EXPERIENCES WITH ULTRA-SHORT ACTING INTRA-VENOUS BARBITURATES COMBINED WITH DECAMETHONIUM BROMIDE FOR ENDOTRACHEAL INTUBATION *

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Early in 1949 a preliminary report (1) was made of our experiences utilizing a combination of evipal sodium and d-tubocurarine chloride for endotracheal intubation. This report contains additional experience with that combination of agents and in addition, a comparison with evipal sodium combined with decamethonium bromide (syncurine, C10); pentothal sodium combined with either d-tubocurarine chloride or decamethonium bromide; spirothal (2) (spiro [2'-ethyl-3', 5'-dimethylcyclopentane] 5, 5-pyramidine-2-thio-4,6-dione sodium) with decamethonium bromide and surital sodium (3, 4) (sodium-5-allyl 5 [1 methyl butyl] 2-thio-barbiturate) with decamethonium bromide.

Preparation of Solutions

d-Tubocurarine chloride will be denoted as dTC and decamethonium bromide as C10.

Each drug employed is prepared as follows (table 1):

**TABLE 1**

AGENTS EMPLOYED FOR ENDOTRACHEAL INTUBATION

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Total Amount</th>
<th>Amount per cc.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Barbiturate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evipal Sodium</td>
<td>5%</td>
<td>500 mgm.</td>
<td>50 mgm.</td>
</tr>
<tr>
<td>Pentothal Sodium</td>
<td>5%</td>
<td>500 mgm.</td>
<td>50 mgm.</td>
</tr>
<tr>
<td>Surital Sodium</td>
<td>4%</td>
<td>400 mgm.</td>
<td>40 mgm.</td>
</tr>
<tr>
<td>Spirothal Sodium</td>
<td>5%</td>
<td>500 mgm.</td>
<td>50 mgm.</td>
</tr>
<tr>
<td><strong>Curarizing Agent</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d-Tubocurarine Chloride</td>
<td></td>
<td>15 mgm.</td>
<td>1.5 mgm.</td>
</tr>
<tr>
<td>Decamethonium Bromide (Syncurine)</td>
<td></td>
<td>4 mgm.</td>
<td>0.4 mgm.</td>
</tr>
</tbody>
</table>

† From the Department of Anesthesiology, Medical College of Georgia, Augusta, Georgia.
Evipal-dTC: One-half gram of evipal is dissolved in 9 cc. of distilled water; 1 cc. of high potency dTC (15 mg.) is added. This represents a 5 per cent solution of evipal. Each cubic centimeter of solution contains evipal 50 mg. and dTC 1.5 mg.

Evipal-C10: One-half gram of evipal is dissolved in 6 cc. of distilled water; 4 cc. (4 mg.) of C10 is added. This again represents a 5 per cent solution of evipal. Each cubic centimeter contains evipal 50 mg. and C10 0.4 mg.

Pentothal is prepared in a 5 per cent solution with dTC or C10 similar to the preparation of evipal.

Spirothal is prepared in a 5 per cent solution with C10 only but similar to evipal-C10.

Surital is prepared in a 4 percent solution with C10. First, a 10 per cent solution of the drug is made with distilled water, 4 cc. (400 mg.) is withdrawn and added to 4 cc. (4 mg.) of C10 and 2 cc. of distilled water is added to make a total of 10 cc. One cubic centimeter contains surital 40 mg. and C10 0.4 mg. The lower concentration and amount of surital compared with the other agents used indicates that our experience parallels that of other investigators who have found surital to have a greater potency than pentothal (5, 6).

In children under 8 years of age a half strength solution was utilized. In each instance a dilution up to 10 cc. was employed.

**Technic of Intubation**

**Adults and Children over 8 Years of Age.**—The full strength solution of the combined agents was employed. An initial dose of 2 to 5 cc. (the average in adults was 4 cc., in children 3 cc.) was injected rapidly into a readily accessible arm vein. The effect on the patient was watched for thirty to sixty seconds; oxygen by mask was given during

