Journal of Steroid Biochemistry, 1977, Vol. 8, pp. 95–97. Pergamon Press. Printed in Great Britain

URINARY EXCRETION OF STEROID HORMONE METABOLITES IN MEN WITH DUODENAL ULCER

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(*Received* 29 *June* 1976)

SUMMARY

Duodenal ulcer is more common and usually more severe in men than in women. One hypothesis put forward to explain this sex difference is that men undergo more stress than women. Therefore, the urinary excretion of androsterone (A), aetiocholanolone (E) and 17-hydroxycorticoids has been determined in 25 normal men, and 22 hospital controls and 35 patients with duodenal ulcer (D.U.) before and after surgery. The excretion of steroids was the same in the normal controls and the preoperative controls and D.U. patients. After surgery the controls showed a significant decrease in E excretion, and the D.U. patients had a decrease in excretion of E large enough to raise the A/E ratio. The results are not consistent with the view that endogenous androgenic or adrenocortical steroids maintain D.U.

INTRODUCTION

Duodenal ulcer is much more common in men than in women. There is considerable epidemiological evidence in man, supported by experimental work with man and animals, that steroid hormones, particularly sex hormones, are at least partly responsible for the sex difference in the occurrence and severity of peptic ulceration in men and women. Two main hypotheses have been put forward to explain this sex difference: (a) men lead more stressful lives than women and are therefore more likely to develop peptic ulceration because of increased secretion of corticosteroids and androgens from the adrenal cortex, and (b) female sex hormones, particularly oestrogens, have a protective action against peptic ulceration. Most of the experimental work carried out over the last three decades has been based on the second hypothesis, and oestrogens and stilboestrol have been used to treat patients with peptic ulcer. However, the clinical trials and experimental work have yielded equivocal results. The primary events leading to peptic ulceration are unknown, although it is virtually taken for granted that ulceration is caused by the acid secretion of the stomach (see the Review by Crean, [1]). Little attention has been paid to the possible role of progestins in peptic ulceration [2], and it is surprising that there has been only one small-scale investigation of the effect of a combined oestrogen-progestin preparation on gastric function and serum gastrin levels [3] and that work was done on cats. No investigations of the production, metabolism and urinary excretion of metabolites of endogenous steroid hormones appear to have been carried out in human subjects with peptic ulcer.

This report presents data on the urinary excretion of metabolites of endogenous androgenic and adrenocortical steroid hormone metabolites in a group of men before and after surgical treatment for duodenal ulcer.

MATERIALS AND METHODS

Subjects investigated. The age-matched groups of subjects were (mean ± S.D. years); 25 normal men (50 ± 12.4) with no history of endocrine or gastrointestinal disorders carrying out their normal activities; 22 patients (50.3 ± 16.6), designated as hospital controls, operated on for hernia or varicose veins; 35 patients (42 ± 15.7) surgically treated for duodenal ulceration which was established by symptomology and radiography and confirmed by postoperative examination of the ulcer regions, none of which showed any signs of malignancy. Since the patients were admitted to the hospital one or two days before surgery only one or two urine samples could be obtained preoperatively. The patients were admitted to one surgical unit of the Royal Victoria Infirmary, Newcastle upon Tyne, and received common preoperative treatment. Because of the large catchment area of this hospital patients were usually transferred to peripheral hospitals or convalescent homes on the fifth day after surgery. Therefore urine samples were collected on the third to fifth day after surgery. All patients made a good recovery and had no renal complications. For the sake of convenience, and to avoid the problem of obtaining complete 24 h urine samples, early morning urine samples (EMUS) were collected from patients and normal subjects.

Steroid analyses. Urinary androsterone (A) and aetiocholanolone (E) were determined by a g.l.c. method [4] and 17-hydroxycorticosteroids (17-OCHS) by the method of Metcalf [5]. Creatinine was measured in an Autoanalyser. Results are expressed as mg or μg steroid/g creatinine.

Table 1. Urinary excretion of androsterone (A), aetiocholanolone (E) and total 17-hydroxycorticosteroids (17-OHCS) in mg/g creatinine, and the A/E ratio in normal subjects, hospital controls and patients with D.U. before (pre-op) and after (post-op) surgery. Means ± S.E.M.; n = number in each group.

	Normals	Controls		D.U. patients	
		Pre-op	Post-op	Pre-op	Post-op
n	25	22		35	
A	2.74 (0.19)	2.60 (0.30)	2.26 (0.27)	2.65 (0.22)	2.20* (0.13)
E	1.88 (0.14)	1.87 (0.27)	1.43 (0.12)	2.18 (0.17)	1.49** (0.14)
A/E	1.53 (0.37)	1.40 (0.14)	1.58 (0.15)	1.33 (0.12)	1.60** (0.12)
17-OHCS	5.42 (0.28)	6.04 (0.34)	5.74 (0.46)	5.29 (0.62)	4.92 (0.50)

The asterisks in the last column indicate that the numbers marked are significantly different from the numbers immediately to the left: * $P < 0.03$, ** $P < 0.001$.

Statistical analyses. Earlier findings that urinary excretion of steroids by groups of subjects has a log normal distribution have been confirmed by others [6], and a log normal distribution was also observed in the present study. Therefore statistical analyses were done on the logarithms to the base 10 of the steroid concentrations expressed as μg steroid/g creatinine. Student's t-test was used to assess the probability of 2-tail differences between groups of subjects, and paired t-tests were done on the data for the pre- and post-operative states of the hospital controls and the patients with duodenal ulcer to evaluate the effect of surgery within these two groups of subjects. The standard of significance was set as $P < 0.05$.

