THE SPEED OF ONSET AND POTENCY OF ALTHESIN

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SUMMARY

The speed of onset of anaesthesia with Althesin has been compared with that of other intravenous anaesthetics. Like thiopentone, Althesin appears to be a truly rapidly acting drug, producing sleep in one arm–brain circulation time. The relative potencies of the drugs studied were approximately Althesin 60 µlitre/kg equivalent to thiopentone 4 mg/kg, equivalent to methohexitone 1.2 mg/kg, although by some criteria Althesin 80 µlitre/kg is required to produce an effect equivalent to thiopentone 4 mg/kg.

Intravenous anaesthetic agents can be classified according to whether or not they produce sleep in one arm–brain circulation time. The latter group includes pentobarbitone and hydroxydione, which have passed out of clinical use, and diazepam, which may be regarded more as a basal sedative than as an anaesthetic drug (Brown and Dundee, 1968). The main disadvantage of drugs of slow onset is that the anaesthetist cannot easily vary the dose in the light of the response of the patient, because of the delay in this response. In addition, side effects such as arterial hypotension appear to be delayed along with the slow onset of sleep. Experimental work with Althesin in animals suggested that the onset of action was rapid (Child et al., 1971) but the present investigation was designed to confirm this in man.

In the context of intravenous anaesthesia it is possible to define potency as the relative amounts of drugs which will produce the same depth of sleep, and accurate estimates of potency are of great importance, particularly in the investigation of new drugs (Clarke et al., 1968). Inaccurate values can lead to erroneous clinical impressions concerning, for example, the relative duration of action of drugs, such as occurred in the case of thiopentone and buthalitone (O'Mullane, 1957). Since the incidence and severity of side effects following induction with intravenous barbiturates are dose-related (Barron and Dundee, 1967) a wrong estimate of potency may cause unfair condemnation of a drug (Lunding and Moller, 1964).

Intravenous injection during a period of reactive hyperaemia following temporary ischaemia of the forearm has been used by Dundee and McArdle (1959) to reduce the time during which an irritant intravenous anaesthetic (hydroxydione) was in contact with a vein wall. In subsequent studies Dundee, Barron and King (1960) and Clarke and his colleagues (1968) made use of this period of hyperaemia to reduce the arm–brain circulation time while investigating the relative potencies of thiopentone and other barbiturates. Varying doses of these drugs were injected as rapidly as possible and the onset time taken as the time from the end of injection until the patient stopped counting aloud. The minimum dose of each drug con-
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sistently causing sleep in one arm–brain circulation
time was taken as a guide to the relative potency
of that drug.

The purpose of the present study was to investi-
gate the rapidity of onset of sleep following various
doses of Althesin, and to determine the potency of
this anaesthetic agent relative to standard barbitu-
rates. Some of the preliminary findings have been
presented by Clarke, Dundee and Carson (1972).

METHOD

Observations were made on 190 healthy women
patients who received atropine sulphate 0.6 mg
i.m. as the sole premedication. The circulation to
one arm was occluded by a sphygmomanometer
cuff, inflated to about 220 mm Hg for 2.5 min
(Clarke et al., 1968). Twenty seconds after releas-
ing the cuff, the predetermined dose of Althesin
was injected as rapidly as possible through a 21
s.w.g. needle into a large antecubital vein. The
patients were asked to count aloud and the time
from the end of injection until counting ceased
was measured with a stopwatch. Conventional
maintenance anaesthesia with nitrous oxide and
oxygen was then implemented until the end of
surgery.

RESULTS

Figure 1 shows the scatter of individual “onset
times” following various doses of Althesin given
during reactive hyperaemia. The average times of
onset of sleep at the different dose ranges of
Althesin are tabulated in table I. These mean times
are also represented in the figure by the con-
tinuous line.