**TABLE 2**

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>E &amp; DTC (325)</th>
<th>E &amp; Sy (454)</th>
<th>P &amp; DTC (60)</th>
<th>P &amp; Sy (73)</th>
<th>STB &amp; Sy (50)</th>
<th>S &amp; Sy (50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>3.6 *</td>
<td>6.8 *</td>
<td>4.5 *</td>
<td>6.7 *</td>
<td>10.0 *</td>
<td>6.0 *</td>
</tr>
<tr>
<td>10-30</td>
<td>26.0</td>
<td>25.8</td>
<td>25.6</td>
<td>24.6</td>
<td>26.0</td>
<td>22.0</td>
</tr>
<tr>
<td>30-50</td>
<td>39.4</td>
<td>39.1</td>
<td>38.4</td>
<td>37.2</td>
<td>42.0</td>
<td>48.0</td>
</tr>
<tr>
<td>50-70</td>
<td>25.0</td>
<td>23.8</td>
<td>27.3</td>
<td>27.4</td>
<td>18.0</td>
<td>24.0</td>
</tr>
<tr>
<td>70-90</td>
<td>6.0</td>
<td>4.5</td>
<td>4.2</td>
<td>4.1</td>
<td>4.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

* All figures refer to percentages.
1. Figures refer to number of patients.

E: Evipal, DTC: d-Tubocurarine, STB: Spirothal, S: Surital, Sy: Syncurine, P: Pentothal
this interval. (Patients invariably demonstrated a very short period of hyperpnea with this initial rapid administration. The thio-
barbiturates showed this more markedly than did evipal.) If apnea
did not occur an additional injection of 3 to 5 cc. was given in adults
and 1 to 3 cc. in children. In the event of the occurrence of apnea
after the initial injection, an additional amount of only 1 to 3 cc. was
given. The end point was judged by the relaxation of the masseter
muscles and the ability of the patient to tolerate exposure of the ep-
iglottis and larynx with minimal reaction. A Macintosh laryngoscope
blade facilitated exposure. Ten cubic centimeters of the combined
drugs was the maximum employed in any one patient.

Children under 8 Years of Age.—A half strength solution of the
combined agents was employed; for example, evipal 250 mg. and C10
2 mg. was diluted to 10 cc. Each cubic centimeter contained 25 mg. of
evipal and 0.2 mg. of C10. Two to 4 cc. of the combination was given

| TABLE 3 |
| AMOUNT OF AGENT USED TO INTUBATE |
| Milligrams | E & DTC | E & Sy | P & DTC | P & Sy | STB & Sy | S & Sy |
| 150 | 0.0 * | 2.5 * | 0.0 * | 1.4 * | 6.0 * | 4.0 * |
| 150-250 | 3.3 | 8.8 | 10.0 | 12.3 | 8.0 | 22.0 |
| 250-350 | 14.6 | 17.8 | 18.5 | 37.0 | 18.0 | 36.0 |
| 350-450 | 26.4 | 41.3 | 21.5 | 48.0 | 36.0 | 16.0 |
| 450-500 | 55.7 | 29.6 | 50.0 | 1.3 | 32.0 | 22.0 |

* All figures refer to percentages.

E—Evipal, DTC—d-Tubocurarine, STB—Spirothel, S—Surital, Sy—Syncurine, P—Pentothal

rapidly intravenously. The child was watched for thirty to sixty
seconds. If apnea did not occur an additional 2 to 5 cc. was injected,
depending on the age and size of the child and the degree of relaxation
of the masseter muscles. In the event of the occurrence of apnea with
the initial injection an additional amount of only 1 to 3 cc. was given.

A means for either controlling or supplementing respiration was
always at hand ready for use.

This study included a wide range of ages (table 2) in both white and
colored, good and poor risk patients.

The amount of combination of agents needed for endotracheal in-
tubation (table 3) varied from 3 to 10 cc. The average used for an
adult was approximately 8 cc. and for children one-third to one-half
of this amount. The amount needed was decreased about one third in
instances of debility and extremes of age. The policy established in
our original report of not exceeding 10 cc. of the combination was fol-
lowed in this series. It is well to point out that with the exception of
the pentothal and evipal group combined with dTC, less than 2 per cent of the total number studied needed a supplemental agent to accomplish intubation (table 4).

The time required for completion of the intubation varied from one minute to more than ten minutes (table 5). It may be noted that intubation was performed in less than five minutes in 96.4 per cent of the group given evipal-C10 and in 96 per cent of the series given surital-C10. This is a distinct difference when compared with the other agents studied and implies a much greater incidence of difficulty and more frequent need for supplemental agents when dTC is employed with either evipal or pentothal.

Apnea following intubation occurred quite frequently (table 6). In most of these cases apnea or hypopnea was usually the direct result of over-dosage; rarely was it the result of reflex stimulus from an endotracheal tube in the trachea. As reported in our preliminary series, the length of apnea was considerably reduced by utilizing 60 to 70 per cent nitrous oxide with oxygen initially as supplemental agents after intubation. As soon as respirations were well established, cyclopropane or ether was used as a supplemental agent when needed. For short procedures such as tonsillectomies frequently only nitrous oxide was required as a supplement. It is worthy of note that pentothal-dTC, spirothal-C10 and surital-C10 combinations seemed to produce apnea of longest duration.

