

Perioperative course of stress in patients confronting cardiac surgery

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Citation

P Bergmann, S Huber, H Mächler, E Liebl, H Hinghofer - Szalkay, P Rehak, B Rigler. *Perioperative course of stress in patients confronting cardiac surgery*. The Internet Journal of Anesthesiology. 1999 Volume 4 Number 3.

Abstract

Background:

Major surgery correlates with high values of perioperative stress and anxiety. We tested the perioperative course of stress, anxiety and well-being in patients confronting cardiac surgery.

Methods:

From admission at the hospital through the late postoperative phase, salivary and plasma cortisol measurements as well as psychological anxiety inventories and well-being tests were performed in 30 patients awaiting open heart surgery.

Results: After medical information state anxiety decreased from 42.1 points (SE 2.1) to 38.7 points (SE 1.8) and remained almost unchanged until the day before surgery (38.6 points, SE 1.6). Preoperatively salivary cortisol decreased continuously but during transport to the operating room salivary cortisol increased significantly from 4.1 nmol/l (SE 0.4) to 39.4 nmol/l (SE 14.8); after induction of anesthesia plasma cortisol decreased from 419.0 nmol/l (SE 17.7) to 186.9 nmol/l (SE 15.4). Postoperatively, well-being deteriorated in all our patients; anxiety decreased after surgery.

Conclusions: Despite preoperative sedation our data demonstrate a high level of stress and anxiety in patients confronting cardiac surgery. Key words: Salivary cortisol, plasma cortisol, anxiety well-being, stress,

INTRODUCTION

Anxiety, and particularly the apprehension of personal injury, is generally considered to be a potent stimulus to ACTH and cortisol secretion.¹ One naturally occurring situation which is associated with anxiety is the prospect of major surgery.

This paper reports a study which demonstrated the course of salivary and plasma cortisol levels as well as psychological state anxiety inventories and well-being tests in patients confronting open heart surgery from admission through the late postoperative phase.

MATERIAL AND METHODS

SUBJECTS

After approval by the Ethics committee of the Karl-Franzens University Graz, Austria, 30 consecutive patients (14 female, 16 male) scheduled for open heart surgery (CABG in 19 pts, heart valve operation in 11 pts) volunteered for the study and provided written and informed consent. Mean age was 59 years (min. 44; max. 75), mean ejection fraction 56% (min. 25; max. 82), average time for cardiopulmonary bypass 100

minutes (min. 47; max. 165), average cross-clamping time 63 minutes (min. 32; max. 92), total operation time 227 minutes (min. 170; max. 320). Patients with acute or recent myocardial infarction (within the last 6 weeks), as well as those undergoing percutaneous transluminal coronary angioplasty, and patients with angina unresponsive to medical therapy and therefore scheduled for urgent operation were excluded.

PREOPERATIVE AND ANESTHETIC MANAGEMENT

From admission until the day before surgery all patients received meprobamate 150 mg 3 times/day. On the evening before surgery 100mg nembutal and 5-10mg diazepam were administered orally.

All patients received 300 mg/kg etomidate and 10mg/kg fentanyl for induction of anesthesia, and 0.08 mg/kg pancuronium for paralysis intravenously. Clinical monitoring included seven-lead electrocardiography, systemic arterial pressure, central venous pressure, pulmonary arterial pressure, pulse oximetry, and

capnography. Anesthesia was supplemented with isoflurane to 0.5% inspired and bolus doses of 50-100 mg fentanyl intravenously as indicated. Cardiopulmonary bypass was performed with a membrane oxygenator using hemodilution and systemic hypothermia of 32°C. St. Thomas Hospital solution was used for cardioplegia.

SALIVARY CORTISOL MEASUREMENT

Saliva was collected using a small cotton swab (Salivette[®] Sarstedt, Rommelsdorf, Germany). Patients were asked to retain the cotton swab in their mouth for at least 2 minutes and then insert it into a special plastic tube which was stored at -20°C until assay (at most 20 days later)¹. Saliva collection did not occur at measuring point VI where the patient is intubated and sufficient salivary extraction is thus impossible. The first two samples were collected to assess stress reactions to the medical information, the fifth sample on the way to the operating room; at all other times salivary cortisol was collected in the evening, when patients were unaffected by routine therapeutic interventions. Table 1 describes the points of measurement of salivary cortisol.

