Prolactin, LH, FSH, GH and cortisol response to surgery and the effect of epidural analgesia

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Abstract. The prolactin, LH, FSH, growth hormone and cortisol responses to surgical stress were studied in female patients receiving halothane (general) anaesthesia or epidural analgesia. Plasma cortisol, prolactin, and growth hormone concentrations increased during surgery, and post-operatively in patients operated under general anaesthesia, but not in patients operated during epidural analgesia. Gonadotrophin concentrations were unchanged in the general anaesthesia group until 9 h after stimulation when levels decreased slightly. In contrast plasma gonadotrophin levels decreased immediately after the administration of epidural analgesia and during the following 9 h. It is concluded that neurogenic blockade inhibits the anterior pituitary response to surgical stress.

Surgical stress has been shown to influence the secretion of the anterior pituitary hormones (Charters et al. 1969; Noel et al. 1972; Aono et al. 1976; Brandt et al. 1976; Wang et al. 1978). The release mechanism of the endocrine-metabolic response is predominantly mediated through neurogenic stimuli from the surgical area (Kehlet 1978).

However, data on prolactin, LH and FSH responses to surgery in women are very limited. In this study we describe the influence of neurogenic blockade on plasma prolactin, LH, FSH, growth hormone and cortisol responses to surgery in female patients.

Material and Methods

Thirteen otherwise healthy, pre-menopausal women undergoing hysterectomy for menorrhagia or cervical cancer in stage 0–1 were studied. Age ranged from 26 to 48 years (average 41 years in the general anaesthesia group and 36 years in the epidural group). None had any signs of cardiac, hepatic, renal or endocrine disease, and none received any hormonal drugs including contraceptives. Menstrual bleeding intervals were regular or slightly irregular. Two women receiving general anaesthesia and one epidural analgesia were studied in the late follicular phase of their menstrual cycle. All other patients studied were in the mid-luteal phase of the cycle.

All patients gave informed concept to participate. Seven patients had general anaesthesia with halothane and six patients epidural analgesia only, induced by 0.5% bupivacaine without adrenaline (Marcaine®) as described previously (Engquist et al. 1977). The analgesia, extending from T₄ to S₅, started before skin incision and was maintained throughout the following 24 h, constantly keeping the patients pain free. Both groups were premedicated with pethidine 1 mg/kg, promethazine 12.5–25 mg, and atropine 0.5 mg. The two groups were comparable with regard to duration of operation (about 90 min), and no one received blood or blood substitutes other than isotonic saline during the study.

Twelve blood samples were taken from a venous catheter: 15 and 10 min before anaesthesia or epidural analgesia, at skin incision, and at ½, 1, 2, 3, 4, 6, 9, 14 and 24 h after skin incision. They were analysed for cortisol by a competitive protein binding technique (Kehlet et al.
Results

The results are summarized in Figs. 1 and 2.

Cortisol in plasma increased during and after surgery in the seven females receiving general anaesthesia (Fig. 1). The values were significantly $(P < 0.05)$ higher than control levels up to 14 h after skin incision. In contrast, no rise in plasma cortisol levels was seen in patients operated under epidural analgesia. Differences between the two groups were significant $(P < 0.05)$ from half an hour to 14 h after skin incision.

Prolactin concentration in plasma showed a marked increase after induction of anaesthesia before skin incision and then a fall in the early post-operative period (Fig. 1). In contrast, plasma prolactin levels were unchanged in patients having epidural analgesia. Differences between groups were significant from skin incision to 4 h after skin incision.

Growth hormone in plasma increased during and after surgery $(P < 0.05)$ in the patients receiving general anaesthesia (Fig. 1). The concentration fell post-operatively, but on the first post-operative day (24 h) growth hormone was significantly $(P < 0.05)$ different.

Plasma cortisol, prolactin and growth hormone concentration during and following hysterectomy in patients anaesthetized with general anaesthesia (●●) and epidural analgesia (●●●).

* In relation to a point indicate that this is significantly $(P < 0.05)$ different from mean of control.

* At bottom indicate that at this time the two groups are significantly $(P < 0.05)$ different.