RESULTS

Table 1 shows the values for A, E and 17-OHCS (mg/g creatine) and the A/E ratios for the normal subjects (normals) and for the pre- and postoperative hospital controls (controls) and duodenal ulcer (D.U.) patients. There are no significant differences between the normals and the preoperative values for the controls and the D.U. patients.

After surgery steroid excretion patterns changed. In the control group there were no significant changes in steroid excretion, but the changes in the D.U. group were significant with respect to A ($P < 0.03$), E ($P < 0.01$) and to A/E ($P < 0.001$). Other changes were not significant. Paired t-tests were carried out on the pre- and post-operative values for the two groups who underwent surgery. The P values are shown in Table 2 (this Table contains fewer subjects than Table 1 because urine was not collected before and after surgery in every case). In the control group surgery caused a significant fall in E excretion, but this was not large enough to produce a significant change in the A/E ratio. In the D.U. group the fall in E excretion was large enough to produce a significant increase in the A/E ratio.

Table 2. The effect of surgery on the patients within each group on the excretion of A, E and 17-OHCS and on the A/E ratio as assessed by paired t-test on logs of data: P values.

	Controls	D.U. patients
n	18	26
A	NS*	NS*
E	0.03	0.001
A/E	NS*	0.006
17-OHCS	NS*	NS*

NS* = not significant at $P < 0.05$.

No significant correlation between age and steroid excretion was found in any of the three groups, and the ages of the subjects in the three groups were not significantly different.

DISCUSSION

The steroids determined in this study are derived entirely (17-OHCS) or partially (A and E) from the adrenal cortex. It is generally accepted that this gland responds to stress by the action of ACTH mediated through the hypothalamo-adenohypophyseal axis, the result being an increased secretion of adrenocortical steroids. Many investigators [3, 6, 7] have suggested that hospitalisation and surgery are stressful situations which should cause an increase in the production of adrenocortical hormones. In the present investigation the pattern of urinary steroids is remarkably similar in the normal group and the control and D.U. groups before surgery (Table 1). Therefore any stress experienced by the patients being hospitalised is not reflected by an increase in urinary 17-OHCS nor in A and E, even though the urine samples were collected on the morning after the patients' entry into hospital. Metcalf [8] has carefully studied some factors which might affect adrenocortical or gonadal function in women. The factor most relevant to the present study is her finding that the 24 h urinary

excretion of A + E decreased by about 50% when obese women are fasted for about 3 days. She measured the steroids over a 24 h period, whereas the patients' steroid excretion patterns were based on EMUS in the present study. These patients were fasted, and usually sedated, overnight prior to surgery, and fasting and sedation may have affected the adrenal function of the patients. Nevertheless, it is doubtful if this is the explanation for the close similarity of the groups of patients shown in Table 1 prior to surgery. The patients may have become stabilized with respect to adrenal and gonadal function during the course of their chronic disease. The results obtained suggest that patients with D.U. do not have abnormally high adrenal function which could contribute to the persistence of their ulcers. However, the possibility that the initiation of the ulcer may have been caused by abnormal steroid hormone production cannot be ruled out.

It is also often stated [3, 6, 7] that the stress of surgery is accompanied by increased adrenocortical hormone secretion. In the present work there was no significant change in urinary 17-OHCS within the third to fifth days after surgery, and the excretion of A and E decreased. In other work of this type [3, 6, 7] the steroid excretion patterns were not analysed by paired *t*-tests before and after surgery. When this was done with the controls and D.U. patients (Table 2) interesting differences were found. After surgery the controls excreted significantly ($P < 0.03$) less E than before surgery, but this decrease in E was not sufficient to affect the A/E ratio. In the D.U. patient group there was a significant decrease in E excretion, sufficiently large to produce a significant increase in the A/E ratio. This suggests that the precursors of A and E are not the same, and formation or metabolism of the E precursor is altered in D.U. patients after surgery. The reduction in E excretion may be related to the observation that A + E excretion is decreased by fasting [8]. The diets of the patients in this study were not monitored, but the D.U. patients were on bland and often liquid diets after surgery. The control patients received the normal hospital diet within a day or two after surgery.

The results obtained are consistent with the view that patients with D.U. do not have an abnormal secretion of adrenocortical hormones when compared with normal subjects and hospital controls of the same age-range. The results indicate that, as judged by excretion of 17-OHCS and A and E, the adrenal cortex of D.U. patients does not respond more readily to stress than normal subjects or patients in hospital for minor surgery. Therefore, there is little evidence to support hypothesis (a) described in the Introduction.

Acknowledgements—I am grateful to the North of England Cancer Research Campaign for financing this project. Mrs. Sandra Gillott gave valuable technical assistance. Dr. J. R. Greenwell and Professor D. J. Newell provided much assistance with the statistics, which is gratefully acknowledged.

REFERENCES

1. Crean G. P.: *Vits. Horms.* **21** (1963) 215–280.
2. Albinus M., Blair E. L., Hirst F., Grund E. R., Reed J. D., Sanders D. J. and Taylor W.: *J. Endocr.* **69** (1976) 449–450.
3. Parbhoo S. P. and Johnston I. D. A.: *Gut* **7** (1966) 612–618.
4. Rao L. G. S.: *Lancet* **1** (1970a) 441–443.
5. Metcalf M. G.: *J. Endocr.* **26** (1968) 415–423.
6. Miller W. R., Hamilton T., Champion H. R., Wallace I. W. J., Forrest A. P. M., Prescott R. J., Cameron E. H. D. and Griffiths K.: *Br. J. Cancer* **32** (1975) 619–627.
7. Rao L. G. S.: *Lancet* **1** (1970b) 390–391.
8. Metcalf M. G.: *J. Endocr.* **63** (1974) 263–274.