A comparison of the curve obtained for Althesin
with those previously determined for methohexi-
tone and thiopentone (derived from the findings of
Clarke and his colleagues, 1968) suggested that the
onset time with the different drugs was similar
(fig. 2). On the basis of a mean onset time of 10.5
sec, 60 μlitre/kg Althesin was noted to be equipotent
with thiopentone 4.0 mg/kg. However, on the basis
of the dose required to induce anaesthesia in 90%
of patients within 11 sec, 80 μlitr/kg Althesin
was required to produce a similar effect to that of
thiopentone 4.0 mg/kg.

In contrast, figure 2 also gives the mean times for
the onset of action of ketamine (derived from the
findings of Bovill and his colleagues, 1971) and the
difference between ketamine and the other drugs is
obvious.

DISCUSSION

The present study shows that, as with the barbitu-
rates, adequate doses of Althesin given at the height
of reactive hyperaemia will produce sleep in 90%
of patients in 11 sec. In addition, the average time
of onset of sleep is 10–10.5 sec.

![Graph](https://academic.oup.com/bja/article-abstract/47/4/512/245848)
This method of measuring potency of drugs is based on the assumption that the arm-brain circulation time is the only major factor affecting the rate of onset of action of the drugs being studied. Other factors such as the degree of ionization and lipid solubility are standard. Mark and his colleagues (1958) have shown that there is no delay because of a "blood-brain barrier" in the action of thio-barbiturates. A similar rapid uptake of radioactively labelled Althesin by the brain, especially in the grey matter, has been demonstrated by Card, McCulloch and Pratt (1972).

Although the onset of anaesthesia with Althesin is not significantly slower than with the barbiturates, there does appear to be a wider scatter in the time of onset of sleep in the clinical range of dosage (40–80 μlitre/kg). It must be concluded, therefore, that a range of 60–80 μlitre/kg is equipotent with thiopentone 4.0 mg/kg or methohexitone 1.2 mg/kg.

REFERENCES


LA RAPIDITE DE DEPART ET L'EFFICACITE DE L'ALTHESINE

RESUME

La rapidité du départ de l'anesthésie avec l'Althesine a été comparée à celle d'autres anesthésiques intraveineux. Comme le thiopentone, l'Althesine semble être un médicamente agissant vraiment rapidement, et provoquant le sommeil en un seul temps de circulation bras-cerveau. L'efficacité relative des médicaments étudiés était la suivante: environ 60 µl/kg d'Althesine correspondent à 4 mg/kg de thiopente et à 1,2 mg/kg de méthohexitone bien que, selon certains critères, on doive avoir 80 µl/kg d'Althesine pour produire un effet équivalent à 4 mg/kg de thiopentone.

DIE GESCHWINDIGKEIT DES NARKOSEEINTRITTS UND DIE STÄRKE VON ALTHESIN

ZUSAMMENFASSUNG

Die Geschwindigkeit des Eintretens der Narkose mit Althesin wurde verglichen mit der bei anderen intravenösen Narkosemitteln. Althesin scheint ebenso wie Thiopentone eine wirklich schnell wirkende Droge zu sein, die innerhalb einer einzigen Zirkulationsperiode zwischen Arm und Gehirn Schlauf hervorruft. Die relativen Stärken der untersuchten Drogen waren ungefähr: 60 µl/kg Althesin waren aquivalent zu 4 mg/kg Thiopentone und zu 1,2 mg/kg Methohexiton, obwohl nach manchen Kriterien 80 µl/kg Althesine erforderlich sind, um eine Wirkung zu erzielen, die 4 mg/kg Thiopentone entspricht.

LA RAPIDEZ DE INICIACION Y POTENCIA DEL ALTESIN

SUMARIO

Se ha comparado la rapidez de iniciacion de la anestesia con Altesin con la de otros anestesicos intravenosos, tales como tiopentono. El Altesin parece ser una droga de accion rapida y segura, produciendo sueno en un tiempo de circulacion brazo-cerebro. Las potencias relativas de las drogas que se estudiaron fueron aproximadamente: Altesin 60 µl/kg equivalente a 4 mg/kg de tiopentono, a 1,2 mg/kg de metohexiton, a pesar que segun algunos criterios se necesitan 80 µl/kg de Altesin para producir un efecto equivalente a 4 mg/kg de tiopentono.