EFFECTS OF KETAMINE ANAESTHESIA ON THE METABOLIC RESPONSE TO PELVIC SURGERY

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SUMMARY

The effects of ketamine anaesthesia on the metabolic and endocrine response to pelvic surgery were investigated, and compared with results obtained in a control group of patients anaesthetized with thiopentone and halothane. Ketamine anaesthesia before the onset of surgery was associated with a significant increase in blood glucose and plasma cortisol concentrations, and in heart rate. However, when surgery was established there were no metabolic, endocrine or haemodynamic differences between ketamine and halothane anaesthesia. We conclude that ketamine does not exacerbate the metabolic response to surgery.

Although the cardiovascular effects of ketamine anaesthesia have been studied in detail (for review see White, Way and Trevor, 1982), little attention has been directed towards the associated endocrine and metabolic changes. Since it has been shown that ketamine causes an increase in circulating catecholamine (Takki et al., 1972; Baraka, Harrison and Kachachi, 1973; Appel et al., 1979), ACTH and cortisol concentrations (Oyama, Matsumoto and Kudo, 1970), it could be argued that the use of this agent may exacerbate the metabolic response to surgery.

Clarke and colleagues (1974) found that ketamine anaesthesia was associated with slightly higher blood glucose and plasma cortisol concentrations, when compared with other induction agents in patients who had undergone minor gynaecological surgery. In contrast, Kaniaris and co-workers (1975) demonstrated a decreased glucose and non-esterified fatty acid (NEFA) response to surgery with ketamine anaesthesia compared with halothane and thiopentone in children. In a recent study by Stefansson, Wickström and Haljämäe (1982a) ketamine anaesthesia was used in elderly patients undergoing surgical correction of fractured neck of femur and changes in circulating and intramuscular metabolites were measured. Unfortunately, a direct comparison of these metabolic results with similar patients anaesthetized with other techniques was not possible because of differences in the preoperative blood glucose concentration (Stefansson, Wickström and Haljämäe, 1982b, c).

In the present study we have attempted to resolve these conflicting reports by examining the effects of ketamine anaesthesia on the concentrations of circulating metabolites, and cortisol, during pelvic surgery.

PATIENTS AND METHODS

Sixteen healthy women admitted for Fallopian tubal surgery were investigated. On admission to hospital their height and body weight were recorded and the body mass index calculated as an estimate of adiposity (Keys, Fidanza and Karvonen, 1972). The patients were allocated randomly to receive supplementation of anaesthesia either with an infusion of ketamine, or with halothane. The nature of the study was explained to the patients and consent obtained for the collection of samples of central venous blood.

All patients were premedicated with papaveretum 15–20 mg and hyoscine 0.3–0.4 mg i.m. 90 min before surgery. On arrival in the anaesthetic room the duration of starvation was determined and a central venous catheter inserted percutaneously from an antecubital fossa vein to permit blood sampling and the administration of fluids. A cannula was inserted to a vein in the contralateral arm for the infusion of ketamine or an equivalent volume of sodium chloride solution 150 mmol litre⁻¹ (halothane patients). After the patient had rested for 10 min a control blood sample was collected and arterial pressure and heart rate measured.

In the ketamine group anaesthesia was induced
with ketamine 2 mg kg\(^{-1}\) i.v., the trachea was intubated with the aid of alcuronium and the lungs ventilated with 70% nitrous oxide in oxygen. Immediately after the induction of anaesthesia an infusion of ketamine 25 \(\mu\)g kg\(^{-1}\) min\(^{-1}\) was started and maintained for the duration of surgery. In the halothane group anaesthesia was induced with thiopentone 3.5–5.0 mg kg\(^{-1}\), the trachea was intubated following the administration of alcuronium and the lungs ventilated with 70% nitrous oxide in oxygen supplemented with 0.5–1.0% halothane. Ventilation was adjusted to maintain an end-tidal carbon dioxide concentration of 4.5–5.0% in both groups of patients. Sodium chloride solution 150 mmol litre\(^{-1}\) was administered i.v. at a rate of 4 ml kg\(^{-1}\) h\(^{-1}\) during the study; measured blood loss did not exceed 200 ml.

