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CLINICAL STUDIES OF CT 1341, A NEW STEROID ANESTHETIC

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Introduction

For many years barbiturates have been known as the sole intravenous anesthetic agents despite their low therapeutic index, local irritation at the site of injection and prolonged after effects. On the other hand steroid derivatives have been known to possess anesthetic properties.

In the present communication we describe the pharmacological properties of a new steroid anesthetic (CT, 1341) and the results of 150 anesthesia performed with this agent.

Chemistry: CT 1314 is a mixture of two steroids, 3 alphahydroxy-5 alpha-pregnane-11, 20-dione (steroid I) and 21-acetoxy-3 alpha-hydroxy-5 alpha-pregnane-11,20-dione (steroid II), Both are anesthetic agents but the former has approximately twice the potency of the latter steroid II, however, greatly increases the solubility of steroid I and the standard solution

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*In Iran (Althesin or Alfathesin).

contains 9 mg of the steroid I with 3 mg of steroid II in each ml of 20% Cremophor EL (1).

Physical properties: CT 1314 is a ready prepared clear solution which is isotonic with the blood and its pH is approximately equal to that of the blood.

Pharmacology: The mechanism of action of CT 1314 is not well understood. However, it seems that its mechanism of action is not different to the other short acting anesthetics. The therapeutic index of the drug is high, thus it possesses a wide margin of safety which is one the remarkable advantages of the drug. The anesthesia is induced rapidly with the drug. This is true also in the case of recovery from anesthesia.

A sleep dose of CT 1314 produces unconsciousness in about 30 seconds. The patient awakens five to ten minutes later. The duration of anesthesia may be prolonged by repeated injections of the drug. Surgical analgesia appears to be present for approximately half period of anesthesia. During the course of anesthesia the pupils may dilate which is not indicative of the depth of anesthesia. In most cases the eyelash reflex disappears some 30 seconds after the onset of unconsciousness but occasionally it persists through out, or until inhalational anesthesia is used. There is good relaxation of the mucles of the abdomen and of the jaw.Muscle twitching may precede this relaxation, more particularly with higher dosage and speed of injection of the drug. The glottic and laryngeal reflexes return quickly as the depth of anesthesia lightenes. Progress to complete recovery is normally more rapid than barbiturates. The cardiovascular changes occuring after a unique doses

of the drug are as follow: peripheral vasodilation, rarely flushing of the skin, leads to the fall of central venous and arterial blood pressure at about 10-20%. Recovery from this fall is very rapid. The cardiac output is maintained or even increased. Blood pressure is maintained by a reflex increase in peripheral vascular resistance. Following the induction there may be a breif apnea or irregularity of respiration. The depth of respiration is decreased.

CT 1314 is used mainly for the rapid induction of anesthesia especially when rapid recovery is desired. Thus the drug is indicated in all circumstances where an intravenous anesthetic is appropriate. except in cases of obstetrics, neurosurgery, in infants up to one year and in patients with obstructive jundice (2).

CT 1314 is removed from the circulation by the liver, and recovery from anesthesia is not dependent upon redistribution in the tissues. The changes in serum cortisol and blood sugar levels are similar to those found after administration of barbiturates.

CT 1314 shows no evidence of teratogenicity in experimental animals, but it should be used with caution in pregnancy. Thrombophlebitis has not been reported. Nausea and vomiting are infrequent. The patient may experience mild euphoria, but hallucinations have not been reported. There is usually amnesia for events immediately prior to the injection of the drug. No vein damage was encountered in any animal and human treated with CT 1314. This is true for hemorrhage, edema, congestion and external damage in surrounding tissues. In addition there was no macroscopic arterial injury.

The drug proved compatible with muscle relaxantes,

premedicant drugs and inhalaion anesthetics in clinical uses (3).

Number of cases	Age	Operation
48	4-20 Years	Tonsilectomy
35	25-43 "	Cur-Tages (D.C.)
26	28-65 "	Appandectomy and Fissure, Fistole
37	25-52 "	Endoscopy
1	28 "	Mitral Valvoltomy
1	56 "	Oesophagos Tumore
2	52-54 "	Hiatal Hernia
150		

Materials

Hundred and fifty patients of both sexes were used in this study Table 1. They were anesthetized for minor and major surgery. The cases of minor surgery consisted of tonsilectomy, hemorrhoid, diffuse abscesses and endoscopy investigations. The cases of major surgery consisted of thoracic surgery for lung manipulations,cardiac surgerymainly mitral valvulotomy and gastro intestinal tract cancers (especially oesophagus) or hiatal hernia.