Figure 1

Table 1: Points of Measurement

I	1 st day Immediately after arrival at the hospital
II	1 st day 20 min after receiving medical information (routine vs extensive)
III	2 nd day in hospital
IV	3 rd day in hospital (day before surgery)
V	On the way to the operating room before induction of anesthesia
VI	After induction of anesthesia, immediately before skin incision
VII	1 st day postoperatively
VIII	6 th day postoperatively

PLASMA CORTISOL MEASUREMENT

Samples of 5 ml of blood were drawn from all patients to measure plasma cortisol levels. Times of blood sampling were defined as following points of measurement (Table 1). At measuring points III and IV, samples were drawn from a peripheral vein in addition to the routine sampling. At points VI, VII and VIII samples were drawn from the vena cava superior via a central venous catheter. Samples were placed in chilled tubes and centrifuged at 3000 g for 10 min at 4°C; the separated plasma was stored at -20°C until assay (at most 20 days later). No plasma cortisol measurements were performed at measuring points I and II to avoid any stress response due to consecutive venipunctures.² For the same reason we did not perform plasma measurement during transport to the operating room (measuring point V).

ASSAY OF CORTISOL

Plasma and salivary cortisol were determined in duplicate with commercial radioimmunoassay kit (CORT-CT2 kit, CIS bio international[®]– ORIS Group/France). The sensitivity of the method is approximately 4.6 nmol/l with plasma cortisol measurement and 0.8 nmol/l with salivary cortisol measurement. Between 8 – 10 a.m. the reference limits in plasma utilizing the CORT-CT2 kit are 154 - 638 nmol/l, between 8 – 10 a.m. saliva reference limits are 5.3 – 61.8 nmol/l and at 8 p.m 1.2 - 12.3 nmol/l (CIS bio international[®]– ORIS Group/France).

PSYCHOLOGICAL VARIABLES - (TRAIT ANXIETY, STATE ANXIETY, PATIENTS' WELL-BEING)

Points of measurement for patients' psychological variables are seen in Table 1. The completion of the psychological test sheets was supervised by the medical psychologist (E.L). The number of tests was limited to four. At point V the patient is sedated, at point VI intubated and at point VII in the intensive care unit and thus cannot fill out test sheets.

Patients' state anxiety were measured by the State-Anxiety test.³ Subjects rated their levels of state anxiety on a 4-point scale ranging from "not at all" (= 1 point) to "almost always" (= 4 points). A total score of 20 to 80 points rose in proportion to anxiety.³

Patients well-being was evaluated by the well-being scale,⁴ a list of 28 pairs of opposite adjectives, one relating to enhanced (= 0 points) and the other to impaired (= 2 points) well-being. An indifferent decision rates one point. A low total of points reflects a rather positive condition, a high total a rather negative one.

STATISTICAL ANALYSIS

Statistical analyses were performed with a 2-way analysis of variance (ANOVA) for repeated measurements with the main effects of gender and points of measurement. Multiple comparisons between the measurement points were done according to Tukey-Kramer. In the text data are described as mean ± standard error. Data in figures are shown as mean (± standard error) by repeated measures analysis of variance (ANOVA).

RESULTS

STATE ANXIETY

There was no significant difference in state anxiety between female and male patients (p = 0.82) comparing all the points

of measurement. State anxiety was significantly higher ($p = 0.0011$) before medical information at measuring point I (42.1 ± 2.1 points) than afterwards at point II (38.7 ± 1.8). The day before surgery, at point IV (38.6 ± 1.6 points), state anxiety remained almost unchanged compared with point II. Six days after surgery at point VIII (34.3 ± 1.7 points) state anxiety decreased significantly ($p = 0.0001$).

Figure 2

Figure 1: Perioperative course of patients' state anxiety - A significantly lower level of state anxiety is seen after medical information and b postoperatively ($p = 0.0011$). Data are shown as means (standard error = SE: 0.7) by repeated measures analysis of variance (ANOVA).

