EPIDURAL ANALGESIA AND THE METABOLIC RESPONSE TO SURGERY

GRISELDA M. COOPER, ANITA HOLDCROFT, G.M. HALL AND J. ALAGHBAND-ZADEH

THE USE OF EPIDURAL ANALGESIA in combination with nitrous oxide and oxygen anaesthesia is a popular technique for lower abdominal and pelvic surgery. The advantages of this technique include good muscular relaxation, a contracted bowel, a reduction in blood loss and the provision of effective postoperative analgesia without central respiratory depression.

There have been several studies of the effect of epidural blockade combined with general anaesthesia on the metabolic and hormonal response to pelvic surgery.[1-5] Most of these investigations were confined to examining changes in blood glucose and plasma cortisol values[1-4] and only Brandt, Kehlet, Binder, Hagen and McNeilly[5] measured other hormones.

The purpose of this study was to examine the effect of the combination of nitrous oxide and oxygen anaesthesia with epidural analgesia on circulating metabolites and hormones during Fallopian tube surgery, with particular reference to fat metabolism. Unfortunately it was not possible to examine the effects of the components of this anaesthetic technique. The use of nitrous oxide and oxygen alone produced awareness during anaesthesia in two of the seven patients studied and the technique was abandoned. Epidural analgesia with the patient awake was associated with severe nausea and occasional vomiting when the uterus was manipulated which was only prevented by the induction of light anaesthesia.

METHODS

Fourteen healthy patients admitted for tubal surgery were investigated. The operation was performed by one surgeon using a standard microsurgical technique and was undertaken either for primary infertility or for reversal of sterilisation. They were premedicated with papaveretum 15–20 mg and hyoscine 0.3–0.4 mg intramuscularly one hour before operation. On arrival in the anaesthetic room the duration of preoperative starvation was determined and a central venous catheter was inserted percutaneously from an antecubital fossa. The patient rested for 10 minutes and a control central venous blood sample was collected.

The patient was then placed in the lateral position and a catheter was inserted into the epidural space at either the L2/3 or L3/4 interspace. Fourteen ml of bupivacaine 0.5 per cent without adrenaline was injected into the epidural space and, when the level of sensory blockade was sufficient for the operation (above T10) general anaesthesia was induced with a sleep dose of thiopentone. Tracheal intubation was undertaken after the administration of pancuronium and anaesthesia was maintained with nitrous oxide and oxygen using a Cape-Waine ventilator with a semi-closed circuit incorporating sodalime. Ventilation was adjusted to maintain an end-tidal carbon dioxide concentration of 4.5–5.0 per cent (Hartmann-Braun URAS 4 infra-red carbon dioxide analyser).

The efficacy of the epidural analgesia during operation was determined by measurement of the skin temperature of the legs and by clinical signs of adequate analgesia. Incremental doses of bupivacaine 0.5 per cent without adrenaline were given as required and the mean dose administered was 98 mg (SEM ± 6 mg).

Hartmann's solution was administered intravenously during surgery at a rate of approximately 6 $ml \cdot kg^{-1}$ body weight/hour. Blood transfusion was not required as the measured blood loss was only 100–150 ml. Systolic arterial pressures were maintained above 13.3 kPa (100 mm/Hg) during the experimental period.

Central venous blood samples were collected every 30 minutes during the operation and were analysed for free fatty acids (FFA), glycerol, β-hydroxybutyrate, acetoacetate, glucose, lactate, pyruvate, cortisol and growth hormone

Griselda M. Cooper, M.B., Ch.B., F.F.A.R.C.S.; Anita Holdcroft, M.B., Ch.B., F.F.A.R.C.S.; G.M. Hall, M.B., B.S., Ph.D., M.I.Biol., F.F.A.R.C.S. Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London, W.12, OHS, England. J. Alaghband-Zadeh, L.M.S.S.A., M.R.C.Path., Department of Chemical Pathology, Charing Cross Hospital Medical School, London, W.12, England.

Correspondence to: Dr. G.M. Hall, Department of Anaesthetics, Royal Postgraduate Medical School, Hammersmith Hospital, London, W.12, OHS, England.

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TABLE I

	Means ± SEM	Ranges
Age (years)	31.8 ± 1.1	(27–39)
Weight (kg)	57.9 ± 2.1	(41–70)
Body fat (%)	26.5 ± 1.6	(23–29)
Preoperative starvation (hours)	14.5 ± 0.8	(12–18)

Anthropometric data from patients studied.
Values represent means ± SEM (and ranges).