There were no serious complications and no deaths in this series (table 7). Drops in blood pressure occurred not infrequently but were
of a minor nature regardless of the agents employed. The decreases in blood pressure (20 to 40 mm. of mercury) were greatest with pentothal combined with either dTC or C10 and least in degree although somewhat more frequent with evipal and surital. Surital seemed to produce the least effect in this respect (20 mm. of mercury or less).

**Table 6**

**INCIDENCE OF APNEA**

<table>
<thead>
<tr>
<th>Time in Minutes</th>
<th>E &amp; B DTC (325)</th>
<th>E &amp; B Sy (454)</th>
<th>P &amp; B DTC (60)</th>
<th>P &amp; B Sy (73)</th>
<th>STB &amp; B Sy (50)</th>
<th>S &amp; B Sy (50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>69.5 *</td>
<td>65.4 *</td>
<td>40.0 *</td>
<td>59.0 *</td>
<td>52.0 *</td>
<td>56.0 *</td>
</tr>
<tr>
<td>1-3</td>
<td>9.1</td>
<td>5.8</td>
<td>5.0</td>
<td>10.9</td>
<td>6.0</td>
<td>8.0</td>
</tr>
<tr>
<td>3-5</td>
<td>8.7</td>
<td>7.3</td>
<td>12.5</td>
<td>9.6</td>
<td>8.0</td>
<td>10.0</td>
</tr>
<tr>
<td>5-10</td>
<td>6.3</td>
<td>11.4</td>
<td>15.0</td>
<td>10.9</td>
<td>18.0</td>
<td>4.0</td>
</tr>
<tr>
<td>10-20</td>
<td>4.9</td>
<td>9.9</td>
<td>12.5</td>
<td>9.6</td>
<td>16.0</td>
<td>22.0</td>
</tr>
<tr>
<td>20*</td>
<td>1.5</td>
<td>0.2</td>
<td>15.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

* All figures refer to percentages.
(1)-Figures refer to number of patients

E-Evipal, DTC-α-Tubocurarine, STB-Spirothal, S-Surital, Sy-Syncurine, P-Pentothal

Rises in blood pressure occurred quite frequently but presented no serious problem with any of the agents. The most frequent and greatest increases (60 to 120 mm.) were produced by the combination of spirothol and C10 and the next greatest by surital-C10 and pentothal with either dTC or C10. These rises in blood pressure seemed to be

**Table 7**

**SIDE EFFECTS OF AGENTS AND INTUBATION**

<table>
<thead>
<tr>
<th></th>
<th>E &amp; B DTC (325)</th>
<th>E &amp; B Sy (454)</th>
<th>P &amp; B DTC (60)</th>
<th>P &amp; B Sy (73)</th>
<th>STB &amp; B Sy (50)</th>
<th>S &amp; B Sy (50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drop in B.P.</td>
<td>15.6 *</td>
<td>14.5 *</td>
<td>10.5 *</td>
<td>12.75 *</td>
<td>12.00 *</td>
<td>14.0 *</td>
</tr>
<tr>
<td>Rise in B.P.</td>
<td>29.6</td>
<td>31.5</td>
<td>45.6</td>
<td>50.6</td>
<td>66.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>0.0</td>
<td>0.45</td>
<td>2.0</td>
<td>1.37</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Bronchospassm</td>
<td>3.3</td>
<td>1.3</td>
<td>5.0</td>
<td>4.1</td>
<td>6.00</td>
<td>0.0</td>
</tr>
</tbody>
</table>

* All figures refer to percentages.
(1)-Figures refer to number of patients

E-Evipal, DTC-α-Tubocurarine, STB-Spirothal, S-Surital, Sy-Syncurine, P-Pentothal

initiated on exposure of the larynx and before intubation and did not seem to be associated with either hypoxia or carbon dioxide retention. Intubation aggravated the picture for a few minutes followed in a very short time by a dramatic leveling off to the original blood pressure reading. The use of topical anesthesia, when thoroughly carried out, abolished most increases in blood pressure. The apparent benign
nature of this circulatory picture in our experience precluded the routine use of topical anesthesia before intubation.

