Pre-induction of Anesthesia in Pediatric Patients with Nasally Administered Sufentanil

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To evaluate nasally administered sufentanil, 1.5–4.5 μg/kg, for pre-induction (i.e., pre-medication/induction) of anesthesia in pediatric patients, the authors studied ASA PS 1 or 2 patients scheduled for elective surgery. Eighty children, ages 6 months to 7 yr, were randomized to receive sufentanil (1.5, 3.0, or 4.5 μg/kg) or placebo (normal saline, 0.03 ml/kg) nasally over 15–20 s. Induction of anesthesia was completed with 5% halothane and O2 via facemask. After tracheal intubation, anesthesia was maintained with N2O (60–70%) and halothane, as clinically indicated. A blinded observer remained with the child from prior to drug administration until discharge from the recovery room. Patients given sufentanil were more likely to separate willingly from their parents and be judged as calm at or before 10 min compared to those given saline. Ventilatory compliance during induction of anesthesia decreased markedly in 25% of subjects given sufentanil, 4.5 μg/kg. Subjects given sufentanil moved or coughed less during tracheal intubation and required less halothane compared to those given placebo. During recovery, patients given sufentanil cried less and fewer needed analgesic recovery times were similar for all groups. However, patients given sufentanil, 4.5 μg/kg, had a higher incidence of vomiting in the recovery room and during the first postoperative day. The authors conclude that nasally administered sufentanil, 1.5 or 3.0 μg/kg, facilitates separation of children from parents, has minimal side effects, may improve intubating conditions, and can provide postoperative analgesia. (Key words: Analgesia: sufentanil. Anesthesia: pediatric. Anesthetics, nasal: sufentanil. Anesthetic techniques: nasal. Induction: anesthesia. Premedication.)

INDUCTION OF ANESTHESIA in the pediatric patient presents a challenge to the anesthesiologist because of the potential for psychological trauma to the patient. Fear of painful or unpleasant procedures and separa-

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Materials and Methods

Following approval by the local Committee on Human Research, informed consent was obtained to study 80 patients 6 months to 7 yr of age (table 1), ASA physical status 1 or 2, scheduled for elective surgery requiring no special anesthetic technique. These unpremedicated patients were brought to a preoperative area, where they were randomly assigned to receive sufentanil (1.5, 3.0, or 4.5 μg/kg) or placebo (normal saline, 0.03 ml/kg). The sufentanil or placebo was drawn into a 1- or 3-ml syringe, the needle was removed, and the undiluted medication was administered nasally from the syringe over 15–20 s. Oxygen and succinylcholine were available at the patient’s bedside. We attempted to separate the child from his/her parents and take him/her to the operating room 4 min after we administered sufentanil or placebo; if unsuccessful, this was repeated at 2 min intervals (at 6, 8, and 10 min) until the child was willing to separate. If the child was not willing to separate from his/her parents at 10 min, he/she was taken to the operating room at that time. Anesthesia was induced with 5% halothane and O2 via facemask. As soon as the patient lost consciousness,
TABLE 1. Age Distribution for Patients Receiving Placebo (Normal Saline) or Sufentanil, 1.5, 3.0, or 4.5 μg/kg, Nasally

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Sufentanil (μg/kg)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td>Patients less than 2 yr of age</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Patients 2–7 yr of age</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>20</td>
</tr>
</tbody>
</table>

ventilation was assisted or controlled and the inspired concentration of halothane was decreased to approximately 2%. The trachea was intubated without the use of muscle relaxants. Halothane was then discontinued and anesthesia maintained with N₂O, 60–70%; halothane was again added as clinically indicated to maintain pulse and arterial blood pressure in the normal range and to prevent movement. Ventilation was controlled to maintain end-tidal P₉O₂ at approximately 35 mmHg. Intraoperatively, no opiates were given; muscle relaxants were used if surgically indicated. At the end of surgery, N₂O and halothane were discontinued and ventilation was halved. If P₉O₂ exceeded 70 mmHg, nal-

oxone, 1 μg/kg, was administered. The trachea was extubated when regular spontaneous ventilation occurred. Supplemental oxygen was administered during transport to, and while in, the recovery room. Patients requiring analgesics were given morphine, 0.1 mg/kg iv. Children were discharged from the recovery room by "usual criteria," and returned either home or to the ward as surgically indicated.

A blinded observer remained with the child from prior to drug administration until discharge from the recovery room, and recorded the following.

Preinduction and Induction. Arterial oxygen saturation (SpO₂) and heart rate by pulse oximetry (Nellcor™), response to administration of nose drops (crying or not crying), willingness to separate from parents, mood (calm or not calm) at the time of separation from parents, response to facemask (accept or reject), the anesthesiologist’s subjective assessment of ventilatory compliance (the ease of delivering positive pressure ventilation after the patient lost consciousness), and response to tracheal intubation (movement or coughing).