(GH) concentrations by methods described previously.[6]

The skinfold thicknesses of the patients were measured on the fourth postoperative day using skin calipers (John Bull, British Indicators Ltd.) and the percentage of fat to body weight was calculated.[7]

The results are presented as mean values (±SEM) and were analysed using a two-way analysis of variance.[8]

Results

The anthropometric characteristics of the patients are shown in Table I.

The changes in the mean values of the substrate and hormonal concentration during surgery are shown in Table II. Plasma FFA and glycerol concentrations decreased significantly ($p < 0.05$) after 30 minutes of surgery but then returned to control values. There was no significant change in total ketone body concentration (β-hydroxybutyrate and acetoacetate). The blood glucose only increased from 3.97 mmol/l to 4.58 mmol/l after 90 minutes of surgery ($p > 0.2$). Blood lactate concentration increased progressively from a control value of 0.75 mmol/l to 1.19 mmol/l after 120 minutes ($p < 0.01$) but there was no associated change in pyruvate concentration. Plasma cortisol and growth hormone were increased significantly after one hour of surgery ($p < 0.05$) and this persisted for the duration of the operation.

Discussion

Fat metabolism

In any clinical study of fat metabolism it is essential to determine the duration of starvation and the degree of obesity of the subjects. As liver glycogen stores are progressively depleted during starvation there is a concomitant increase in the breakdown of triglycerides in adipose tissue (lipolysis) with a sparing effect on the utilisation of glucose.[9] Lean patients readily mobilise free fatty acids, whereas triglyceride synthesis (lipogenesis) predominates in obese patients.

Table I shows that the duration of preoperative starvation and percentage of body fat were similar in the patients studied.

The significant decrease in plasma free fatty acids and glycerol found after 30 minutes of surgery (Table II) was also observed in a previous study[6] and appears to be independent of the anaesthetic technique used. The most likely cause of this sudden decline in lipolysis is the removal of preoperative fear and apprehension by the induction of anaesthesia. Lipolysis is particularly sensitive to stimulation by catecholamines and has been used as an indirect estimate of sympathetic activity.[10] The absence of a significant increase in free fatty acids and glycerol during surgery suggests that the overall level of sympathetic activity was not increased. Thus, the effect of the local analgesic on blocking the thoraco-lumbar sympathetic fibres was balanced by increased autonomic activity in the upper limbs, causing vasoconstriction.[11]

The measurement of plasma glycerol concentration was undertaken to verify the use of changes in plasma free fatty acid concentrations as an indication of lipolysis. Circulating free fatty acid values are determined mainly by the balance between lipolysis and immediate re-esterification in adipose tissue.

Plasma glycerol, on the other hand, indicates lipolysis alone, since the glycerol phosphate necessary for re-esterification is derived solely from glycolysis. Table II shows that plasma free fatty acid and glycerol change similarly and a regression analysis of individual FFA and glycerol concentrations determined from the same plasma sample showed a highly significant correlation ($r = 0.42$, $p < 0.001$). Thus, the plasma level of free fatty acids is a true indicator of lipolysis during epidural analgesia.

Glucose and hormone values

The failure of the glucose concentration to increase despite a significant rise in plasma cortisol and growth hormone values (Table II) confirms the results of Brandt, *et al.*[5] Engquist, Brandt, Fernandes and Kehlet[4] suggested that the total abolition of the cortisol response to pelvic surgery was only obtained with an epidural blockade extending from T4 to S5. As autonomic blockade is always more extensive than the sensory loss,[12,13] we considered that this technique may

TABLE II

TIME (MINUTES)

Substrate	0	30	60	90	120
FFA (mmol/l)	0.71 ± 0.09	0.51 ± 0.09*	0.69 ± 0.08	0.76 ± 0.14	0.69 ± 0.12
Glycerol (mmol/l)	0.15 ± 0.02	0.10 ± 0.01*	0.15 ± 0.02	0.13 ± 0.02	0.13 ± 0.02
Ketone bodies (mmol/l)	0.13 ± 0.03	0.15 ± 0.05	0.12 ± 0.02	0.16 ± 0.03	0.17 ± 0.05
Glucose (mmol/l)	3.97 ± 0.24	4.14 ± 0.18	3.87 ± 0.15	4.58 ± 0.21	4.55 ± 0.32
Lactate (mmol/l)	0.75 ± 0.09	0.95 ± 0.10*	0.98 ± 0.10†	1.04 ± 0.14†	1.19 ± 0.19†
Pyruvate (μmol/l)	22 ± 4	23 ± 6	17 ± 4	17 ± 3	21 ± 7
Hormones					
Cortisal (mmol/l)	220 ± 37	216 ± 39	463 ± 110*	529 ± 66†	551 ± 94*
Growth hormone (mμ/l)	1.3 ± 0.2	4.6 ± 2.3	18.0 ± 6.5*	12.6 ± 3.8†	13.3 ± 6.5*

