Brit. J. Anaesth. (1971), 43, 496

ALTERATIONS IN RESPONSE TO SOMATIC PAIN ASSOCIATED WITH ANAESTHESIA

XX: KETAMINE

BY

J. G. BOVILL AND J. W. DUNDEE

SUMMARY

Subhypnotic doses of ketamine cause a transient decrease in sensitivity to somatic pain. Analgesia can be detected up to 40 minutes after normal (2–3 mg/kg) anaesthetic doses. In contrast to the action of barbiturates, antanalgesia does not occur after ketamine.

Ketamine hydrochloride is a parenteral anaesthetic agent which has been claimed to produce profound analgesia (Domino, Chodoff and Corssen, 1965). Corssen and Domino (1966) reported that analgesia produced by ketamine was insufficient to protect against visceral pain but was effective against pain involving the extremeties and skeleton; on this basis they suggested the term "somatoanalgesia".

Most of the information on ketamine analgesia has been deduced from clinical observations. Painful surgical procedures can be carried out under ketamine anaesthesia alone, without patients showing clinical signs of pain and many have commented on the duration of analgesia outlasting the period of anaesthesia (Bjarnesen and Corssen, 1967; Aguado-Matorras and Nalda-Felipe, 1970). On the experimental side Domino, Chodoff and Corssen (1965) used crushing haemostats on the skin of volunteers to determine the onset of analgesia. Nolte and associates (1968) used a standard pain stimulus with a spring "algometer" and demonstrated analgesia in the postoperative period after ketamine. In a limited study on six patients, Iwatsuki and associates (1967) measured the pain response to pressure on the anterior surface of the tibia in patients recovering from ketamine anaesthesia and demonstrated analgesia lasting for up to 1 hour.

In view of the limited amount of controlled data available on ketamine analgesia, it was felt that further studies of its effect on experimentally-induced somatic pain were required. This paper reports such an investigation in twenty-eight patients, using a method of measurement with which we have had considerable experience. It also compares the findings with those previously obtained with thiopentone.

METHOD

Studies were carried out on female subjects undergoing minor gynaecological operations. Premedication consisted of either atropine 0.6 mg alone or with morphine 10 mg. This latter is referred to as the "opiate" series.

Sensitivity to somatic pain was measured by the application of an increasing degree of pressure to the anterior surface of the tibia and subjects were asked to identify two end points, (a) first feeling of pain and (b) when pain became unbearable. These are referred to as "threshold" and "response" readings respectively and the point on the scale of the algesimeter at which these occurred was noted. Readings are not given in any absolute units, each 1-lb. division on the scale of the balance simply being designated as 1 pain unit. The average of the threshold and response readings are used throughout and all findings are expressed as changes from the pre-anaesthetic control.

It will be appreciated that a method of algesimetry which depends on the patient's clear definition of one or two end points can only be used in the conscious subject. Its application and limitations have been described by Dundee and

J. G. BOVILL, M.B., F.F.A.R.C.S.; J. W. DUNDEE, M.D., PH.D., F.F.A.R.C.S.; The Queen's University of Belfast, Northern Ireland.

Moore (1960) who have also investigated the expected range of variation in repeated observations in normal subjects. All algesimetry readings were made by the authors.

In all patients duplicate control readings were carried out immediately before injection of the ketamine. These had to be within 2 units of each other, otherwise the subject was excluded from the trial.

The study was divided into two parts. The first was carried out prior to surgery. Subhypnotic doses (10 and 20 mg) were injected and readings taken at minute intervals for 6–8 minutes. The smaller dose was repeated at the 6th minute and readings taken for a further 6 minutes.

The second study was carried out in the postoperative period on patients receiving normal anaesthetic doses (2–3 mg/kg). Observations were made as soon as they could respond to commands and were continued at 5–10-minute intervals for up to an hour.

RESULTS

Figure 1 shows the findings with the small doses. While 10 mg had no obvious effect on the level of consciousness, patients were often drowsy for a few minutes after the 20 mg dose, but none actually fell asleep. Analgesia was detected in all nine patients given the 20 mg dose. This had occurred within 1 minute of injection and lasted between 5 and 8 minutes. The 10 mg dose produced less marked analgesia, but when it was repeated the effects were more striking. With this dose analgesia lasted about 5 minutes. Antanalgesia did not occur with subhypnotic doses and the duration and intensity of ketamine analgesia did not appear to be affected by the premedication.

