A CLINICAL EVALUATION OF ISOPROPYL CHLORIDE ANESTHESIA

HOWARD S. LIANG, M.D., AND ROBERT B. DODD, M.D.

Isopropyl chloride is currently being used as an anesthetic agent in Europe. Killian (1) states that it offers some advantages over the generally accepted inhalation agents. He claims that isopropyl chloride (IPC) is a potent and non-irritating volatile agent characterized by a fast induction and rapid recovery, and comparable in its action to cyclopropane. Killian describes the physical and chemical characteristics of IPC and reports on the results of 175,000 trials, animal experiments and "light" anesthesias. On the basis of 30,000 "light" anesthesias, using IPC as the principal agent, he favors isopropyl chloride over trichloroethylene for the production of analgesia for short procedures. It is interesting to note that IPC had been abandoned earlier by Cope (2), Lockett (3), and by Elam and Newhouse (4) because the agent produced cardiac arrhythmias and apparently had a low margin of safety.

Since IPC is being produced commercially in Europe for clinical use and has been recommended recently as an anesthetic agent (1, 5, 6, 7), it is our opinion that our series of 22 cases, though limited, is worth reporting. Our primary aim in this clinical study was to learn the general characteristics of IPC and its limitations, if any, in clinical usage.

Physical and Chemical Characteristics. Isopropyl chloride is a saturated halogenated hydrocarbon with the formula (CH₃)₂—CH—Cl. It is a colorless liquid with a not unpleasant garlic-like odor. It is flammable and explosive both in air and oxygen and decomposes when exposed to sunlight or heat. It has a boiling point of 36.5 C., a molecular weight of 78.54 and a specific gravity of 0.8588 at 20.6 C. Its solubility in water is 0.308 Gm. in 100 cc. at 20 C. and it dissolves readily in ether or alcohol. The anesthetic potency of IPC, as shown by animal experiments, is double that of diethyl ether. It produces anesthesia in dogs at 0.5 to 1.2 volumes per cent of the inspired atmosphere (8).

Clinical Studies

We limited our techniques of administration to three methods: Open drop, either as an induction agent or as the principal agent; semiclosed, for induction and maintenance; and semiclosed with intravenous induction (that is, following a Penthathal® sodium, nitrous oxide-

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297
TABLE 1

Methods of Administration

<table>
<thead>
<tr>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction and maintenance 11*</td>
</tr>
<tr>
<td>Induction only 4</td>
</tr>
<tr>
<td>Semiclosed induction and maintenance 2</td>
</tr>
<tr>
<td>Intravenous induction, semiclosed maintenance 5</td>
</tr>
</tbody>
</table>

* Three cases in which IPC was used as the sole agent were completed by changing to open drop ether because of: (1) Ventricular tachycardia, (2) fallen blood pressure and pallor, or (3) QRS depression and technical difficulty.

The gaseous vehicle for vaporizing IPC in the semiclosed system was 2 to 1 mixture of nitrous oxide and oxygen with total flows varying according to the size of the patient. The patients received a barbiturate or opiate and a belladonna alkaloid one half to one hour preoperatively. Distribution by technique is shown in table 1.

The age distribution and types of operation performed are shown in table 2. Two of the infant patients for craniotomy were female; the other patients were males. Duration of anesthesia varied from ten minutes to two hours and ten minutes.

RESULTS

In the majority of the cases in which anesthesia was induced by either the open drop or semiclosed method the patients entered the third stage of anesthesia within from two to five minutes. The clinical evaluation of the drug was based upon the following effects: analgesia, narcosis and relaxation. The reaction of the patient to such surgical manipulations as cutting, pulling, and stitching, was noted to ascertain the degree of analgesia or anesthesia. The degree of relaxation was estimated by testing the muscular tone of the abdominal wall and extremities. Our evaluation of the clinical effects of IPC anesthesia is given in table 3. The stages and planes cited are comparable to Guedel's levels for ether anesthesia (9). Our impression is that IPC