Mean (+SEM) values of metabolites and hormones during surgery. The significance of the difference from Time 0 indicated by $^*p < 0.05$ and $^\dagger p < 0.01$, otherwise differences are not significant.

cause severe circulatory disturbances with consequent changes in metabolism. Therefore, we followed our usual clinical practice of establishing a level of blockade sufficient for the operation.

Blood lactate and pyruvate concentrations

The increase in lactate concentration without an associated rise in pyruvate (Table II) was similar to the observations of Hall, Young, Holdcroft and Alaghband-Zadeh[6] in which nitrous oxide and oxygen anaesthesia for pelvic surgery was supplemented by halothane 0.5–1.0 per cent. This slight lacticacidaemia was not due to hyperventilation and was not influenced by β-adrenergic blockade, which inhibits the stimulation of muscle glycogenolysis by catecholamines (authors' unpublished results). It is unlikely that there was an important contribution from the lactate in the Hartmann's solution (28 mmol/l) as a similar lacticacidaemia was observed when 150 mmol/l saline solution was used for fluid replacement during operation.

It is possible that both halothane and epidural analgesia reduce muscle blood flow, so that the oxygen requirements of muscle are no longer matched by the oxygen delivery. Anaerobic muscle metabolism is therefore increased. This phenomenon is analogous to the $\dot{V}/\dot{Q}$ abnormality of the lung, only in this "metabolic $\dot{V}/\dot{Q}$". $\dot{V}$ represents the local oxygen consumption of the muscle and $\dot{Q}$ represents the local capillary blood flow. Some support for this concept is provided by the results of Wright and Cousins[14] who showed that although lower limb blood flow was increased by epidural blockade, this was due entirely to an increase in skin flow. Muscle capillary blood flow, as measured by a 133 Xe clearance method, was decreased by half. Thus, the redistribution of blood flow caused by epidural blockade may induce small but significant changes in muscle metabolism.

In conclusion, the results demonstrate that the only significant changes in metabolites during epidural analgesia are a transient decrease of free fatty acids and glycerol in plasma after 30 minutes and a sustained increase in blood lactate. It is important to note that the abolition of the hyperglycaemic response to surgery occurred despite significant increases in plasma cortisol and growth hormone concentrations. Thus changes in blood glucose values alone do not accurately reflect the endocrine response to surgery.

Summary

The effect of epidural blockade on the metabolic and hormonal responses to pelvic surgery was investigated in 14 female patients. Central venous blood samples were collected every 30 minutes and analysed for free fatty acids, glycerol, β-hydroxybutyrate, acetoacetate, glucose, lactate, pyruvate, cortisol and growth hormone concentrations. There was no change in fat and glucose metabolism except for a transient decrease in lipolysis after 30 minutes of surgery. Cortisol and growth hormone values were significantly increased ($p < 0.01$) after 60 minutes. A small but statistically significant increase in blood lactate concentration was observed ($p < 0.01$) and the concept of a "metabolic $\dot{V}/\dot{Q}$" abnormality is postulated to explain the lacticacidaemia.

Résumé

L'effet du bloquage épidural sur les réponses métabolique et hormonale provoquées par la chirurgie du bassin a été étudié chez 14 patientes. Des échantillons de sang veineux central ont été prélevés et analysés dans le but de doser les acides gras libres, le β-hydroxybutyrate, l'acéto-acétate, le glucose, le lactate, le pyrunate, le cortisol et l'hormone de croissance. Aucun changement dans le métabolisme lipidique et glucidique n'a été noté à l'exception d'une baisse transitoire de la lipolyse après 30 minutes de chirurgie. Quant au cortisol et à l'hormone de croissance, leur concentration a subis une hausse significative ($p < 0.01$) après 60 minutes. Une augmentation significative bien que faible a aussi été notée pour le lactate sanguin ($p < 0.01$); le concept du pliquer cette lactacidémie.

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