Journal of Steroid Biochemistry, 1973, Vol. 4, pp. 439–440. Pergamon Press. Printed in Great Britain

SHORT COMMUNICATION

EFFECT OF AMPICILLIN TREATMENT ON THE URINARY EXCRETION OF ESTRIOL CONJUGATES IN PREGNANCY

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(*Received* 5 *March* 1973)

SUMMARY

The effect of ampicillin treatment on the urinary estriol conjugate pattern was studied in six normal pregnancies. It was shown that the decrease in the urinary excretion of estriol-3-glucuronide accounted for most of the fall in total urinary estriol which occurred. This indicates that the drug effect is brought about by the interference of ampicillin with the enterohepatic circulation of estriol.

ADMINISTRATION of ampicillin [1], phenoxymethylpenicillin [2] or neomycin [3] decreases the urinary excretion of estriol in normal human pregnancy. We have explored this matter further by employing a gas–liquid chromatographic method [4] which enables the four known urinary estriol conjugates to be measured separately. Twenty-four-hour urines from six mothers (33–37 weeks pregnant) were collected on seven successive days (days 1–7). Each woman was given 500 mg ampicillin (Doktacillin ®, Astra, Sweden) four times daily on days 3, 4 and 5. One per cent of the total volume was removed from each 24 h urine sample and pooled with the other five 1% samples for the corresponding day. In this way, a urine sample representative of the six mothers' 24 h excretion was prepared for each of the seven days. The concentrations of estriol-16α-glucuronide† (E_3-16Gl), estriol-3-glucuronide (E_3-3Gl), estriol-3-sulfate, 16α-glucuronide (E_3-3S,16Gl) and estriol-3-sulfate (E_3-3S) were determined in these samples. The results (Table 1) indicate a fall in the urinary excretion of estriol on days 4, 5 and 6, with partial return to the normal level on day 7. As compared to days 1 and 2, the decrease in total urinary estriol averages 4·5 mg/24 h. An average fall of 4·2 mg/24 h can be seen in the corresponding values for E_3-3Gl. This seems to indicate that the diminished excretion of E_3-3Gl accounts for most of the decrease in total urinary estriol.

E_3-3Gl is known to be formed exclusively in the intestinal mucosal cells [5, 6] and its formation is dependent on an intact enterohepatic circulation of estrogens [7]. Hence, ampicillin probably interferes with the enterohepatic circulation of estrogens causing increased fecal loss of estriol and decreased production of E_3-3Gl. Future studies will show if the proposed effect is brought about by reduc-

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†Trivial names and abbreviations used: Estriol-16α-glucuronide (E_3-16Gl) = 3,17β-dihydroxyestra-1,3,5(10)-trien-16α-yl-β-D-glucopyranosiduronate; estriol-3-glucuronide (E_3-3Gl) = 16α,17β-dihydroxy-estra-1,3,5(10)-trien-3-yl-β-D-glucopyranosiduronate; estriol-3-sulfate, 16α-glucuronide (E_3-3S,16Gl) = 17β-hydroxyestra-1,3,5(10)-trien-3-yl-sulfate-16α-yl-β-D-glucopyranosiduronate; estriol-3-sulfate (E_3-3S) = 16α,17β-dihydroxyestra-1,3,5(10)-trien-3-yl-sulfate.

Table 1. Urinary excretion of estriol conjugates in 6 normal pregnant women treated with ampicillin*

Day	1	2	3†	4†	5†	6	7
E_3-16Gl	7·55	7·49	10·5	6·76	9·24	7·66	8·89
E_3-3Gl	4·99	5·59	5·04	1·32	0·94	1·03	2·38
E_3-3S,16Gl	1·31	1·16	1·05	0·96	0·68	0·54	0·96
E_3-3S	0·33	0·32	0·24	0·25	0·20	0·08	0·19
Total estriol	14·2	14·6	16·8	9·29	11·1	9·31	12·4

*Values are estriol mg/24 h.
†Ampicillin treatment.

tion of the intestinal microflora. Since steroid conjugates are poorly reabsorbed, diminished bacterial hydrolysis of steroid conjugates could conceivably result in insufficient supply of estriol to the intestinal glucuronidating enzyme system in the mucosal cells. In any case, it is of interest that the cause of the decreased urinary output of estriol due to ampicillin treatment is an altered metabolism in the maternal compartment rather than impaired production in the fetoplacental unit.

ACKNOWLEDGEMENTS

The authors wish to thank Mr. Henrik Brunholm for skilful technical assistance. This investigation was supported by the National Research Council for Medical Sciences in Finland (M. J. T.) and Ford Foundation (H. A.).

REFERENCES

1. Willman K. and Pulkkinen M. O.: *Amer. J. Obstet. Gynec.* **109** (1971) 893.
2. Pulkkinen M. O. and Willman K.: *Brit. med. Jl* **4** (1971) 48.
3. Pulkkinen M. O. and Willman K.: *Amer. J. Obstet. Gynec.* (1973) (in press).
4. Tikkanen M. J. and Adlercreutz H.: *J. steroid Biochem.* **3** (1972) 807.
5. Dahm K. and Breuer H.: *Z. klin. Chem.* **4** (1966) 153.
6. Stoa K. F. and Levitz M.: *Acta Endocr. (Kbh.)* **57** (1968) 657.
7. Tikkanen M. J. and Adlercreutz H.: *Amer. J. Med.* **54** (1973) 600.