Twenty minutes after the induction of anaesthesia a second blood sample was collected and surgery commenced. Further samples were obtained after 30, 60, 90 and 120 min of surgery and were analysed in duplicate for glucose, NEFA, lactate, pyruvate and cortisol concentrations, and haematocrit, by methods described previously (Walsh et al., 1981). Plasma concentrations of ketamine, norketamine (metabolite I) and dehydronorketamine (metabolite II) were determined in duplicate as described by Chang and Glazko (1972), except that nitrogen was used as the carrier gas. At the same time as the blood samples were collected the arterial pressure and heart rate were measured.

The results are expressed as mean values (± SEM). Statistical evaluation of the results was undertaken using two-way and one-way analysis of variance as appropriate.

**RESULTS**

Details of the patients studied are shown in table I. There were no significant differences between the two groups.

<table>
<thead>
<tr>
<th>Table I. Details of patients studied</th>
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<tbody>
<tr>
<td>Control group (n = 8)</td>
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<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Age (yr)</td>
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<td>Wt (kg)</td>
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<td>Duration of starvation (h)</td>
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<td>Body mass index (kg m(^{-2}))</td>
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Changes in the concentrations of the circulating metabolites and plasma cortisol, and in the haematocrit, are shown in table II. The blood glucose concentration in the halothane group did not change significantly during 20 min anaesthesia, but increased from 3.48 to 4.55 mmol litre\(^{-1}\) after 60 min surgery (\(P < 0.01\)). Ketamine anaesthesia before surgery, on the other hand, was associated with a significant increase in glucose concentration from 3.60 to 4.19 mmol litre\(^{-1}\) (\(P < 0.05\)). There was a further increase in blood glucose during surgery in the ketamine group to 4.95 mmol litre\(^{-1}\) (\(P < 0.001\)) after 60 min. Although the glycaemic response to surgery was always greater in the ketamine patients, there was no significant difference between the two groups.

Plasma NEFA, blood lactate and pyruvate concentrations did not change significantly during the study in either group of patients.

The pattern of the cortisol response was similar to that described for glucose. In the halothane patients plasma cortisol concentrations increased only after surgery had started and reached 614 nmol litre\(^{-1}\) at 120 min (\(P < 0.001\)). Ketamine anaesthesia before surgery produced a significant increase in cortisol concentration from 198 to 336 nmol litre\(^{-1}\) (\(P < 0.01\)), and this increased further to 646 nmol litre\(^{-1}\) after 120 min (\(P < 0.001\)). During the operation there were no significant differences in the cortisol values between the two groups.

The haematocrit declined similarly in both groups, from 40.0 to 36.8% (\(P < 0.001\)) in the halothane patients and from 40.3 to 37.3% (\(P < 0.001\)) in the ketamine patients.

Plasma ketamine concentrations increased slowly from 5.11 \(\mu\)mol litre\(^{-1}\) at the start of surgery to 6.97 \(\mu\)mol litre\(^{-1}\) after 120 min (fig. 1). The concentration of norketamine (metabolite I) increased during surgery to 1.66 \(\mu\)mol litre\(^{-1}\) after 120 min. Dehydronorketamine (metabolite II) was detected in occasional samples in only four of the patients.

Ketamine anaesthesia before surgery produced a significant increase in heart rate from 93 to 113 beat min\(^{-1}\) (\(P < 0.001\)), but no change in mean arterial pressure (fig. 2). During surgery there were no significant differences in heart rate and mean arterial pressure between the two groups.

**DISCUSSION**

The most important finding of the present study was that, once surgery was established, there was no difference in the metabolic response between
**Fig. 1.** Mean (± SEM) plasma concentrations of ketamine (solid circles) and norketamine (open circles).