1974), and for growth hormone, prolactin, LH, and FSH by radioimmunoassays (Ørskov et al. 1968; McNeilly & Hagen 1974). In the assays used, the normal ranges for plasma prolactin (standardized against human pituitary prolactin supplied by Dr. H. Friesen and the M.R.C. prolactin standard A 71/222, assuming 10 mU per ampoule, 1 ng equals 28.1 μU) were 5–30 μU/l; for LH (M.R.C. standard 68/40, 77 IU/ampoule) in normal females in the luteal phase 1.9–7.9 μU/l; for FSH (M.R.C. standard 69/104, 10 IU/ampoule) in normal female subjects in the luteal phase 1.2–7.4 μU/l.

The significance of changes within groups was determined by the paired Student’s $t$-test and between groups by the unpaired Student’s $t$-test.
0.05) higher than the pre-operative level in both groups. Except for the 24-h sample, growth hormone showed no significant changes in patients receiving epidural analgesia. When compared with the general anaesthesia group patients receiving epidural analgesia had significantly (P < 0.01) lower growth hormone levels during surgery, but not post-operatively.

Gonadotrophin concentrations in plasma were unchanged during operation performed in general anaesthesia (Fig. 2). Compared with control levels there was a gradual fall in circulating gonadotrophin concentrations after the operation which became significant (P < 0.05) 9 h post-operatively (Fig. 2). There was a significant (P < 0.05) fall in circulating LH and FSH levels after epidural analgesia (Fig. 2), with a return towards pre-operative levels at 9 and 14 h, respectively. Plasma LH was significantly (P < 0.05) higher in patients receiving general anaesthesia compared with the epidural group during surgery, but not post-operatively.

Discussion

Surgery represents a stimulus to cortisol, prolactin and growth hormone release in female patients (Charters et al. 1969; Noel et al. 1972; Brandt et al. 1976). The present study confirms these observations. In contrast to cortisol and growth hormone the general anaesthetic agents themselves stimulate prolactin release in accordance with previous studies (Noel et al. 1972; Brandt et al. 1976).

The release mechanisms involved in cortisol, growth hormone, and prolactin response to surgery are apparently different, since cortisol continued to increase post-operatively concomitant with a decrease in plasma growth hormone and prolactin levels. This discrepancy cannot be explained solely on differences in 'half-life' of the hormones as suggested by Sowers et al. (1977).

Plasma gonadotrophins showed no significant intraoperative changes, but the concentrations of LH and FSH decreased post-operatively, as demonstrated previously in female patients (Charters et al. 1969; Aono et al. 1976).

The release mechanisms of the endocrine-metabolic response to surgery are predominantly afferent neurogenic stimuli from the surgical area to the central nervous system (Kehlet 1978). This is confirmed in the present study by the blockade of the cortisol and growth hormone response to surgery by epidural analgesia. Similarly, the prolactin response to surgery was blocked by neurogenic blockade, but this may partly be due to omission of general anaesthesia, which itself increases plasma prolactin (Brandt et al. 1976).

It might therefore be argued that the main release mechanism of prolactin to surgery is due to the anaesthetic agents, since epidural analgesia in addition to general anaesthesia did not inhibit the prolactin response to surgery in our previous study (Brandt et al. 1976). However, in that study epidural analgesia extended only to T4 which neither was sufficient to block the cortisol response to surgery. Therefore, sympathetic afferent pathways from T4 to T8 which were blocked in the present study probably are an important pathway for the release of prolactin and cortisol to surgery (Engquist et al. 1977).

Furthermore, since trauma such as gastroscopy leads to increased prolactin levels independent of anaesthesia (Noel et al. 1972; Sowers et al. 1977), it may be suggested that prolactin response to surgical stress is mediated by neurogenic stimuli. Since patients receiving medications known to elevate plasma prolactin were excluded from the study, the high plasma prolactin concentrations encountered pre-operatively in three of the six women in the epidural group may be ascribed to the effects of anxiety and psychological stress.

Neurogenic blockade provoked a fall in plasma LH and FSH during surgery. This finding is unexplained, and no data exist on changes and possible influence of sex steroids on the gonadotrophins during surgery and epidural analgesia in women.

In summary, this study has shown that neurogenic blockade prevents the prolactin, GH and cortisol responses to surgical stress and decreases LH and FSH per- and post-operatively in female patients.

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References


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