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# PLASMA TESTOSTERONE, LH AND FSH DURING THE FIRST 24 HOURS AFTER SURGICAL OPERATIONS

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## SUMMARY

A statistically significant increase of plasma LH was observed at the end of the surgical operations. Premedication did not influence plasma testosterone, LH or FSH concentrations in samples taken 1 h later. The concentrations of testosterone were essentially unchanged until 4·5 h after the end of the operations. Between 4·5 and 10·5 h postoperatively there was a significant decrease of both testosterone and LH concentrations in plasma. After that time LH was restored to normal concentrations while the decrease in testosterone persisted throughout the observation period of 24 h. There was no change in plasma FSH concentrations. The hormone concentrations were compared to the patients' own preoperative values as well as to diurnal levels of two healthy male hospital employees working and sleeping in the same ward as the patients. No great diurnal variation was observed in any of the hormones studied. It was concluded that the sequence of events was general anaesthesia, LH increase, surgical trauma and concomitant LH and testosterone decrease. In some cases general anaesthesia was followed by a decrease in plasma testosterone. In most cases an increase occurred 1 h after surgery as compared with the post-anaesthetic levels. Decreased testosterone concentrations were seen in a patient with perforated gastric ulcer; partial gastrectomy caused a further decrease.

## INTRODUCTION

In previous work [1] we were unable to relate the post-operative decrease of plasma testosterone concentrations in male patients to any decrease of plasma LH or FSH, when the first samples were taken one day after the operation. We therefore decided to look for the events taking place during the first 24 h after surgery. Charters *et al.* [2] found an early postoperative decrease of both LH and FSH concentrations. More recently Aono *et al.* [3] reported a significant increase of LH concentrations 0·5 h after induction of anaesthesia and during the operation. Testosterone concentrations decreased 0·5 and 2 h after the start of the operation. However, the hormone levels of the patients were not studied during the following 24 h period. A study of the immediate postoperative period may contribute to an understanding of why testosterone concentrations decrease after surgery.

## MATERIALS AND METHODS

*Subjects.* Ten patients were selected for this study. Premedication was morphine + scopolamine or, in Patients IV and IX, pethidine chloride + atropine. Anaesthesia was induced by barbiturate iv (Narkotal[R]) supplemented with a muscle relaxant (Celocurin[R]), and sustained with halothane + $N_2O + O_2$.

Cholangiography was carried out during the operation in Patient IX. Patient X was admitted to the hospital because of perforation of a gastric ulcer. Two healthy hospital employees were used as controls with regard to possible diurnal variations of the hormones. They worked in the same ward as the patients and had their sleeping quarters in an adjoining room. Preoperative blood samples were taken between 8 and 9 a.m., then 1 h after premedication, 30 min after the anaesthesia was started, followed by a sample immediately at the end of the operation approx. 1 h later. A further sample was taken 1·5 h after the end of the operation. Samples were taken at 3 h intervals until 9 a.m. the next morning. The blood sampling did not interrupt the sleep to any great extent. Details of the operations are given in Table 1.

*Hormone determinations.* Testosterone concentrations in plasma were determined using a competitive protein binding assay after one paper chromatography step as previously reported [1]. Interassay variation coefficients for duplicate determinations were 32·7% below 200 ng/100 ml, 14·1% between 200 and 500 ng/100 ml and 13·1% between 500 and 1200 ng/100 ml. In our laboratory the normal values in males for testosterone were 775 ± 332 (S.D.) ng/100 ml. FSH and LH levels were determined by a radioimmunosorbent technique [4, 5]. The normal range for LH in men was 0·46–2·2 ng/ml in the age group 37–56 years and 0·39–3·1 ng/ml in the age group 17–36. The normal range for FSH in men was 0·47–3·5 ng/ml and 0·35–3·3 ng/ml, respectively [5].

## RESULTS

*Normal controls.* A small decrease in plasma testosterone concentrations was noticed in the controls but this was insignificant as compared to the decreases in the patient series (Table 2). No consistent changes were observed in plasma LH (Table 3) or FSH levels (Table 4).

*Premedication.* There was no effect of premedication on testosterone, LH or FSH concentrations in plasma one hour after the drugs were injected (Table 2–4).

*General anaesthesia.* During the observation period of 30 min no significant changes were noted in the cross-sectional study in the plasma levels of any of the hormones studied. However in individual cases (II, IV, VI and VIII) a small decrease was observed in the plasma testosterone concentration (Table 2).

*End of surgical operation.* A significant increase in plasma LH levels was noted at the end of these operations of approx. one hour's duration (Table 3). In individual cases (I, III, IV, VI and VII) the plasma testosterone concentrations showed a small increase as compared with the post-anaesthetic levels (Table 2). Normal LH levels were restored 1·5 h later, except in case VII, changing to subnormal levels between 4·5–10·5 h after the operations ended. At the same time plasma testosterone concentrations decreased significantly and remained low throughout the observation period (Table 2). FSH levels did not change (Table 4).