TABLE 2

Operations Performed with IPC as Anesthetic Agent

<table>
<thead>
<tr>
<th>Operation</th>
<th>Infant 4 mo.-2 years</th>
<th>Child 5-11 years</th>
<th>Adult</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circumcision</td>
<td>3</td>
<td>4</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Hernia</td>
<td></td>
<td>5</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Dental</td>
<td></td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Skin graft</td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>I &amp; D, extremities</td>
<td></td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Craniotomy</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22</td>
</tr>
</tbody>
</table>
TABLE 3

CLINICAL EVALUATION OF IPC EFFECTS FOR STATED LEVEL OF ANESTHESIA

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Analgesia</th>
<th>Narcosis</th>
<th>Relaxation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Stage III (plane 1)</td>
<td>?</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>(plane 2)</td>
<td>+</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>(plane 3)</td>
<td>++</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+++++</td>
</tr>
</tbody>
</table>

A good analgesia and relaxation was given in all stages. All patients retained stimuli or regained consciousness within a few minutes of discontinuance of IPC. There were no deaths in the series.

RESPIRATORY CHARACTERISTICS

Depression of Respiration. Respiratory movement was gradually depressed as anesthesia progressed. On occasion a patient went into complete apnea during the early third stage. This sign occurred early when the anesthetic was administered rapidly. Respiration were depressed both in rate and tidal volume. The process could be reversed by giving oxygen by bag and mask.

Lack of Secretions. There was a remarkable lack of mucus and salivation during anesthesia.

Agreeable Odor. The patients offered little resistance to administration of IPC by open or semiclosed methods. This was especially notable in young subjects.

TABLE 4

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Pt.</th>
<th>Age</th>
<th>Operation</th>
<th>Anesthetic Method</th>
<th>Time, min.</th>
<th>EKG</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-7</td>
<td>WR</td>
<td>9</td>
<td>Dental extraction</td>
<td>Open drop</td>
<td>10</td>
<td>Normal</td>
<td>Brief convulsion</td>
</tr>
<tr>
<td>I-14</td>
<td>MJ</td>
<td>25</td>
<td>I &amp; D. jaw</td>
<td>Semiclosed</td>
<td>20</td>
<td>Normal</td>
<td>Pentothal induction</td>
</tr>
<tr>
<td>I-15</td>
<td>GG</td>
<td>5</td>
<td>Hernia</td>
<td>O.D. + semiclosed</td>
<td>50</td>
<td>Depressed QRS, sinus tachycardia</td>
<td>Pentothal induction, technical difficulty</td>
</tr>
<tr>
<td>I-16</td>
<td>WP</td>
<td>5</td>
<td>Circumcision</td>
<td>Open drop</td>
<td>35</td>
<td>Regular sinus tachycardia</td>
<td>Pulse 150-172</td>
</tr>
<tr>
<td>I-17</td>
<td>WA</td>
<td>30</td>
<td>Skin graft</td>
<td>Semiclosed</td>
<td>120</td>
<td>Sinus tachycardia</td>
<td>Pentothal induction, obstruction</td>
</tr>
<tr>
<td>I-18</td>
<td>JG</td>
<td>9</td>
<td>Circumcision</td>
<td>Open drop</td>
<td>80</td>
<td>Ventricular tachycardia</td>
<td>C$_2$HCl discontinued after 3 minutes</td>
</tr>
<tr>
<td>I-19</td>
<td>LC</td>
<td>11</td>
<td>Circumcision</td>
<td>Semiclosed</td>
<td>60</td>
<td>Extrasystole</td>
<td>Pentothal induction, obstruction</td>
</tr>
<tr>
<td>I-20</td>
<td>CC</td>
<td>9</td>
<td>Hernia</td>
<td>Semiclosed</td>
<td>130</td>
<td>Depressed QRS, sinus tachycardia</td>
<td>Fall of B.P. 120/80 to 80/50, hiccup</td>
</tr>
</tbody>
</table>
Laryngospasm. Laryngospasm of a slight degree occurred twice in the series. Both instances occurred while IPC was given at a fairly rapid rate. Patients tolerated tracheal intubation well.

Circulatory Characteristics

Tachycardia. A rapid pulse occurred in over half of our cases. Since tachycardia is quite common in children under anesthesia regardless of the agent used, we had assumed that this characteristic was not of great significance.