Patients were able to co-operate in algesimetry studies between 10 and 15 minutes after normal anaesthetic doses (2–3 mg/kg) of ketamine. Figure 2 shows that nearly all patients showed profound somatic analgesia in the postoperative period, which lasted between 35 and 45 minutes after the injection of ketamine. Its occurrence and duration was not obviously affected by the premedication. Antanalgesia was only detected in one patient (atropine premedication) who was apprehensive and gave very high control readings, and who was restless and upset at the time when the apparent increased sensitivity to somatic pain occurred.

Figure 3 compares the mean findings in the postoperative period in fourteen patients who received large doses of ketamine with those in twelve patients who received clinical doses of thiopentone (Dundee, 1960). The difference between the two drugs is obvious.

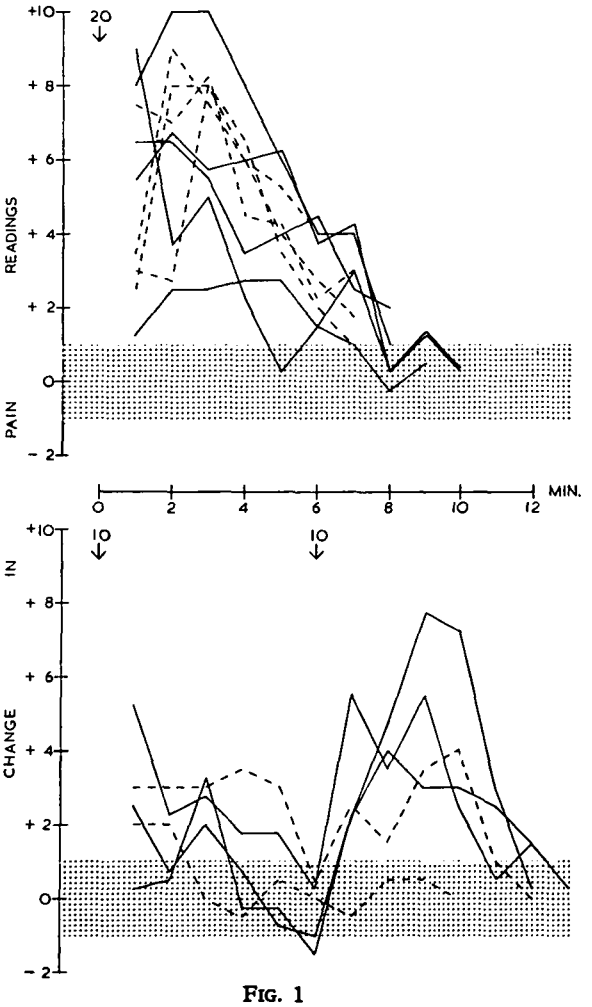

FIG. 1

Effects of small (10 mg and 20 mg) doses of ketamine on experimentally induced somatic pain. Findings are expressed as changes from control.

--- Atropine premedication.

—— Opiate premedication.

Stippled area indicates accepted experimental error of this method of algesimetry.

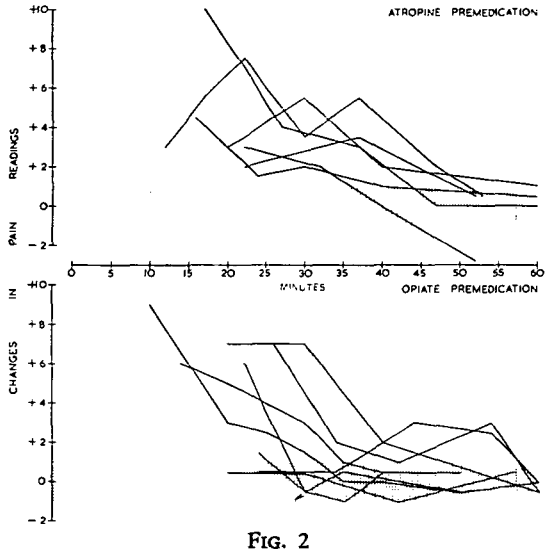

FIG. 2

Algesimetry studies carried out in the postoperative period after ketamine anaesthesia. Findings are expressed as changes from pre-operative control. Stippled area indicates accepted experimental error of this method of algesimetry.

