INTERRVENEUS METHAQUALONE:
A NEW NON-BARBITURATE ANAESTHETIC

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SUMMARY
Methaqualone, a non-barbiturate hypnotic, was used as the sole anaesthetic for short surgical procedures in 27 patients. In a further 13 it was, in addition, injected intermittently during nitrous oxide anaesthesia for longer operations. Rapid loss of consciousness followed intravenous injection of adequate doses. Transient generalized muscle spasm followed the onset of sleep, after which there was muscle relaxation. Recovery was uneventful and after a single dose consciousness began to return in 10–15 minutes.

For many years the barbiturates were the agents of choice for the intravenous induction of anaesthesia, but recently non-barbiturate drugs, such as propanidid, diazepam and ketamine, have been studied. Each of these has some advantages and some disadvantages over thiobarbiturates but none could be called ideal. There is obviously a need for continued research in this field.

The hypnotic property of methaqualone was first discovered in this laboratory (Gujral and Kohli, 1955). The oral preparation (Melsed, Quaalude, Sedaquin) is now commonly employed as a hypnotic since it has a wider margin of safety than the barbiturates (Soncin, 1961; Gujral, Kohli and Saxena, 1956). It is a 2,3-disubstituted quinazolone with the following structural formula:

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\text{Chemical structure of methaqualone} \quad \begin{array}{c}
\text{CH}_3 \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{CH}_3
\end{array}
\]

Its chemical configuration is unlike that of any other commercially available hypnotic. Methaqualone base is a stable crystalline compound which is colourless, odourless and bitter in taste. As a free base it has a melting point of 115–116°C. It is insoluble in water and most other solvents. However, it can be dissolved in propylene glycol, glycerol, acetone, benzene, arachis oil, spans and tweens.

Trials of intramuscular methaqualone, dissolved in propylene glycol, were encouraging in cases of tetanus. It abolished the muscular spasm and produced deep hypnosis (Saxena et al., 1967). After intramuscular injection of 200–400 mg of the drug the effects were apparent within 5–10 minutes and lasted for about 2 hours. Intravenous injections were also tried, the onset of deep hypnosis occurring within 1/4–1 minute with relaxation of spasms lasting for 15–20 minutes. For these reasons it was considered worthwhile to investigate the possibility of using intravenous methaqualone (1) alone for short surgical procedures, (2) for induction of anaesthesia in place of thiopentone and (3) to produce relaxation during surgical procedures.

Presentation. A 10 per cent solution of methaqualone base in boiling propylene glycol was made and immediately placed in dry 2- and 4-ml ampoules. The ampoules were sealed and sterilized. The shelf life of the preparation is at least 1 year. The solution is precipitated in the presence of moisture; therefore it is essential to use an absolutely dry syringe for intravenous injection. It is advisable to use a wide-bore needle because the solution is slightly viscous.

METHOD AND RESULTS
Patients. The study was carried out on 40 otherwise healthy adult patients undergoing surgery of the ear, nose and throat (chronic tonsillitis, deviated septum, foreign bodies in ear and nose) or general surgery (appendicectomy, cholecystectomy). Consent was

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obtained from each patient to use methaqualone intravenously. Patients were free from intercurrent disease of a kind which might influence the drug trial.

Premedication. Hyoscyamine 0.5 mg was injected intramuscularly at least half an hour before the induction of anaesthesia.

The cases were grouped as follows:

Series 1. In 27 patients aged 15–65 years a single intravenous injection of methaqualone (5 mg/kg) was the sole anaesthetic agent for short procedures such as the removal of foreign bodies from the ear and nose and diagnostic bronchoscopy (21 cases). In the first 7 of the 21 patients having diagnostic bronchoscopy, there was reaction to the passage of the instrument. Thereafter the larynx and trachea were sprayed with 1–2 ml of 4 per cent lignocaine solution. Respiration was spontaneous throughout and no other anaesthetics were required for maintenance. Intubation was not carried out in this series.

Series 2. In 13 patients (6 for tonsillectomy and 7 for laparotomy) a standard dose of methaqualone (300 mg) was injected intravenously for induction of anaesthesia, the cords were sprayed with lignocaine, and anaesthesia was maintained with 70 per cent nitrous oxide in oxygen. This single dose, in addition to putting the patient to sleep, produced sufficient relaxation to permit endotracheal intubation without the use of a short-acting muscle relaxant.

For laparotomy, injection of methaqualone in a dose of 200 mg was repeated 2–3 times to produce muscular relaxation adequate for intra-abdominal surgery and for closure of the peritoneal cavity. The interval between the first and second doses was in the region of 25 minutes whereas between the second and third it was slightly longer (approximately 35 minutes). Under these circumstances, when anaesthesia was being maintained with nitrous oxide/oxygen, methaqualone produced apnoea lasting for 2–3 minutes. During this period respiration was controlled and on return of spontaneous breathing, assisted ventilation was required for a further 15–20 minutes.

At the end of operation breathing was always clinically adequate. Consciousness returned as soon as nitrous oxide had worn off and patients quickly responded to command.

Course of anaesthesia.