*Ulcer perforation.* Low testosterone concentrations (161 ng/100 ml) were observed in Subject X (Table 2) 1·75 h after the perforation of a gastric ulcer. A further decrease occurred 13·5–19·5 h after the end of the operation (67, 32 and 71 ng/100 ml). At the same time LH was in the high normal range. FSH showed no consistent changes.

*Cholangiography.* The expected postoperative decrease in plasma testosterone failed to occur in Patient IX who underwent cholangiography during the operation (cholecystectomy). A postoperative decrease was observed in Patient IV who had a cholecystectomy without cholangiography.

Table 1. Data concerning the patients undergoing surgery and normal subjects

| | | Age | Diagnosis | Operation | Remarks |
|---|---|---|---|---|---|
| Patient | I | 49 | Hernia disci intervertebralis | Laminectomy | |
| | II | 40 | Ileitis regionalis | Extirpation + Colostomy | Unilateral orchidectomy |
| | III | 51 | Duodenal ulcer | Partial ventricular resection | |
| | IV | 41 | Cholelithiasis | Cholecystectomy | |
| | V | 40 | Hernia disci intervertebralis | Laminectomy | |
| | VI | 42 | Thrombosis of the right popliteal artery | Bypass | |
| | VII | 39 | Duodenal ulcer | Partial ventricular resection | |
| | VIII | 45 | Duodenal ulcer | Partial ventricular resection | Cardiac arrest for 1–2 min. during operation |
| | IX | 54 | Cholelithiasis | Cholecystectomy | Cholangiography during operation |
| | X | 53 | Perforated gastric ulcer | Partial ventricular resection | |
| Normal subjects | C–I | 28 | Healthy | | |
| | C–II | 20 | Healthy | | |

Table 2. Plasma testosterone concentrations of male patients after premedication, anaesthesia and a surgical operation of about one hour's duration. The blood samples under "Control" were taken between 8–9 a.m. except for Patient X in whom the sample was obtained at 5 p.m. He was admitted for acute perforation of a gastric ulcer. Patient IX had a cholangiography during cholecystectomy. Patients IX and X were excluded from the statistical comparison

| | | | | | | Hours after operation or hours after noon | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Control | PR* | AN** | OP*** | 1·5 | 4·5 | 7·5 | 10·5 | 13·5 | 16·5 | 19·5 | 22·5 |
| Patient | I | 392 | 277 | 316 | 426 | 279 | 307 | 310 | 206 | 286 | 206 | 279 | 411 |
| | II | 614 | 543 | 446 | 377 | | 188 | 140 | 91 | 59 | 273 | 327 | 158 |
| | III | 846 | 394 | 835 | 1008 | 605 | 209 | 273 | 266 | 397 | 295 | 360 | 439 |
| | IV | 538 | 328 | 375 | 470 | 299 | 202 | 94 | 115 | 97 | 131 | 50 | 349 |
| | V | 340 | 375 | 512 | 513 | 737 | 223 | 265 | 158 | 63 | 257 | 69 | 190 |
| | VI | 1072 | 1098 | 725 | 1001 | | | 715 | 350 | 72 | 641 | 424 | 279 |
| | VII | 869 | 888 | 733 | 904 | 1109 | 638 | 497 | 332 | 403 | 248 | 191 | 158 |
| | VIII | 1000 | 889 | 770 | 787 | 474 | 379 | 162 | 85 | 127 | 401 | 275 | 310 |
| Mean | | 709 | 599 | 589 | 686 | 584 | 307 | 307 | 200 | 188 | 307 | 247 | 287 |
| S.D | | 277 | 314 | 199 | 267 | 312 | 162 | 207 | 106 | 149 | 155 | 134 | 111 |
| S.E.M. | | 98 | 111 | 71 | 95 | 127 | 61 | 73 | 37 | 53 | 55 | 47 | 39 |
| Excluded | IX | 653 | 625 | 624 | 576 | 523 | 672 | 247 | 447 | 610 | 440 | 390 | 624 |
| patients | X | 161 | 182 | 131 | 124 | 261 | 230 | 168 | 149 | 67 | 32 | 71 | 161 |
| Normal | C–1 | 614 | | | | 842 | 615 | 748 | 482 | 699 | 821 | 678 | |
| subjects | C–2 | 934 | | | | 772 | 596 | 530 | 830 | 702 | 809 | 712 | 604 |
| P values | | | | | | | | | | | | | |
| I–VIII *v* Control | | — | NS | NS | NS | NS | < 0·01 | < 0·01 | < 0·001 | < 0·001 | < 0·01 | < 0·001 | < 0·01 |
| I–VIII *v* Normal subjects | | NS | | | | NS | < 0·05 | NS | NS | < 0·01 | < 0·01 | < 0·05 | |