Maintenance. End-tidal halothane concentrations and end-tidal P₉O₂ (both by mass spectrometry).

Emergence and Recovery. SpO₂, skin-surface P₉O₂ (SensorMedics™), need for naloxone, airway complications (surgical trauma following tracheal extubation, postextubation cough, need for airway support), vomiting, mood, and analgesic requirements.

One Day Following Surgery. Parents were asked whether their child vomited, had pain, or showed change of appetite or sleeping habits.

During the pre-induction period, data for SpO₂, heart rate, and willingness to separate from parents were recorded before, and at 2-min intervals after, administration of sufentanil or placebo. During maintenance of anesthesia, recordings were made at 15-min intervals. The maximum end-tidal halothane concentration intraoperatively was determined for the period beginning 15 min after tracheal intubation until the completion of surgery. During recovery, SpO₂ and skin-surface P₉O₂ were recorded at 5-min intervals during the first 20 min and, thereafter, at 10-min intervals until discharge.

We also recorded the times of administration of sufentanil/placebo, separation from parents, start of induction, loss of consciousness, tracheal intubation, end of surgery, discontinuation of N₂O, spontaneous ventilation, tracheal extubation, arrival in post-anesthetic recovery room (PARR), and discharge from PARR.

Data are reported as incidence (%) or mean ± SD. Data were analyzed using χ² analysis (with Yates's correction where indicated), Fisher's exact test, or analysis of variance and the Student-Newman-Keuls test. P < 0.05 was considered statistically significant.

**TABLE 2. Characteristics of Patients Receiving Placebo Normal Saline) or Sufentanil, 1.5, 3.0, or 4.5 μg/kg, Nasally. Data Reported as Percent**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Sufentanil (μg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 10)</td>
<td>(n = 20)</td>
</tr>
<tr>
<td>Willing to separate from parents:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 4 min</td>
<td>21*</td>
<td>40</td>
</tr>
<tr>
<td>At or before 10 min</td>
<td>55*</td>
<td>85</td>
</tr>
<tr>
<td>Calm at time of separation from parents</td>
<td>47*</td>
<td>85</td>
</tr>
<tr>
<td>Accepts facemask</td>
<td>11</td>
<td>25</td>
</tr>
<tr>
<td>Ventilatory compliance (assessed subjectively; see text for explanation):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mildly decreased</td>
<td>0*</td>
<td>45</td>
</tr>
<tr>
<td>Markedly decreased</td>
<td>0*</td>
<td>0</td>
</tr>
<tr>
<td>Movement or coughing during tracheal intubation</td>
<td>42*</td>
<td>25</td>
</tr>
<tr>
<td>Airway complications after tracheal extubation:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Need for airway support</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Croup</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting in PARR‡</td>
<td>33</td>
<td>25</td>
</tr>
<tr>
<td>Crying in PARR</td>
<td>90*</td>
<td>55</td>
</tr>
<tr>
<td>Analgesics in PARR</td>
<td>74*</td>
<td>35</td>
</tr>
<tr>
<td>Vomiting after release from PARR‡</td>
<td>42</td>
<td>25</td>
</tr>
<tr>
<td>Normal appetite one day following surgery‡</td>
<td>61*</td>
<td>77</td>
</tr>
</tbody>
</table>

* Different from sufentanil (all doses combined) by χ² analysis or Fisher's exact test (P < 0.05).
† Different from other doses of sufentanil by χ² analysis (P < 0.05).
‡ Excludes patients with nasogastric tubes.
§ Excludes patients who were NPO.
Table 3. Duration (Min) of Induction of Anesthesia, Surgery, and Recovery in Patients Receiving Placebo (Normal Saline) or Sufentanil, 1.5, 3.0, or 4.5 µg/kg, Nasally. Data Reported as Mean ± SD; Range in Parentheses

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 19)</th>
<th>1.5 (n = 20)</th>
<th>3.0 (n = 21)</th>
<th>4.5 (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from induction of anesthesia to tracheal intubation</td>
<td>7 ± 3*</td>
<td>5 ± 4</td>
<td>4 ± 2</td>
<td>4 ± 1</td>
</tr>
<tr>
<td></td>
<td>(3–15)</td>
<td>(2–17)</td>
<td>(2–8)</td>
<td>(2–6)</td>
</tr>
<tr>
<td>Time from induction of anesthesia to end of surgery</td>
<td>136 ± 81</td>
<td>120 ± 77</td>
<td>143 ± 74</td>
<td>128 ± 72</td>
</tr>
<tr>
<td></td>
<td>(46–331)</td>
<td>(32–218)</td>
<td>(40–270)</td>
<td>(32–287)</td>
</tr>
<tr>
<td>Time from end of surgery to tracheal extubation</td>
<td>4 ± 4</td>
<td>3 ± 3</td>
<td>5 ± 5</td>
<td>5 ± 5</td>
</tr>
<tr>
<td></td>
<td>(0–17)</td>
<td>(0–8)</td>
<td>(0–19)</td>
<td>(1–19)</td>
</tr>
<tr>
<td>Time in PARR</td>
<td>110 ± 34</td>
<td>100 ± 31</td>
<td>95 ± 58</td>
<td>104 ± 63</td>
</tr>
<tr>
<td></td>
<td>(70–207)</td>
<td>(52–159)</td>
<td>(52–225)</td>
<td>(36–318)</td>
</tr>
</tbody>
</table>

