PLASMA VOLUME DURING SURGERY IN UNSUPPLEMENTED GLUCOCORTICOID-TREATED PATIENTS

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SUMMARY
Changes in plasma volume and plasma cortisol concentrations were investigated in seven unsupplemented and three supplemented glucocorticoid-treated patients and in eight control patients subjected to abdominal surgery. No differences in postoperative plasma volume deficit could be demonstrated between normal and glucocorticoid-treated patients, or between patients with a normal or an impaired adrenocortical response to surgery. These results may lend further support to observations indicating that arterial hypotension during operation in glucocorticoid-treated patients is not caused by adrenocortical insufficiency.

Experimental studies in the adrenalectomized dog have all demonstrated major decreases in plasma volume during stress-induced adrenocortical insufficiency (Swingle et al., 1938; Swingle et al., 1959; Marks et al., 1965), but there are no corresponding studies in humans. We have found previously a high incidence of arterial hypotension during operation in unsupplemented glucocorticoid-treated patients, which is not related to plasma cortisol concentrations (Kehlet and Binder, 1973b). However, it has been suggested (Cope, 1965) that during long-term glucocorticoid therapy the tissues become adapted to a higher glucocorticoid concentration, so that a decrease towards normal concentrations represents, relatively, a hypoadrenal state.

The present study was undertaken to investigate whether changes in plasma volume take place during surgery in glucocorticoid-treated patients where no exogenous glucocorticoid was given, and to correlate these findings with the clinical course and the adrenocortical function.

PATIENTS AND METHODS
Eight normal and ten glucocorticoid-treated patients undergoing elective major abdominal surgery (cholecystectomy, hysterectomy) were studied. Age, sex, weight and the dose of glucocorticoid are shown in table I.

In order to secure complete catabolism of exogenous glucocorticoid, glucocorticoid treatment was stopped 36 hours before operation. Supplementary glucocorticoids were administered to three of the glucocorticoid-treated patients (table I) as follows: 100 mg cortisol phosphate-ester* i.m. at the time of premedication and 100 mg cortisol phosphate-ester* i.v. at the time of skin incision. Operative blood loss was calculated by weighing the sponges and measuring suctioned blood. Neither plasma nor blood transfusions were given. After premedication with pethidine and atropine, anaesthesia was induced with thiopentone, endotracheal intubation being facilitated by suxamethonium, and anaesthesia was maintained with droperidol, fentanyl, nitrous oxide and oxygen. Arterial pressure and heart rate were recorded at 5-min intervals during each surgical procedure.

Plasma volume was determined 24 hours before, and 2 hours after skin incision using the T1824 Evans Blue technique as described by Leth and Binder (1970). Plasma for spectrophotometric T1824 analysis was sampled from a contralateral cubital vein 15, 30, 45 and 60 min after injection of the dye. The concentration of T1824 in plasma at zero time was determined by extrapolation of the calculated regression line of the disappearance of dye from plasma. The patients were fasting and confined to bed.

During the 2-hour period from skin incision to injection of T1824, the patients received isotonic saline intravenously in an amount of 20 ml/kg. The duration of surgery varied between 50 and 180 min and was similar in the normal and glucocorticoid-treated groups of patients. Plasma cortisol was

*Equivalent to 90 mg cortisol (hydrocortisone).
in figure 1. In the control group the average volume and plasma cortisol after operation is shown increased. (16-18) the plasma cortisol concentration was In the supplemented glucocorticoid-treated patients response and four (12-15) an impaired response. Of supplemented glucocorticoid-treated patients (9, 10). Of the remaining unsupplemented glucocorticoid-treated patients, one (11) showed an intermediary response and four (12-15) an impaired response. In the supplemented glucocorticoid-treated patients (16-18) the plasma cortisol concentration was increased.