*1 h after premedication

**0·5 h after induction of anaesthesia.

***At the end of the operation (duration approx. 1 h).

Table 3. Plasma LH concentrations of male subjects as described in Table 1

| | | | | | | Hours after operation or hours after noon | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Control | PR | AN | OP | 1·5 | 4·5 | 7·5 | 10·5 | 13·5 | 16·5 | 19·5 | 22·5 |
| Subject | I | 0·93 | 1·4 | 1·2 | 1·5 | 0·72 | 0·58 | 0·74 | 0·92 | 0·89 | 0·87 | 0·95 | 0·94 |
| | II | 0·75 | 0·87 | 1·8 | 1·5 | 1·2 | 0·89 | 0·70 | 0·44 | 1·9 | 1·8 | 1·2 | |
| | III | 1·5 | 0·30 | 1·2 | 1·9 | 0·99 | 0·70 | 0·63 | 0·76 | 0·97 | 0·88 | 1·5 | 1·2 |
| | IV | 1·4 | 0·93 | 1·6 | 1·8 | 1·3 | 0·82 | 0·83 | 0·73 | 0·73 | 0·66 | 0·92 | 0·76 |
| | V | 0·90 | 1·1 | 0·81 | 1·4 | 0·73 | 0·32 | 0·46 | 0·57 | 0·42 | 0·87 | 0·40 | 0·39 |
| | VI | 0·85 | 0·91 | 1·23 | 1·4 | | 0·62 | 0·49 | 1·5 | 0·90 | 0·69 | 1·2 | |
| | VII | 1·1 | 0·91 | 1·1 | 2·3 | 2·0 | 1·7 | 1·5 | 1·1 | 0·82 | 0·80 | 0·86 | 0·86 |
| | VIII | 0·72 | 0·73 | 1·2 | | 0·86 | 0·68 | 0·49 | 0·49 | 0·98 | 0·95 | 0·57 | 0·73 |
| Mean | | 1·02 | 0·90 | 1·27 | 1·69 | 1·11 | 0·79 | 0·73 | 0·81 | 0·95 | 0·94 | 0·95 | 0·81 |
| S.D. | | 0·29 | 0·31 | 0·30 | 0·33 | 0·45 | 0·41 | 0·34 | 0·35 | 0·42 | 0·36 | 0·36 | 0·27 |
| S.E.M. | | 0·10 | 0·11 | 0·11 | 0·13 | 0·17 | 0·14 | 0·12 | 0·13 | 0·15 | 0·13 | 0·13 | 0·11 |
| Excluded | IX | 1·1 | 0·89 | 1·3 | 1·6 | 0·97 | 1·1 | 0·64 | 0·68 | 1·2 | 0·91 | 0·81 | 0·69 |
| | X | 1·8 | 1·5 | 1·4 | 1·1 | 1·0 | 0·99 | 1·5 | 2·2 | 1·9 | 2·2 | 2·1 | 2·1 |
| Untreated | C–1 | 1·5 | | | | 1·2 | 1·6 | 1·1 | 1·5 | 1·1 | 1·1 | 0·97 | |
| | C–2 | 1·4 | | | | 1·2 | 1·4 | 1·4 | 1·9 | 1·2 | 1·3 | 1·0 | |
| P values | | | | | | | | | | | | | |
| I–VIII *v* Control | | — | NS | < 0·2 | < 0·01 | NS | NS | < 0·1 | NS | NS | NS | NS | NS |
| I–VIII *v* Normal subjects C–1, C–2 | | < 0·1 | | | | NS | < 0·1 | NS | < 0·1 | NS | NS | NS | |