* Different from sufentanil (all doses combined) by analysis of variance and the Student-Newman-Keuls test (P < 0.05).

Results

Sixty-one percent of the children cried, all transiently, during administration of sufentanil or placebo; there was no difference among groups. Subjects given sufentanil were more likely to separate willingly from their parents at or before 10 min compared to patients given placebo (table 2); 51% of the patients given sufentanil separated at 4 min compared to 21% of the patients given placebo. Patients given sufentanil were also more likely to be judged as calm when they separated from their parents. Subjects judged calm after nasally administered sufentanil were either relaxed (71%), drowsy (25%), or asleep (4%). Prior to induction of anesthesia, no patients had an $SpO_2$ less than 95%. One patient given sufentanil, 3 µg/kg, vomited prior to induction of anesthesia; this patient’s anesthetic and postoperative courses were uneventful. No children complained of nausea.

Patients given sufentanil and placebo responded similarly to the anesthesia facemask. Sufentanil was associated with decreased ventilatory compliance (assessed subjectively) in many patients. The decrease was judged mild in 49% of patients given sufentanil, 1.5 or 3.0 µg/kg, and did not compromise oxygenation. One subject, given sufentanil, 3.0 µg/kg, had a marked decrease in compliance, and $SpO_2$ fell below 95%; this improved following succinylcholine, oxygen, and positive pressure ventilation. Although the decrease in compliance was marked in 25% of the subjects given sufentanil, 4.5 µg/kg, induction of anesthesia and tracheal intubation proceeded uneventfully and administration of muscle relaxants was not needed. Patients given sufentanil moved or coughed less frequently during tracheal intubation (table 2), despite a shorter time from the beginning of induction to tracheal intubation (table 3). Intraoperatively, maximum end-tidal halothane concentrations were lower in patients given sufentanil (table 4). Skin-surface $PCO_2$ at the time of tracheal extubation was lower in patients given placebo. Two patients (both given sufentanil, 4.5 µg/kg) required naloxone for respiratory depression prior to tracheal extubation; duration of surgery for these patients was 59 and 112 min.

Time from end of surgery to tracheal extubation and time in the recovery room were similar for all groups. The incidence of vomiting in the PARR and during the first postoperative day was similar after placebo and sufentanil, 1.5 and 3.0 µg/kg. However, children given sufentanil, 4.5 µg/kg, had a higher incidence of vomiting in the PARR and during the first postoperative day. Patients given sufentanil cried less frequently, and fewer required analgesics in the PARR. No patients had significant decreases in $SpO_2$ while in the PARR. Skin surface $PCO_2$ increased more than 3 mmHg after admission to the PARR in only one subject; that subject re-

Table 4. Maximum End-tidal Halothane Concentration Intraoperatively and Skin Surface $PCO_2$ at Tracheal Extubation in Patients Receiving Placebo (Normal Saline) or Sufentanil, 1.5, 3.0, or 4.5 µg/kg, Nasally. Data Reported as Mean ± SD

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 19)</th>
<th>1.5 (n = 20)</th>
<th>3.0 (n = 21)</th>
<th>4.5 (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum end-tidal halothane concentration (%)</td>
<td>1.6 ± 0.6*</td>
<td>1.0 ± 0.4</td>
<td>0.8 ± 0.3</td>
<td>0.7 ± 0.4</td>
</tr>
<tr>
<td>Skin-surface $PCO_2$ at tracheal extubation (mmHg)</td>
<td>46 ± 8*</td>
<td>50 ± 11</td>
<td>53 ± 10</td>
<td>54 ± 9</td>
</tr>
</tbody>
</table>

* Different from sufentanil (all doses combined) by analysis of variance and the Student-Newman-Keuls test (P < 0.05).
ceived sufentanil, 4.5 µg/kg, and was the only patient
given naloxone in the recovery room. Airway complica-
tions occurred rarely, and did not differ between pa-
tients given placebo versus sufentanil.

One day after surgery, there was no difference in
pain or sleep habits among the groups. However, more
patients given sufentanil had a normal appetite.