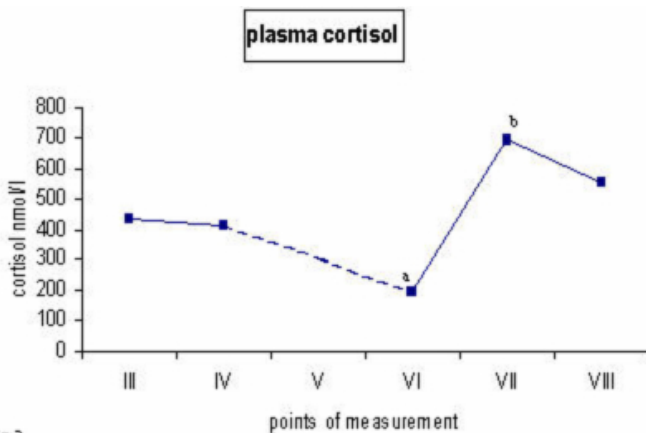


Fig 3

WELL-BEING

Simultaneously with the state - anxiety test all the patients were asked to complete the well-being test. Overall, there was no significant difference between female and male patients ($p = 0.82$). Patients' well-being was better ($p = 0.0299$) before surgery at measuring points II (13.2 ± 1.5 points) and IV (13.5 ± 1.8 points) than afterwards at measuring point VIII (17.6 ± 2.4 points). Preoperative medical information leads to an improvement of well-being (measurement point I 16.5 ± 2.1 versus measurement point II 13.2 ± 1.5).

Figure 3

Figure 2: Perioperative course of patients' state anxiety - A high total of points reflects a rather negative well-being. Preoperatively, patients' well-being does not improve significantly. Well-being deteriorates after surgery ($p = 0.0299$). Data are shown as means (SE: 0.9) by repeated measures analysis of variance (ANOVA).

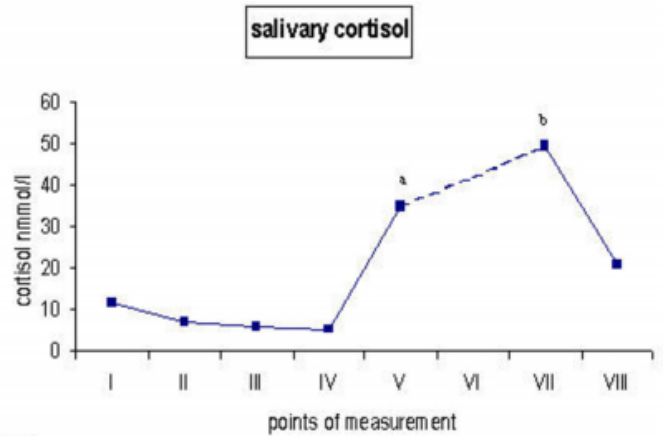


Fig 4

PLASMA CORTISOL

Plasma cortisol did not differ significantly between genders ($p = 0.55$) comparing all five points of measurement. Preoperatively, no significant difference ensued between measuring points III (446.1 ± 22.6 nmol/l) and IV (419.0 ± 17.7 nmol/l). After induction of anesthesia, immediately before skin incision at measuring point VI ($186.9.5 \pm 15.3$ nmol/l) plasma cortisol levels were lower ($p = 0.0033$) than at any other time. Plasma levels increased ($p = 0.0033$) postoperatively at measuring point VII (783.9 ± 44.7 nmol/l) and also six days postoperatively at point VIII (589.5 ± 33.5 nmol/l).

Figure 4

Figure 3: Perioperative course of plasma cortisol concentration - A Significantly reduced level at point VI after induction of anesthesia before skin incision ($p = 0.0033$). b High concentration at the first day postoperatively at point VII ($p = 0.0033$).--- no plasma cortisol measurement at point V to prevent stress induction by venipuncture. Data are shown as means (SE: 19.5) by repeated measures analysis of variance (ANOVA).

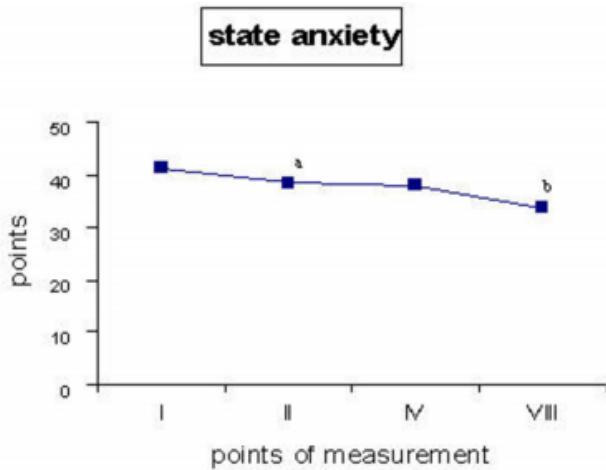


Fig 1

SALIVARY CORTISOL

Again, men and women did not differ in level of salivary cortisol ($p = 0.25$) comparing all measuring points. During the preoperative course, salivary cortisol concentration decreased slowly comparing measuring points I (13.6 ± 4.6 nmol/l), II (7.8 ± 1.4 nmol/l), III (5.1 ± 0.9 nmol/l) and IV (4.1 ± 0.4). During transport to the operating room at measuring point V salivary cortisol level (39.4 ± 14.8 nmol/l) increased significantly ($p = 0.0005$). Peak salivary cortisol concentration (45.7 ± 7.4 nmol/l) was reached after surgery at measuring point VII. This value was significantly higher ($p = 0.0005$) versus measuring points I, II, III, IV and VIII (20.3 ± 4.1 nmol/l).

