. Elliott, W. H. & Elliott, D.C. Biochemistry and molecular biology, Oxford, Oxford University Press, p. 375, 1997.
5. Heilmeyer, L. Hyposideremia. In: "Iron metabolism" (Ed.) F. Gross, Berlin, Springer-Verlag, p. 201, 1964.
6. Kaneko, K. Acta Haematol. Jap. 33: 857, 1970.
7. Prato, V., Mazza, U., Massaro, A.I., Bianco, G. and Battistini, V. Porphyrin synthesis and metabolism in iron deficiency anemia. In vitro studies. Blut, 17, 14, 1968.
8. Sharma, D. C., Mathur, R. and Singh, P.P. Indian J. Clin Biochem. 8: 80; 1993.
9. Tietz, N.W. Fundamentals of clinical chemistry, Philadelphia, Saunders, p. 926, 1976.
10. Varley, H. Practical clinical biochemistry, London Heinemann, p. 603, 1974.