

## EFFECT OF ORAL CONTRACEPTIVES ON URINARY PORPHYRINS

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### Summary

Urinary porphyrins were measured in thirty women on oral contraceptives who constituted the study group and in ten women using conventional methods of contraception who constituted the control group. The difference of the means of urinary copro and uroporphyrin in the two groups was found to be statistically insignificant. Further, the effect of duration of treatment on females using oral contraceptives was also studied. The difference of means was not significant between the cases using oral contraceptives for a period of less than six months and the cases using the same for more than six months.

In 1896 Saillet<sup>1</sup> for the first time observed the presence of porphyrins in normal urine. He called the pigment urospectrine. Over 95 per cent or possibly all the urinary coproporphyrin is excreted by the kidneys in the form of coproporphyrinogen which is oxidised immediately into coproporphyrin. Urine contains coproporphyrin in the range of  $166 \pm 95$  ug in males and  $134 \pm 42$  ug in females in 24 hours<sup>2</sup> but the figures can vary depending upon the body weight<sup>3</sup>, diet and ingestion of alcohol<sup>4</sup>. Normal urine contains small quantities of uroporphyrin also.

Oral contraceptives are now being widely used all over the world. The side effects of oral contraceptives

have an important bearing on our family planning programme. The object of the present paper was to investigate whether oral contraceptives used by healthy women of child bearing age had any effect on porphyrin metabolism. Watterberg<sup>5</sup> reported exacerbation of acute intermittent porphyria after administration of oestrogen as such or as it is present in oral contraceptives. The appearance of cutaneous porphyria in men with prostatic carcinoma and who were treated with oestrogen suggested that oestrogen contained in the contraceptive pill might affect adversely those individuals with pre-existing abnormalities of porphyrin metabolism (Walshe)<sup>6</sup>.

Copeman et al<sup>7</sup> reported the development of cutaneous hepatic porphyria which developed within a year after prostatectomy and subsequent oestrogen therapy. The urinary porphyrin excretion increased many fold after oestrogen administration and it did not decrease when oestrogen was stopped. Urinary excretion of porphyrin precursors and coproporphyrin in

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Received for publication on 20—9—1980

healthy females on oral contraceptive was reported by Koskelo et al<sup>8</sup> in 1966. Studies regarding porphyrins in healthy females have been undertaken by Wranne<sup>9</sup>. Previous research indicates that porphyrins are also influenced by age, weight, diet, alcohol intake and certain drugs, viz. barbiturates, arsenic, lead, hexachlorobenzene<sup>10</sup>, chloroquin<sup>11</sup>, griseofulvin<sup>12</sup> and oestrogen<sup>13</sup>.

To the best of our knowledge no complete study has been made in this country regarding the effects of oral contraceptives on levels of porphyrins in urine in non-porphyrin individuals.

Various methods have been evolved for the quantitative estimation of porphyrins. In the present paper the method of Rimington<sup>14</sup> has been used.

## Material and Methods

### Study Area

The study area consisted of Patiala city and the villages surrounding the Primary Health Centre, Bhadson with a population of approximately 0.2 million. Forty healthy women of child bearing age, attending the Family Planning Clinic of Rajendra Hospital, Patiala and Primary Health Centre, Bhadson were selected at random for quantitative estimation of urinary porphyrins. These forty women belonged to the age group 21-40 years. Out of these forty women, thirty were treated with oral contraceptives for at least

a period of three months and formed the study group. Thorough clinical examination and routine laboratory tests on blood, urine and stool and liver function tests had been done to exclude any who had abnormality. Cases with history of having consumed either hepatotoxic drugs or alcohol had also been excluded. The oral contraceptives used were primovlar (Norgestrol 0.5 mg and ethinyloestradiol 0.05 mg), lyndiol (Lynestrenol 1.0 mg and ethinyloestradiol 0.05 mg) and orlest (Norethisterone acetate 1 mg and ethinyloestradiol 0.05 mg). Control group consisted of the remaining ten women who had used other methods of contraception like condom, tubectomy and I.U.C.D.

## Method

Quantitative estimations of urinary porphyrins were done by the method of Rimington et al based on broadsheet No.70 (Revised broadsheet No.36) August, 1971. The urinary coproporphyrin and uroporphyrin were extracted in 5 per cent HCl.

## Results

The levels of urinary porphyrins for the study group and control group are analysed and tabulated. (Tables 1 & 2). The comparison of the means of the two groups which are different in size was done by applying t-test.

TABLE 1

Showing comparison of urinary coproporphyrin in 30 women on oral contraceptives (Study group) and 10 women on conventional methods of contraception (Control group) in ug/24 hours

S. No.	Group	Number of cases	Mean	Range	S.D.	S. E.
1.	Study group	30	62.637	14.187-233.523	49.758	9.084
2.	Control group	10	40.366	15.066-102.523	25.406	8.035

TABLE 2

Showing comparison of urinary uroporphyrin in 30 women on oral contraceptives (Study group) and 10 women on conventional methods of contraception (Control group) in ug/24 hours

S. No.	Group	Number of cases	Mean	Range	S. D.	S. E.
1.	Study group	30	4.846	0-20.958	7.563	1.381
2.	Control group	10	4.413	0-19.968	5.779	1.827

It was observed that the mean urinary uroporphyrin was higher in the study group than in the control group. However, the difference was not statistically significant. Similar results were also noted in regard to urinary coproporphyrin.

It was also thought desirable to study the effect of duration of therapy. For this the study group was further divided into two categories viz., those who had taken oral contraceptives for more than 3 months but less than six months and those who had oral contraceptives for more than six months. The means of urinary coproporphyrin and uroporphyrin were 57.098 and 5.911 respectively for the former group and 68.843 and 3.785 respectively for the latter. However, the difference between these means is statistically insignificant though slightly higher values of urinary coproporphyrin is obtained for those who had taken oral contraceptives for a longer period.

Taking the normal range of urinary coproporphyrin in ug/24 hours as 0-150, it is observed that one woman (3.3 per cent) taking oral contraceptive had a raised urinary coproporphyrin as compared to none in control group. There was one woman in the study (3.3 per cent) who had raised urinary uroporphyrin levels (more than 30 ug/24 hours) as compared to none in control group.

### Discussion

Urinary porphyrins in fifty normal females has been studied by Garg<sup>15</sup>, <sup>16,17</sup> who found the values of mean and S. D. for urinary coproporphyrin as 36.630 and 16.930 respectively, and for urinary uroporphyrin as 4.210 and 4.510 respectively. These results compared favourably with the present results for the control group.

The present study on urinary coproporphyrin excretion in women on oral contraceptives has been compared with similar study conducted by Burton et al<sup>18</sup>. Our results are in agreement with those of Burton.

Finally we conclude from the present study that duration of therapy with oral contraceptives have no bearing on the porphyrin metabolism even though there is likelihood of raised urinary porphyrin levels if the oral contraceptives are administered. However, the difference in means of urinary porphyrins in the study group and control group are statistically insignificant.

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Indian Association of  
Dermatologists, Venereologists and Leprologists  
will be held in  
Hyderabad during January 1982