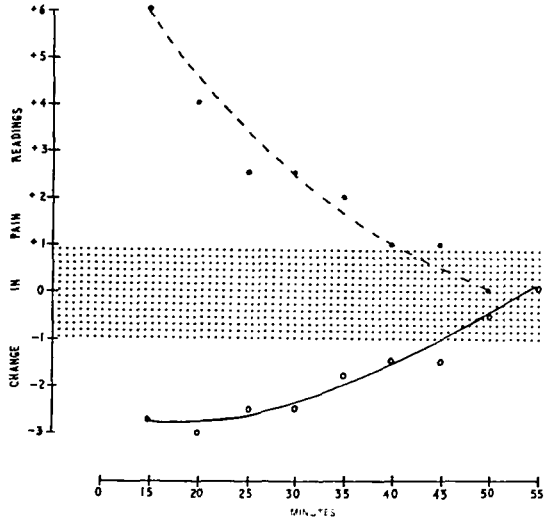

FIG. 3

A comparison of the mean effect of clinical doses of thiopentone (——) and ketamine (- - - -) on post-operative algesimetry readings. Stippled area indicates accepted experimental error of this method of algesimetry.

DISCUSSION

This paper confirms that ketamine produces profound somatic analgesia. This occurs with subhypnotic doses and outlasts the period of sleep produced by normal anaesthetic doses. This latter finding is contrary to the view expressed by Wilson, Fotias and Dillon (1969) but is in keeping with the clinical impressions of other workers.

REFERENCES

Aguado-Matorras, A., and Nalda-Felipe, M. A. (1970). Selection of indications on the use of CI-581 and observations on 198 cases; in *Progress in Anaesthesiology*, p. 1000. Amsterdam: Excerpta Medica.

Bjarnesen, W., and Corssen, G. (1967). CI-581: a new non-barbiturate short acting anesthetic for surgery in burns. *Mich. Med.*, **66**, 177.

Corssen, G., and Domino, E. F. (1966). Dissociative anesthesia: further pharmacologic studies and first clinical experience with the phencyclidine derivative CI-581. *Anesth. Analg. Curr. Res.*, **45**, 29.

Domino, E. F., Chodoff, P., and Corssen, G. (1965). Pharmacologic effects of CI-581, a new dissociative anesthetic in man. *Clin. Pharmacol. Ther.*, **6**, 279.

Dundee, J. W. (1960). Alterations in response to somatic pain. II: The effect of thiopentone and pentobarbitone. *Brit. J. Anaesth.*, **32**, 407.

—— Moore, J. (1960). Alterations in response to somatic pain associated with anaesthesia. I: An evaluation of a method of analgesimetry. *Brit. J. Anaesth.*, **32**, 396.

Iwatsuki, K., Aoba, Y., Sato, K., and Iwatsuki, N. (1967). Clinical study on CI-581, a phencyclidine derivative. *Tohoku J. exp. Med.*, **93**, 39.

Nolte, H., Teuteberg, H., Dudeck, J., Munchhoff, W., and Rumpf, K. (1968). Vergleichende untersuchungen uber die analgesie nach anaesthesien mit ketamine, thiopental und propanidid. *Der Anaesthesist*, **18**, 24.

Wilson, G. H., Fotias, N. A., and Dillon, J. B. (1969). Ketamine: a new anesthetic for use in pediatric neuroroentgenologic procedures. *Amer. J. Roentgenol.*, **106**, 434.

ALTERATIONS, DU FAIT D'UNE ANESTHESIE, DE LA REPONSE A UNE DOULEUR SOMATIQUE

XX: CETAMINE

SOMMAIRE

L'administration de doses subhypnotiques de cétamine a provoqué une diminution transitoire de la sensibilité à la douleur somatique. L'analgésie peut être mise en évidence au bout de 40 minutes après l'injection de doses anesthésiques normales (2–3 mg/kg). A l'inverse de l'effet des barbituriques, il ne se produit pas d'antanalgésie après administration de cétamine.