**Fig. 2.** Mean (± SEM) heart rate and mean arterial pressure (MAP) in the ketamine (open circles) and halothane groups of patients (closed circles).
ketamine and halothane anaesthesia. However, in
the 20 min before surgery ketamine anaesthesia was
associated with significant increases in blood glu-
cose and plasma cortisol concentrations (table II),
and heart rate (fig. 2). This glycaemic response is
compatible with the well-documented activation of
the sympathetic nervous system by ketamine
(White, Way and Trevor, 1982), although it is
curious that there were no changes in circulating
lactate and NEFA concentrations which are, in part,
mediated sympathetically (Clutter et al., 1980). The
increase in plasma cortisol concentration during
ketamine anaesthesia (table I) confirms the stimula-
tion of the hypothalamic-pituitary-adrenal axis
described by Oyama, Matsumoto and Kudo (1970).

Plasma ketamine concentrations were compara-
tively stable during anaesthesia using a fixed infu-
sion rate of 25 µg kg ⁽ min ⁽ (fig. 1) and were ap-
proximately twice the value at which consciousness
has been noted to return (Idvall et al., 1979; Domino
et al., 1982). None of the patients who received
ketamine experienced any emergence reactions dur-
ding recovery from anaesthesia and all were willing to
have the same anaesthetic technique again if re-
quired. The absence of any unpleasant sequelae may
be related to the low plasma ketamine concentra-
tions achieved with this technique (Idvall et al.,
1979; Klausen, Wiberg-J0rgensen and Chraemmer-
J0rgensen, 1983).

Stenberg and Idvall (1981) have suggested that
the occurrence of dehydronorketamine (metabolite II)
may be an artefact resulting from the extraction
and derivatization of the ketamine sample. It is of
interest that, in those few patients in whom de-
hydronorketamine was detected, there were de-
creased concentrations of ketamine and nor-
ketamine, indicating a more rapid metabolism of
ketamine and its primary metabolite. Even if de-
hydronorketamine does not exist in vivo, its produc-
tion probably reflects the rate of formation of
metabolites III and IV from metabolite I, in vivo.

We conclude that ketamine produces only trans-
ient hormonal and metabolic changes which are
minor in comparison with the superimposed surgi-
cal stimulation. The use of ketamine anaesthesia in
the severely injured patient is unlikely to cause
further adverse metabolic effects.

ACKNOWLEDGEMENTS
We wish to thank Mr Raoul Margara for permission to study the
patients, and Miss Tracey Harrison for secretarial assistance.
REFERENCES


LES EFFETS DE L’ANESTHÉSIE PAR LA KETAMINE SUR LA REPONSE METABOLIQUE A LA CHIRURGIE PELVIENNE

RESUME

Nous avons étudié les effets de l’anesthésie à la kétamine sur les réponses métaboliques et endocriniennes à la chirurgie pelvienne et nous les avons comparés aux résultats obtenus dans un groupe contrôle de patients anesthésiés avec pentothal et halothane. L’anesthésie à la kétamine était responsable avant le début de la chirurgie d’une augmentation significative des concentrations plasmatiques de glucose et de cortisol ainsi que de la fréquence cardiaque. Cependant, après le début de la chirurgie, il n’y avait plus de différences métaboliques, endocriniennes ou hémodynamiques entre l’anesthésie à la kétamine et l’anesthésie à l’halothane. Nous en déduisons que la kétamine n’augmente pas la réponse métabolique à la chirurgie.

WIRKUNGEN DER KETAMIN-NARKOSE AUF DIE METABOLISCHE REAKTION BEI OPERATIONEN IM BECKENBEREICH

ZUSAMMENFASSUNG


EFFECTOS DE LA ANESTESIA POR QUETAMINA SOBRE LA RESPUESTA METABOLICA EN CIRUGIA PELVICA

SUMARIO

Se llevaron a cabo investigaciones sobre los efectos de la anestesia por quetamina sobre la respuesta metabólica y endocrina en cirugía pélvica y se compararon con los resultados obtenidos en un grupo de control de pacientes anestesiados con tiopentona y halotano. La anestesia por quetamina antes del principio de la cirugía se encontró asociada con un aumento significante de las concentraciones de cortisol en el plasma y de glucosa en la sangre y del ritmo cardíaco. Sin embargo, cuando la cirugía progresaba, no hubo diferencias metabólicas, endocrinas o hemodinámicas entre la anestesia por quetamina y por halotano. Concluimos que la quetamina no exacerba la respuesta metabólica a la cirugía.