Figure 5

Figure 4: Perioperative course of salivary cortisol concentration - A Significantly higher level during transport to the operating room ($p = 0.0011$). b The peak concentration is seen on the first postoperative day. --- no salivary cortisol measurement at point VI (intubated patient). Data are shown as means (SE: 4.4) by repeated measures analysis of variance (ANOVA).

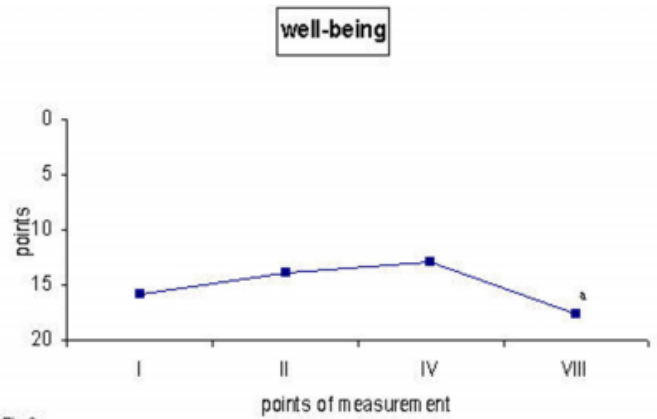


Fig 2

COMMENT

Increases in cortisol secretion may be observed not only with an acute stressor but also in anticipation of a stressful experience.⁵ Especially in situations with high ego involvement, low predictability, low controllability and novelty, corticotropin-releasing hormone (CRH) and adenocorticotrophic hormone (ACTH) are released, with subsequent rise in cortisol levels.⁶ One naturally occurring situation which is associated with anxiety is the anticipation of major surgery.⁷ Patients awaiting elective cardiac surgery were chosen for this study, since most of these patients feel that the operation poses a significant threat which they consent to undertake in hope of successful relief of their symptoms. Consequently, such patients are expected to demonstrate a major adrenocortical response.

Recently it has been demonstrated that cortisol concentrations in saliva provide a good index of free plasma cortisol levels.¹ As saliva is easily collected by non-invasive, painless procedures, and easily processed for cortisol measurement, this technique provides good information in addition to the psychoendocrinological determination of state anxiety and patients' well-being. State anxiety decreases significantly after medical information, which shows the positive influence of the preoperative routine information. Despite premedication with meprobamate 200 mg 3 times per day, from admission until the evening before surgery, in our patients levels of salivary and plasma cortisol remained almost unchanged. Gender did not influence our

results, supporting some previous observations,^{8,9} but opposing others which describe a larger cortisol response to stress in male than in female patients.^{10,11}

Episodic 24-hour measurements of plasma cortisol on the day before major surgery in patients awaiting elective cardiac surgery are reported by Czeisler et al.¹² but no data in the literature describe patients' cortisol reaction on the way to the operating room. Although all our patients received Nembutal 100mg and Diazepam 5-10mg on the evening before surgery and so were sedated during the transport to the operating room, levels of salivary cortisol were approximately three times higher during the transport than immediately after admission to the hospital. Forthcoming studies will show whether more generous preoperative sedation can reduce patients' increase of stress during transport to the operating room.

After induction of anesthesia cortisol levels decreased considerably in our patients. Postoperatively however, salivary and plasma cortisol went up again, to finally return to high-normal values until the 6th postoperative day. These results are confirmed by other studies which describe a decreasing plasma cortisol concentration during anesthesia and surgery before cardiopulmonary bypass, a significant increase during CPB, and a gradual normalization postoperatively.^{13,14,15}

State anxiety decreased significantly six days after surgery while well-being deteriorated postoperatively. Burker et al.¹⁶ describe anxiety as a significant predictor of pre- and postoperative depression and suggest that measures to reduce anxiety are indicated. In summary, cardiac surgery is associated with high values of patients' stress, anxiety and reduced postoperative well-being. This supports psychological care given to these patients perioperatively.

ACKNOWLEDGMENT

We thank Thomas Lang, MD; Hans-Jürgen Semmelrock, PhD, Andreas Rothaler, CTA and the Austrian Society of Aerospace Medicine (Institute for Adaptive and Spaceflight Medicine), Graz, Austria for laboratory analysis; Eugenia Lamont for language editing.

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