Flunitrazepam for the Intravenous Induction of Anaesthesia in Children

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SUMMARY

Flunitrazepam (Rohypnol) was compared with thiopentone as an anaesthetic induction agent in children between 4 and 12 years of age who underwent elective minor surgical procedures.

Successful induction of anaesthesia was achieved in both groups of patients. With flunitrazepam the induction time was longer but not statistically different from that with thiopentone. The incidence of apnoea was higher with thiopentone, but not significantly so.

It is concluded that flunitrazepam could prove a reasonable alternative to thiopentone as an intravenous induction agent in children who have to undergo elective minor operations.


Flunitrazepam (Rohypnol) is a tranquilizer of the benzodiazepine group, chemically closely related to nitrazepam. In animal experiments and clinical trials, the drug was shown to possess marked sedative, muscle relaxant and spasmylic properties. The hypnotic qualities of flunitrazepam suggest its use both as a sedative before anaesthesia and as an intravenous anaesthetic induction agent. However, no studies in the English-language literature have reported the use of flunitrazepam as an intravenous induction agent in children. This article presents the results of the effects of this drug compared with those of thiopentone as an intravenous induction agent in children who underwent elective minor procedures.

PATIENTS AND METHODS

Forty children (12 girls and 28 boys) between 4 and 12 years old who underwent elective minor surgical procedures were studied. The children were classified according to the American Society of Anesthesiologists' rating and all were either in category I or category 2. As premedication they received trimetrazine 3 mg/kg and atropine 0,01 mg/kg by mouth 1 - 2 hours before operation. The patients were allocated randomly to two groups based on hospital numbers. Those with even numbers received flunitrazepam (group I) and those with uneven numbers received thiopentone (group II) for induction of anaesthesia.

Anaesthesia was induced with either flunitrazepam 0,03 mg/kg or thiopentone 3 mg/kg. The dose of flunitrazepam was based on the recommendations of Hare. In a preliminary study, we used a smaller dose of flunitrazepam 0,015 mg/kg, but found the induction time to be unacceptably long; hence the dose selected was 0,03 mg/kg. The drugs were injected through a 23-gauge butterfly needle into a dorsal vein of the hand at an even speed over 20 seconds. The dead space of the needle had previously been filled with the relevant drug. The time from the start of injection of the agent to loss of eyelid reflex was recorded. Any excitatory movements, tremors, apnoea, cough or hiccups were noted. Induction was further classified as uneventful, minor (not interfering with general anaesthesia), more severe (interfering with general anaesthesia), or severe upset (endangering life). After the eyelid reflex had disappeared and the patient was considered anaesthetized, nitrous oxide in oxygen with enflurane (Ethane) was introduced for maintenance.

The pulse rate, measured by radial artery palpation and continuous ECG recording, and blood pressure, measured with the Riva Rocci method, were monitored regularly every 3 - 4 minutes after induction for 15 minutes, and then every 10 minutes throughout the procedure. Patients were observed for evidence of possible awareness during the operation, including changes in blood pressure and pulse rate, facial sweating, lacrimation, or body movements.

The duration of emergence from anaesthesia was timed from the end of induction of the anaesthetic until the patient was awake enough to understand spoken commands when he was considered fit to be discharged from the recovery room. In the recovery room, patients were observed for evidence of nausea, vomiting, respiratory depression or any other adverse effects attributed to the anaesthetic. No analgesic or infiltration with local anaesthesia was permitted during the study period. However, when the patient was considered awake, analgesia was administered, if required, in the routine manner.

The results were statistically analysed using a Student's t test for unpaired data and the chi-squared test.

RESULTS

The clinical data of the two groups of patients are given in Table I.

The mean age of patients in group I was 7,5 years (SEM 0,56), and that of patients in group II 7,4 years
The induction properties of flunitrazepam and thiopeptone were investigated in 40 children who received trimethazine 3 mg/kg and atropine 0,01 mg/kg per mouth 1 - 2 hours pre-operatively. Successful induction of anaesthesia was achieved in both groups of patients.

Halothane is still commonly used, but unacceptable cardiorespiratory depression often accompanies satisfactory operating conditions, especially in the very young. Enflurane was chosen because it leads to faster induction of anaesthesia than halothane. Furthermore, enfurane has muscle relaxant properties, and there is rapid emergence without a hangover.

Induction was trouble-free, and apnoea was encountered in group II only. Changes in blood pressure and heart rate, either during or after induction, were minimal. These findings confirm previous results. A small, but statistically insignificant fall in cardiac index was noted after the induction of anaesthesia with flunitrazepam 0,03 mg/kg in patients who required mitral valve replacement. Excitation during induction was attributed mainly to the too early introduction of the inhalational agent.

In group I, there was an obvious difference between the time to loss of response to verbal command and that to loss of eyelid reflex. The patients, when unresponsive to a spoken command, still had eyelid reflexes; hence the latter would seem not to be a good endpoint of anaesthesia. These findings confirm previous work. Flunitrazepam is a relatively slow-acting induction agent, but this in itself does not preclude its use as an induction agent before elective surgical procedures. Flunitrazepam has been claimed to be a better specific hypnotic than diazepam.

No patients had any major problems during recovery. Those in group I were certainly more drowsy than those in group II. This could be attributed to a greater sedative synergism between the flunitrazepam and the long-acting premedicant trimiprazine, than that between trimiprazine and thiopentone. There was no incidence of restlessness, excitatory movement, salivation, crying, or hypertonous in any of the children studied. Nausea and vomiting did not occur during the recovery phase.

In view of the above results, flunitrazepam would seem a reasonable alternative to thiopentone as an intravenous induction agent for elective minor operations in children, the main advantage being no clinically recognizable respiratory depression.

**REFERENCES**


**GROUP I**

Eyelid reflex disappeared on average 63,8 seconds (SEM 6,94) (range 17-113 seconds) after the administration of flunitrazepam. The average time from the end of general anaesthesia to when the patient was fully awake and could be discharged from the recovery room was 36,6 minutes (SEM 3,81), with a range of 15 - 60 minutes. Nine patients showed evidence of slight excitation on induction, but no patient experienced apnoea after induction.

**GROUP II**

After the administration of thiopentone eyelid reflex disappeared on average at 37,7 seconds (SEM 4,09), with a range of 15 - 100 seconds. The average time from the end of general anaesthesia to full awakening of the patients was 22,3 minutes (SEM 1,73), with a range of 12 - 40 minutes. Six patients had evidence of excitation on induction, but no patient experienced apnoea after induction.

**TABLE I. CLINICAL DATA OF GROUPS I AND II**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
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</thead>
<tbody>
<tr>
<td>Loss of eyelid reflex (s)</td>
<td>63,8 ± 6,94</td>
<td>37,7 ± 4,09</td>
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<tr>
<td>Waking-up time (min)</td>
<td>36,3 ± 3,81</td>
<td>22,3 ± 1,73</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>35,8 ± 4,46</td>
<td>20,45 ± 1,54</td>
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<tr>
<td>Mass (kg)</td>
<td>21,9 ± 1,73</td>
<td>20,45 ± 1,54</td>
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<tr>
<td>Age (yrs)</td>
<td>7,5 ± 0,56</td>
<td>7,4 ± 0,48</td>
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(0x0) The mean body mass of patients in group I was 21,9 kg (SEM 1,73), and that of patients in group II was 20,45 kg (SEM 1,54). The operating time was 35,8 min (SEM 4,46) in group I and 37,7 min (SEM 5,02) in group II. There was no statistical difference between the two groups regarding the above data.

**DISCUSSION**

The induction properties of flunitrazepam and thiopen-