There were several complications in addition to the
episode of vomiting and the episode requiring succinyl-
choline described earlier. Two patients given placebo
had hypotension with induction of anesthesia. One pa-
tient given sufentanil, 4.5 µg/kg, had a transient epi-

dose of rhythmic motor activity after tracheal intuba-
tion. This patient, a 7-month-old, ASA PS 1 girl, with
no prior medical history and receiving no medications,
presented for removal of a dermoid cyst. After adminis-
tration of sufentanil, the child was calm and separated
willingly from her parents. Induction of anesthesia and
tracheal intubation proceeded uneventfully. After in-
tubation, nitrous oxide (60%) and halothane (0.25%)\nwere administered and ventilation was controlled. Sev-

eral minutes later, we noted tonic-clonic activity of the
left upper extremity which rapidly spread to all extre-
mities, lasting 90 s. The SpO₂ was 100% and the pa-
tient was normocaric and normotensive at the begin-
ning of this event. Electrolytes and a venous blood gas
drawn immediately were also normal.

Discussion

Children present a special challenge to anesthesiolo-
gists because of the desire to minimize the psychological
trauma resulting from separation from parents and the
induction of anesthesia. As such, we seek new drugs and
better techniques to improve the quality of the anes-
thetic experience. Although oral transmucosal fentanyl
is an excellent premedication,¹ there are two disadvan-
tages associated with its use: slow onset time (25–45 min
to peak effect)⁴ and an increase in gastric volume com-
pared to unpremedicated subjects (15.9 ± 1.0.8 ml com-
pared to 9.0 ± 6.2 ml [mean ± SD]).⁴ We investigated
the use of nasally administered sufentanil as an adjunct
for induction of anesthesia. This technique resulted in
children being more willing to separate from their par-
ents, facilitated induction and maintenance of anes-
thesia, and improved the quality of the recovery period.

To standardize the induction of anesthesia and to as-
sess the rapidity with which we could intubate the tra-
chea, we used 5% halothane in oxygen for induction of
anesthesia. This produced a rapid loss of consciousness
in all subjects; however, this technique may not be ap-
propriate for all children. We avoided administering
nitrous oxide during induction of anesthesia because,
during preliminary investigations, muscle tone often in-
creased soon after nitrous oxide was administered, a
known, undesirable effect of the combination of an
opiate and nitrous oxide.⁷⁻⁹

Even in the absence of nitrous oxide, we found that
sufentanil often decreased ventilatory compliance dur-
ing the induction of anesthesia. The higher dose of su-
ftenanil, 4.5 µg/kg, was sometimes associated with a
marked decrease in ventilatory compliance, which was
transient and resolved without the use of muscle relax-
ants. Lower doses of sufentanil, 1.5 and 3.0 µg/kg,
were frequently associated with a mild decrease in ven-
tilatory compliance with the introduction of halothane.
This was not a problem (except in one patient described
earlier) because it was transient, resolved as the inhala-
tion induction continued, and was not associated with a
decrease in SpO₂. All patients with markedly decreased
ventilatory compliance became easier to ventilate as the
induction of anesthesia continued.

We observed generalized tonic-clonic activity appear-
ing to be a grand-mal seizure in one patient given su-
ftenanil, 4.5 µg/kg. Seizure activity, documented by
electroencephalography (EEG), occurs in rats given su-
ftenanil, 5 µg/kg.¹⁰,¹¹ Although tonic-clonic activity has
been seen in humans after small doses of sufentanil
(0.6–0.8 µg/kg),¹²,¹³ EEG evidence of seizures has not
been reported.¹⁴ Benthuysen and Stanley¹⁵ speculated
that narcotic-induced motor activity may be a form of
rigidity rather than seizures.

Anesthesiologists who administer sufentanil nasally
will find its effects different from those of other pre-
medicants, such as methohexital, i.e., nasally adminis-
tered sufentanil usually did not produce drowsiness or
sleep. Children given sufentanil became relaxed, occa-
nionally euphoric, and usually calm and cooperative.
Because the shortest surgical procedures ranged from
32–46 min, we do not know whether nasally adminis-
tered sufentanil can be used for shorter cases. We also
do not know whether sufentanil doses lower than 1.5
µg/kg are effective. However, we found that a higher
close of sufentanil, 4.5 µg/kg, offers few advantages
over the lower doses studied and was associated with
more adverse effects, including rigidity, postoperative
vomiting, perhaps convulsive activity, and, occasionally,
a need for antagonism of its respiratory depressant ef-

In summary, administering sufentanil nasally to chil-
dren is a useful adjunct for inducing anesthesia. The
nasal route is probably less traumatic than intramuscu-
lar injection, and is more aesthetic than rectal adminis-
tration, particularly in older children. Although not an
induction agent at the doses studied, nasally adminis-
tered sufentanil, in doses of 1.5 and 3.0 µg/kg, usually
facilitates separation of children from parents and results in a pleasant postoperative course.

References