The duration of anesthesia was dependent to the disease for which the patient was under operation.
It ranged from 7-15 minutes in the case of minor surgery and up to 6 hours in the case of major one. In minor surgery cases, in which the patients were anesthetized only with CT 1314, depending on the time course of surgery CT 1314 administration was repeated for up to 3 times. In the cases of major surgery only one injection of the drug was made and the anesthesia was continued by halotane, nitrous oxide and mucle relaxants like d-tubocurine. In addition the patients received oxygen
As mentioned in the introduction the drug was used only for the induction of anesthesia.

Results

The induction of anesthesia was very short and almost less than one minute. The duration of anesthesia was about 7-10 minutes. The time of action between Tiopenton and Methohexitone. In the case of minor surgery the drug was used repeatedly up to three times.
The patient tolerance to the drug was excellent. One of the major inconveniences we encountered was a fall in blood pressure and rarely respiratory depression which was (A) always due to rapid injection of the drug. Moreover, in the cases of repeated injections of the drug there was a remarkable increase in the recovery time which was about 30 minutes. This was less than 5 minutes in cases the patients received only one injection of CT 1314. We have no observed techycardia,irritation of

injection side, or hallucination.

Premedication was standard, atropine 0.6 mg i.m. one hour before anesthesia. The usual dosage was 0.6-0.9 mg/kg body weight of the drug which was equivalent to 0.05-0.075 ml/kg body weight of the standard solution. Younger children usually required higher doses. The drug was dissolved in 0.85% sodium chloride or in plain water. In some instances we encountered hypotension which could be prevented only slow injection of the drug. This was made by injecting the drug over about one minute. Because the drug is known to be metabolized in the liver we never used it in patients with impaired liver function. Respiratory depression occured rarely and in such cases it was due to overdosage of thedrug. In this event we supported respiration mechanically,in accordance with standard anesthetic pactise, rather than by analeptic drugs alone.

Discussion

CT 1314 is a new short acting intravenous anesthetic containing two steroids. It is useful for the induction of anesthesia. According to our experience and reports of the other investigators it is a safe drug for the induction of anesthesia in cases of minor and major surgery. It has no appreciable local or systemic side effects. The induction time as well as the time course for recovery is very rapid. Cardio-pulmonary depression may occur which we believe could be prevented by the slow injection of the drug.

Of the great advantages of this drug is its large

therapeutic index ($\frac{\text{lethal dose 50}}{\text{Anesthetic dose 50}}$. The anesthetic does is also verylow. It is 1.8 mg/kg in mice compared to 6.9 mg/kg for sodium thiopentone and 7.4 mg/kg for sodium methohexitone (4).

Bacause the drug is metabolized in the liver it is suggested that it should not be used in patients with liver dysfunction. It does not show incomoatibility With other anestetics or premedicant drugs. There have been no reports also ofundue summation of effect with sedatives, premedicant drugs and other anesthetics. In patients with condition allergic (such as Asthmatic) CT 1314 should be used with caution.

SOMMAIRE

CT 1314 est un nouvel anesthesique intraveineux qui semble etre depourvu des desavantages des steroides anesthesiques precedents. La fomule est un melange de deux steroides. La dose optimale pour l'induction est 50-60 mog/kg. Des doses beaucoup plus elevees peuvent etre administrees sans effets secondaires remarquables. Avec l'augmentation de la dose la frequence des mouvements musculaires, de la depression respiratoire et de l'hypo-tention s'accroient. La duree d'action est intermediaire entre celle des barbituriques et de propanidid.

Summary

CT 1314 is a new steroid anesthetic which is used for the rapid induction of anesthesia. Its duration of action as well as the time course for the recovery is rapid. It has a high therapeutic index and proved compatible with other drugs used in anesthesiology.No

appreciable side effects has been encountered during anesthesia with thisdrug. To avoid any disturbance in cardio-pulmonary system it is recommended to be injected slowly.

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