The tendency of the vocal cords to adduct at the time of exposure with the laryngoscope was frequently encountered in the group given Pentothal combined with either curarizing agent and in the series given spiriothal-C10. This tendency of the larynx to go into spasm was rarely encountered when evipal-dTC or evipal-C10 was used. Moreover, this tendency to adduct was never sustained for more than a few seconds. Patients given surital-C10 followed the same pattern and showed very little tendency toward adduction of the cords. Severe laryngospasm, although rare with any of the agents employed (table 7) was most frequently encountered in the series given pentothal-dTC and pentothal-C10.

Bronchospasm shortly after intubation (table 7) was most annoying and occurred more frequently in the groups given pentothal and spiriothal-C10. Those patients given evipal-C10 and surital-C10 showed very little if any tendency toward bronchospastic phenomena. This latter observation is more remarkable inasmuch as patients with asthma or a tendency toward asthma were given evipal-C10 for intubation. In only 2 patients of this series were the symptoms of asthma aggravated somewhat when evipal-C10 was employed. This aggravation occurred twenty to twenty-five minutes following the administration of the agents and before adequate amounts of supplemental anesthetics were administered.

Blind nasal intubation, although at times successful, failed not infrequently when any of the above combination of agents were employed. Nasal intubation with direct exposure of the larynx and direct exposure of the larynx and direct guidance of the endotracheal tube into the trachea was readily accomplished with the technic outlined. The best incidence of success for direct nasal intubation was obtained with evipal or surital combined with C10. This is most probably because of the low incidence of laryngospastic phenomena whenever these agents were employed.

Comment

In our experience the combination of evipal-C10 for endotracheal intubation has proved safe and superior to any of the other combinations of agents tried. Surital-C10 followed the pattern of evipal-C10 quite closely, but produced much longer periods of apnea. It is worthy of further investigation. There are many instances in which rapid endotracheal intubation is desired. This technic in our hands has proved safe and very satisfactory not only for children and adults in good physical condition but also for the extremely poor risk patient, for example, the patient with acute intestinal obstruction with distention and fecal vomitus; the patient in shock whether from toxemia, hemorrhage or trauma; the bronchospastic patient having either
asthma, emphysema or both; the "wet lung" patient with lung abscess, bronchiectasis or hemorrhage; the short-neck and stocky type of individual; the patient with a depressed skull fracture, and the intracranial tumor type of case with increased intracranial pressure. Induction of anesthesia and its maintenance have been greatly simplified in all of the instances listed. The use of topical anesthesia preliminary to endotracheal intubation has not been found necessary. Controlled or supplemented respirations were used whenever apnea or hypopnea occurred.

**Summary and Conclusions**

A comparative study is presented of four ultra-short acting barbituric acids: evipal, pentothal, sipothol and surital, each combined with C10 and utilized for endotracheal intubation. Two of these, evipal and pentothal, were also combined with dTC.

In the series studied all of the agents used were capable in most instances of producing adequate conditions for endotracheal intubation.

The combination of evipal-C10 yielded the best results for intubation and produced the fewest complications.

Surital-C10 produced results similar to evipal-C10, but apnea occurred more frequently and was more prolonged.

It must be stressed that this technic for endotracheal intubation should be employed only by individuals adequately trained in the use of direct laryngoscopy and endotracheal intubation.

C10 (syneurine) was employed only for the initial endotracheal intubation. d-Tubocurarine chloride was used for any additional relaxation needed during the surgical procedure.

Adequate means for controlling or supplementing respiration should always be at hand.

Since this paper was presented Evipal combined with triiodothyrate of tri(beta diethylaminoethoxy) 1, 2, 3 benzene (flaxedil—80 to 100 mg. combined with 500 mg. of 5 per cent evipal) was tried in a series of 25 patients. The relaxation of the jaw and the abduction of the vocal cords approached that obtained with evipal-C10 combination; however, an increase in the heart rate of 30 to 60 beats per minute was very frequently encountered. This increase usually persisted for ten to twenty minutes.

Evipal combined with dimethyl d-tubocurarine chloride (meocostrin) (evipal, 500 mg. of a 5 per cent solution with meocostrin, 5 mg.) was used for endotracheal intubation in 25 patients. This combination has proved inferior when compared with evipal-C10. Evipal-mecostrin, in our experience, has produced less adequate relaxation of the jaw, a greater tendency toward laryngospastic phenomena and a much greater incidence of need for a supplementary agent for intubation.

The combination of evipal-C10 remains the first choice in our hospital for routine endotracheal intubation.

The drugs for this study were furnished by the following: evipal sodium by Winthrop-Searls, Inc.; surital sodium by Parke, Davis and Company; syneurine by Burroughs Wellcome and Company; meocostrin by E. R. Squibb and Sons, and sipothol by Eli Lilly and Company.

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