Consciousness was lost almost immediately following the intravenous injection of an adequate dose of methaqualone, the rapidity of the onset of sleep being similar to that following injection of thiopental. Transient generalized muscle spasm followed the onset of sleep and lasted for about a minute. This was followed by muscular relaxation. Apart from this, induction was quite smooth.

In one patient intravenous premedication was given rather late and violent coughing followed but this was not seen in other patients where timing of premedication was correct.

Despite relaxation of masseters (which permitted easy insertion of the laryngoscope blade), loss of corneal and conjunctival reflexes, the cough reflex appeared to remain intact. There was no obvious depression of respiration and patients did not respond to painful stimuli. Bronchospasm was not observed in this series.

No marked changes in blood pressure and pulse rate were found during induction and maintenance of anaesthesia or during the postoperative period.

Relaxation was adequate for abdominal surgery, the effect lasting for about 15 minutes. There was no protrusion of abdominal contents. Retraction of the abdominal wall could be performed with ease and peritoneal closure presented no problem.

In this series, although single doses did not depress respiration to the point of apnoea, it was interesting to note that methaqualone when used repeatedly with nitrous oxide and oxygen did produce apnoea lasting for 2–3 minutes. The mechanism of this is not clear. It would appear that methaqualone has a cumulative action because with repeated injections the duration of apnoea was progressively prolonged, and while initial doses were 300 mg, subsequent doses of 200 mg were adequate.

As a special study in one otherwise healthy patient methaqualone 300 mg was given intravenously as the sole anaesthetic agent for oesophageal dilatation. In order to detect if it has any neuromuscular blocking effect, myography was performed after ulnar nerve stimulation. For this purpose, methaqualone injections were repeated intermittently at intervals of 15–20 minutes up to a total dose of 1200 mg (20 mg/kg) over a period of 1½ hours. No evidence of neuromuscular blockade was found. This patient remained deeply sedated for 12 hours, although his conjunctival and corneal reflexes returned to normal after 60 minutes of the last dose. He responded only to painful stimuli or to loud commands. The same patient was given nitrous oxide and suxamethonium for a further oesophageal dilatation and it is of interest to note that the patient requested methaqualone for his subsequent dilatation.
Recovery.

Recovery could only be assessed in patients who were given methaqualone as sole anaesthetic agents for minor procedures. Following the intravenous dose of 5 mg/kg consciousness began to return in about 10–15 minutes and recovery appeared to be complete in 15–20 minutes as judged by the return of ocular and pharyngeal reflexes and response to painful stimuli and simple commands. A striking feature of recovery from methaqualone was the rapid return of purposeful reflexes and response to queries and there appeared to be no residual depression such as is found with thiopentone.

No nausea and vomiting followed the use of the drug as sole agent. Thrombophlebitis was not noted at the site of injection.

As a further special study in 5 cases, serum transaminase and alkaline phosphatase estimations were carried out as tests of liver function before and at 1, 3 and 8 days after the use of methaqualone. Also the blood and urine were examined to detect any haematological derangement. No significant hepatotoxic effects or alterations in blood pressure or renal function were noted in the series.

From a limited observation it would appear that the drug is fairly non-toxic because after 20 mg/kg total dose no changes in vital signs were noted.

The use of methaqualone as an induction agent and as a muscle relaxant during laparotomy should be explored further.

ACKNOWLEDGEMENTS

We express our gratitude to Sarabhai Chemicals, Standard Pharmaceuticals and Boots Pure Drug House for general supplies of methaqualone and to the Indian Council of Medical Research for financial support.

REFERENCES


METHAQUALONE ADMINISTRER PAR VOIE INTRAVEINEUSE: UN AGENT ANESTHESIQUE NOUVEAU, NON-BARBITURIQUE

SOMMAIRE

Méthéqualone, un agent hypnotique non-barbiturique, a été utilisé comme seul anesthésique dans des interventions chirurgicales de courte durée chez vingt-sept malades. Chez treize autres malades, cet agent a été administré en injections intermittentes, en tant qu'adjacent, au cours d'anesthésies au protoxyde d'azote, pendant des opérations plus longues. Une rapide perte de conscience a succédé à l'injection intraveineuse de doses adéquates. Un spasme musculaire généralisé et transitoire a fait suite à l'installation du sommeil, après quoi un relâchement musculaire a été observé. La guérison des malades s'est déroulée sans incident et une reprise de conscience s'est opérée au bout de 10 à 15 minutes après administration de doses uniques.

METHAQUALONE: EIN NEUES BARBITURATFREIES ANASTHETIKUM ZUR INTRAVENOSEN INJEKTION

ZUSAMMENFASSUNG


METACUALONAINTRAVENOSA: UN NUEVO ANESTESICO NO BARBITURICO

RESUMEN

La metacualona es un hipnótico no barbitúrico que fue utilizado como único anestésico para intervenciones quirúrgicas breves en veintisiete pacientes. En otros trece, fue inyectado intermitentemente durante la anestesia por óxido nítrico para operaciones más largas. La inyección intravenosa de dosis suficientes fue seguida por una rápida pérdida de la conciencia. El comienzo del sueño fue seguido por un espasmo muscular generalizado transitorio, después de cual hubo relajación muscular. El restablecimiento fue sin complicaciones y después de dosis únicas la conciencia comenzó a reaparecer a los 10-15 minutos.