VERÄNDERUNGEN DER REAKTION AUF SOMATISCHE SCHMERZEN DURCH ANAESTHESIERUNG

XX: KETAMIN

ZUSAMMENFASSUNG

Subhypnotische Dosen von Ketamin verursachen eine vorübergehende Abnahme der Sensitivität für somatische Schmerzen. Bis zu vierzig Minuten nach der Verabreichung einer normalen Dosis des Anaesthetikums (2–3 mg/kg) konnte eine Analgesie beobachtet werden. Im Gegensatz zur Wirkungsweise der Barbiturate entsteht nach Ketamin keine Antanalgesie.

ALTERACIONES EN LA RESPUESTA A DOLOR SOMATICO DURANTE LA ANESTESIA

XX: QUETAMINA

RESUMEN

Dosis subhipnóticas de quetamina causan una disminución transitoria de la sensibilidad al dolor somático. La analgesia puede ser detectada hasta 40 minutos después de dosis anestésicas normales (2–3 mg/kg). Al contrario de la acción de los barbituratos, después de la quetamina no ocurre antanalgesia.

BOOK REVIEW

Obstetrical Anesthesia: Current Concepts and Practice. Edited by Sol M. Shnider, M.D. Published by the Williams and Wilkins Co., Baltimore. Price £5.50.

In few areas of medicine does practice in the United States and Great Britain differ so much as in obstetrics and obstetric anaesthesia. The reasons for this are many, but the fact makes for difficulty when reviewing books on the subject from the opposite side of the Atlantic.

Dr Shnider's book has a long list of eminent contributors but the chapters are disappointingly short, with the result that arguments cannot be properly developed. Fewer chapters would allow each author to penetrate the subject more deeply and improve the usefulness of the book as a standard reference.

The quality of the many sections varies considerably and the editing could have been somewhat tighter. For example, Dr Bonica gives an excellent account of the circulatory and respiratory changes during pregnancy but the salient points of this are largely ignored in a chapter on hypotension by Dr Asling. Because of the high incidence of the use of regional anaesthesia, particularly spinal anaesthesia, hypotension is rightly feared but it always appears to be equated with a low cardiac output. Thus the emphasis is on treatment of the hypotension and not on increasing flow. Vasoconstrictors are extensively used both prophylactically and therapeutically and one has the impression that, if the book was squeezed hard, ephedrine would drip from its pages. It is little wonder that a special chapter on post-delivery hypertension is included. Hypotension with a low cardiac output involves a large component of inferior vena caval occlusion and its relief is essential. Mention is made of left uterine displacement (abbreviated horribly to L.U.D.) but recourse to vasopressors appears to be the main form of treatment. No mention is made of turning the patient into the semilateral position or of rapid foetal delivery. This last point emphasizes particularly one difference between our two countries. According to the data available in the book, delivery by Caesarean section seldom takes place within 20 minutes and it frequently takes more than 30 minutes.

Dr Moya writes well about utero-placental transfer of drugs, but it is disappointing that he makes no mention of the particular problem of bolus intravenous injection.

British anaesthetists will be disappointed by the section on general anaesthesia which is only recommended if regional block is contraindicated. In dealing with the question of inhalation of gastric contents the prophylactic passing of stomach tubes is largely discounted. Although this does not guarantee an empty stomach, the aspiration of considerable quantities of fluid can be achieved and this must make for a safer situation. Cricoid pressure is mentioned several times but no warning is given that this manoeuvre can distort considerably the normal view of the larynx. How many anaesthetists would agree that, if the maternal veins are difficult, cyclopropane induction should be given while an assistant sets up a drip?

No mention is made of the hypertensive effects of ergometrine in pre-eclampsia; of concealed accidental haemorrhage with its unique combination of blood loss and hypertension; or the use of beta-sympathetic stimulators in premature labour. The circulatory effects of the Valsalva manoeuvre are incorrectly described as are the action of ephedrine and the effects of sympathetic blockade. Contrary to what is stated in the book, the foetus can be monitored in utero with external microphones and an external tochograph. The idea that all doctors should be trained in obstetric anaesthesia can only be regarded with extreme apprehension.

In summary, there is much useful information in this book, but the reader must retain a certain amount of scepticism about some of the opinions.

D. B. Scott