The relationship between the changes in plasma volume and plasma cortisol after operation is shown in figure 1. In the control group the average measured at the time of skin incision, and at 1 and 3 hours later, employing a fluorometric technique (Binder, 1972). The operative changes in plasma cortisol during surgery in normal patients have been described previously (Kehlet and Binder, 1973a).

Haematocrit and haemoglobin, albumin and total protein concentrations in plasma were measured 24 hours before and 2 hours after skin incision.

### RESULTS

In table I the plasma volume determinations before and after surgery are shown together with the cortisol values. According to our earlier defined criteria (Kehlet and Binder, 1973a), the adrenocortical response to surgery was normal (plasma cortisol equal to or greater than 30 µg/100 ml 1 hour after skin incision and equal to or greater than 26 µg/100 ml 3 hours after skin incision) in all patients in the control group and in two of the unsupplemented glucocorticoid-treated patients (9, 10). Of the remaining unsupplemented glucocorticoid-treated patients, one (11) showed an intermediary response and four (12-15) an impaired response. In the supplemented glucocorticoid-treated patients (16-18) the plasma cortisol concentration was increased.

The relationship between the changes in plasma volume and plasma cortisol after operation is shown in figure 1. In the control group the average decrease in plasma volume was 8.7% (range +3.5 to −18.3%). In the unsupplemented glucocorticoid-treated patients, the average postoperative decrease in plasma volume was 6.9% (range +7.4 to −15.3%). In addition it was noted that the decrease in plasma volume was, if anything, less marked in the five patients with impaired adrenocortical response to surgery as compared with the two
normally responding patients (fig. 1). In the three supplemented glucocorticoid-treated patients, changes in plasma volume were within the normal range (mean —13.2%).

There was no difference between the average preoperative plasma volume in normal and glucocorticoid-treated patients (50.4 ml/kg (SD 4.8) and 48.0 ml/kg (SD 6.2), respectively).

The mean values of haemoglobin, haematocrit and albumin and total protein in plasma did not show any significant changes after surgery. Neither could any difference be demonstrated between any group, normal and glucocorticoid-treated or normal and glucocorticoid-treated showing an impaired adrenocortical response.

In one patient (13) systolic arterial pressure decreased to 80 mm Hg 3 hours after the skin incision. At this time the plasma cortisol concentration was reduced (20 µg/100 ml), but hypotension could not be attributed to a decrease in plasma volume, which increased by 2.9% after operation. No patient showed hypotension (a systolic arterial pressure less than 80 mm Hg) during the surgical procedure.

**DISCUSSION**

During abdominal surgery a decrease in plasma volume amounting to 6-18% has been demonstrated (Williams et al., 1962; Pfaff et al., 1966; Hoye et al., 1972). This is caused by a functional extracellular fluid volume deficit and by the abnormal loss of albumin from the intravascular compartment (Hoye et al., 1972).

A major decrease in plasma volume has been shown to be an accompaniment of hypotension and shock during stress-induced adrenocortical insufficiency. Thus, Swingle et al. (1938, 1959) and Marks et al. (1965) found a 25–50% deficit in plasma volume after the application of surgical stress to adrenalectomized dogs.

Kehlet and Binder (1973b) have demonstrated previously a high incidence of arterial hypotension during operation in unsupplemented glucocorticoid-treated patients, which did not correlate with the adrenocortical response to surgery, and was not associated with abnormal changes in plasma catecholamines (Kehlet et al., 1974).

The results of the present study concerning postoperative changes in plasma volume in normal patients are similar to others (Williams et al., 1962; Pfaff et al., 1966; Hoye et al., 1972). However, abnormal changes in plasma volume during surgery could not be demonstrated in glucocorticoid-treated patients. Also, the postoperative plasma volume deficit was no larger in patients with an impaired adrenocortical response to surgery. Therefore, as an indication of absolute or relative (Cope, 1965) adrenocortical insufficiency, a reduced plasma volume does not seem to be an important factor contributing to hypotension in glucocorticoid-treated patients during surgery.

**REFERENCES**