![Heart rate tracings](image1)

**Fig. 1.** Case 1-16: (A) preanesthetic record, rate 85/min. (B) Increased pulse rate at 7 minutes followed induction with IPC. (C) and (D) Further progression of sinus tachycardia, with depressed S-T segments and low voltage.

![Heart rate tracings](image2)

**Fig. 2.** Case 1-18: (A) Preanesthetic record. (B) Multifocal ventricular arrhythmia occurring 6 minutes after induction with isopropyl chloride. (C) Regular rhythm, 20 minutes following discontinuance of IPC.

Arrhythmia. A series of electrocardiograms was recorded. The first few tracings were generally satisfactory but, as more anesthesias were given, the findings were less favorable as shown in table 4. EKG recordings made in cases 1-15 and 1-18 are shown in figures 1 and 2.

Blood Pressure Fall. The blood pressure often fell during surgery, varying from 10–20 millimeters of mercury below the preanesthetic systolic level. The most severe drops were to 50 per cent of the preanesthetic reading. On those cases monitored by ECG, it was noted that
the falls occurred concomitantly with depression of the QRS complex. There is some reason to assume that the blood pressure fall may be due to direct myocardial depression.

Digestive System

There were two cases of vomiting on emergence, but no patient vomited after he had returned to his room.

Subjective Impression

The three adult patients stated that they felt no ill effects upon recovery from anesthesia. They all had pleasant memories of the experience.

Comment

Isopropyl chloride was introduced as a clinical agent by MacDonald (10) in 1950. Subsequently, Cope (2), Lockett (3) and Elam and Newhouse (4) reported unfavorably on the clinical use of the drug. Recent articles by Killian (1), Mayrhofer (5), Ebbinghaus (6) and Nissen (7) give the impression that IPC is gaining in favor in the European countries. Killian implied that the fatality reported by Ronalle (11) (cardiac arrest in a patient with thyrotoxicosis) should not incriminate IPC solely on the basis of a direct toxic action on the heart produced by the drug. He believed that IPC, being a rapidly absorbed and eliminated volatile agent, could still be used to advantage to produce unconsciousness for a short period of time despite its inherent qualities as a cardiac irritant. He thought that the use of trichloroethylene should be discontinued and IPC used in its stead.

Trichloroethylene, however, possesses the advantage of having a high boiling point, so that vaporization has to be forced in order to exceed the toxic level of 0.5 per cent in the inspiratory mixture (12). Furthermore, trichloroethylene has the advantage of usually producing respiratory signs, such as coughing or tachypnea, when the concentration is getting too high, whereas IPC produces no irritative phenomena in the respiratory tract.

We are of the opinion that IPC falls into the same category as ethyl chloride, which offers apparently satisfactory anesthesia but progressively blocks the conductive tissue of the heart and exerts a direct toxic effect upon the myocardium. Killian discounted the probability of any direct effect of IPC on the myocardium but did admit to its adverse effect on the conductive tissue of the heart. The ECG findings in our series were very similar to those noted by Bush et al. (13), using ethyl chloride as a general anesthetic, and by Elam and Newhouse (4), using IPC. Although IPC has several very favorable characteristics, we are of the opinion that a drug that is so difficult to handle
when it is administered with extreme care should not be released for
general usage.

SUMMARY AND CONCLUSIONS

1. Isopropyl chloride was administered in 22 selected cases. There
were 6 infants, ranging in age from 4 months to 2 years, of whom 4
were male and 2 female; and 13 children, ranging in age from 5 to 11
years, and 3 adults, all of the male sex.

2. Anesthesins were generally satisfactory when IPC was used as
the principal or induction agent. There were 3 cases in which the
use of IPC was discontinued due to complications.

3. Isopropyl chloride is a potent anesthetic agent producing a rapid
induction and emergence.

4. Anesthesia with IPC is characterized by respiratory depression
without apparent irritation to the pharynx or larynx, minimal secre-
tions, excellent relaxation and little analgesic potency.

5. Because of arrhythmias and electrocardiographic findings of the
same type as seen with certain other halogenated compounds which
have a direct toxic effect on the myocardium, it is concluded that
isopropyl chloride has insufficient merit to be recommended as a clinical
anesthetic agent.

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chloride used in the clinical trial.

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