Table 4. Plasma FSH concentrations of male subjects as described in Table 1

| | | Control | PR | AN | OP | 1·5 | 4·5 | 7·5 | 10·5 | 13·5 | 16·5 | 19·5 | 22·5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Hours after operation or hours after noon | | | | | | | |
| Subject | I | 0·86 | 0·83 | 0·77 | 1·0 | 0·56 | 0·62 | 0·84 | 0·63 | 0·73 | 0·65 | 0·66 | 0·68 |
| | II | 0·95 | 0·58 | 0·80 | 0·65 | 0·65 | 0·65 | 0·91 | 0·58 | 0·55 | 0·85 | 0·58 | |
| | III | 1·8 | 0·51 | 1·5 | 1·8 | 1·5 | 0·98 | 1·3 | 1·2 | 1·3 | 1·3 | 1·3 | 1·2 |
| | IV | 1·1 | 0·95 | 0·86 | 0·88 | 0·78 | 0·79 | 0·70 | 0·64 | | 0·58 | 0·63 | 0·79 |
| | V | 0·58 | 0·38 | 0·24 | 0·56 | 0·17 | 0·26 | 0·47 | 0·48 | 0·17 | 0·39 | 0·16 | 0·40 |
| | VI | 1·3 | 1·4 | 0·93 | 1·1 | | 0·94 | 0·80 | 1·8 | 0·96 | 1·4 | 1·4 | |
| | VII | 1·2 | 1·8 | 1·9 | 2·2 | 2·2 | 1·7 | 1·6 | 1·8 | 2·3 | 1·9 | 1·3 | 1·6 |
| | VIII | 1·8 | 2·2 | 2·2 | | 2·0 | 1·8 | 2·2 | 1·5 | 1·7 | 1·7 | 2·0 | 1·9 |
| Mean | | 1·20 | 1·08 | 1·15 | 1·17 | 1·12 | 0·97 | 1·10 | 1·08 | 1·10 | 1·10 | 1·00 | 1·10 |
| S.D. | | 0·43 | 0·66 | 0·66 | 0·61 | 0·78 | 0·53 | 0·57 | 0·56 | 0·73 | 0·56 | 0·59 | 0·58 |
| S.E.M. | | 0·15 | 0·23 | 0·23 | 0·23 | 0·29 | 0·19 | 0·20 | 0·20 | 0·27 | 0·20 | 0·21 | 0·24 |
| Excluded | IX | 0·42 | 0·32 | 0·30 | 0·40 | 0·76 | 0·42 | | 0·24 | 0·36 | 0·28 | 0·38 | 0·28 |
| | X | 2·2 | 1·8 | 1·6 | 0·75 | 1·1 | 0·65 | 1·0 | 1·7 | 1·4 | 2·0 | 1·7 | 1·6 |
| Untreated | C-1 | 1·2 | | | | 1·2 | 1·2 | 0·86 | 1·5 | 1·1 | 1·4 | 1·2 | |
| | C-2 | 2·9 | | | | 3·2 | 2·5 | 1·7 | 1·8 | 2·5 | 2·0 | 2·5 | |
| P values | | | | | | | | | | | | | |
| I–VIII *v* Control | | — | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| I–VIII *v* Normal subjects C–1, C–2 | | NS | | | | NS | NS | NS | NS | NS | NS | NS | |

## DISCUSSION

We have recently discussed the decrease in plasma testosterone found 1–2 days after surgery without significant change in LH levels [1]. The aim of the present investigation was to observe how soon this decrease occurred.

Decreased plasma concentrations of testosterone have been found 4·5 h after the end of surgical operations of approx. 1 h duration (Table 2). Both when compared to the patients own preoperative levels and to levels in two healthy volunteers studied simultaneously this decrease was highly significant and persisted throughout the 24 h observation period. This decrease occurred concomitantly with a temporary decrease in plasma LH levels. However it continued even though LH returned to normal levels. Aono *et al.* [3] observed a significant increase of plasma LH levels 30 min after induction of anaesthesia, this increase being more pronounced half an hour later during the operation. We observed a similar increase at the end of the operations. Some factor connected with the anaesthesia may therefore have stimulated pituitary LH secretion without increasing plasma testosterone levels. In fact plasma testosterone decreased somewhat in the investigation of Aono *et al.* [3] 0·5 and 2 h after the incision. However in some cases we noticed a small increase of plasma testosterone concentrations at the end of surgery as compared with the post-anaesthetic levels. The difference between the results of Aono *et al.* and ours may be ascribed to the degree and duration of surgical trauma, being more pronounced in their work.

Much evidence points to surgical trauma as an important factor in causing the postoperative decrease of plasma testosterone. This has been reviewed earlier by us [1]. One factor would be general trauma. For example a decrease in plasma testosterone has been found in two patients with perforated ulcer before surgery (present investigation, Patient X; [1]). However, the surgical procedures described here caused a definite long-lasting further decrease in Subject X, Table 2, as well as in the other patients. In individual cases we found a small decrease in plasma testosterone levels 0·5 h after the start of general anaesthesia while the levels returned to preanaesthetic values at the end of surgery. We therefore conclude that the possibility remains that some factor in connection with the complicated narcosis (barbiturate + muscle relaxant + halothane + nitrous oxide + oxygen) may be operating to lower plasma testosterone for an extended period, as well as possibly LH for a shorter period and later on FSH, as we have previously reported.

We will later on report on the effect of surgery on plasma testosterone binding capacity in male patients, as well as on dog experiments where we have studied the influence of the individual components of premedication, general anaesthesia and surgical trauma on testosterone plasma concentrations, production rates and metabolic clearance rates. In the human the high plasma testosterone binding capacity may slow down the rate of decrease of plasma testosterone after surgery as compared with the dog in which the hepatic extraction of testosterone was shown to be 90–95%. In these experiments we will demonstrate to what extent the different factors studied operate on production or on metabolism of testosterone.

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