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Anesthesiology

"A STUDY OF EFFECTS OF ANTICHOLINERGIC DRUGS ON THERMOREGULATION IN PAEDIATRIC PATIENTS UNDERGOING AMBULATORY ANAESTHESIA WITH KETAMINE"

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ABSTRACT **Aims and objectives:** A randomized, double-blind, prospective study to evaluate the effect of anticholinergic drugs on thermoregulation in paediatric patients undergoing ambulatory anaesthesia with ketamine.

Methodology: Patients were randomized to receive either 0.005mg/kg glycopyrrolate or the equivalent volume of normal saline (placebo) at 30min before ketamine anaesthesia. Body temperature was measured tympanically at baseline and at 0, 30, 60 and 90min postoperatively. The quantity of saliva prodiced during surgery and incidence of fever were recorded.

Results: Body temperature was significantly higher in the glycopyrrolate group (n=42) than the placebo group (n=42) at 30, 60 and 90min after surgery, and higher than baseline at 0, 30, 60 and 90min after surgery. In the placebo group, body temperature was significantly higher than baseline at 0 and 30 min after surgery. Saliva secretion was significantly lower in the glycopyrrolate group than the placebo group.

KEYWORDS : ketamine, thermoregulation.

Introduction:

Ketamine has been widely used in minor procedures for children for its quick sedative and analgesic effects with minimal impact on airway reflexes and respiratory depression.1 However, adverse effects such as nausea, vomiting, rash, emergence reactions, increased bronchial secretions and hypersalivation have also been related to ketamine sedations.2,3 Increased bronchial and oral secretions hinder oral and bronchial-related procedures, and the suction to remove excessive mucosal secretions can result in laryngospasm.2,3 Therefore, adjunctive anticholinergics, such as atropine or glycopyrrolate, have been used prior to ketamine administration. Anticholinergics are used as a premedication in oral or bronchial procedures because they reduce mucosal secretions and the resulting reflexive bronchospasms, thereby preventing vagus-induced bradycardia and improving surgical visibility.4–6 However, anticholinergics inhibit muscarinic acetylch oline receptors, exerting antimuscarinic actions such as dry mouth and fever. Thermoregulation is more dependent on sweating in children than in adults, and children may be more susceptible to higher body temperatures after injection of anticholinergics.7–9

Delayed discharge of paediatric patients due to postsurgical fever is frequently observed in patients anaesthetized with ketamine and adjunctive anticholinergics. Fever accounts for 4.7% of complications in paediatric outpatients after surgery,10 and may be caused by underlying disease, dehydration after preoperative fasting, or medication. Surgery is usually postponed in paediatric patients with fever or cold symptoms, reducing the likelihood that underlying conditions cause fever in this patient group. Although dehydration after preoperative fasting can cause fever,11 the fact that body temperature was normal before surgery suggests that fasting is unlikely to be the cause of fever in these cases. Of the medications used routinely in these patients (including Hartmann's solution, normal saline, adjunctive anticholinergics, ketamine and anti-inflammatory analgesic drugs), anticholinergics alone are reported to cause fever as an adverse effects.7,8 Ketamine has also been reported to cause fever, but this is not generally regarded as an adverse event.12 The other listed medications (fluid and anti-inflammatory drugs) are used to treat fever, and are not the cause.13

The aim of this study was to evaluate the fever-causing effects of adjunctive anticholinergics in children under ambulatory anaesthesia using ketamine.

Materials and methods:

This randomized, double-blind, placebo-controlled, prospective study recruited sequential paediatric outpatients aged 12 months – 8 years who were scheduled for procedures requiring ketamine sedation (including v-tube insertion, simple incision for cyst removal, incision and drainage of abscess and frenuloplasty of the tongue) between October 2016 to October 2017 at the Department of Anaesthesia in a tertiary hospital in central India. Inclusion criteria were: (i) American Society of Anaesthesiologists class I14; (ii) surgery performed between 08.00 and 09.00 (to minimize variation due to body temperature fluctuations and duration of preoperative fasting). Patients who required endotracheal intubation due to respiratory failure during the procedure and patients who received medications other than ketamine were excluded. Data were presented as n or mean ± SD. Between group comparisons were made using independent t-test, with repeated measures analysis of variance used to evaluate between group differences in body temperature.

Results:

The study recruited a total of 84 patients, who were randomized between group G (n=42; 22 males/20 females; mean age 3.5 ± 1.6 years; age range 1 – 7 years) and group N (23 males/19 females; mean age 3.7 ± 2.2; age range 1 – 8 years). Demographic and clinical characteristics of the patients are shown in Table 1.

Data regarding mean postoperative body temperature are shown in Figure 2. Overall, mean body temperature was significantly higher in group G than group N (P= 0.001). In addition, mean body temperature was significantly higher in group G than group N at 30, 60 and 90min after surgery (P< 0.05 for each comparison, Figure 2).

The study shows the emergence characteristics of both groups. The emergence time was significantly shorter in the D group (mean difference 1.4min and 95% CI: 0.5–2.3min). There were no group differences in recovery time (mean difference 0.4min and 95% CI: –2.1 to 1.2min), the incidence of vomiting, and the incidence of overall respiratory adverse events (relative risk 1.05 and 95% CI: 0.74–1.47).

Discussion:

Premedication with an anticholinergic drug resulted in increased postoperative body temperature compared with placebo in the present study. This finding could be regarded as clinically negligible because the overall mean body temperature of both groups was 37 – 37.5 degree C, a small difference from the baseline body temperature (37.0 degree C), and requiring no treatment. Higher body temperatures persisted until 90 min after surgery in patients treated with anticholinergic drugs in the current study, whereas temperatures in the placebo group returned to baseline by 60 min after surgery. Of clinical importance, however, was the significantly higher incidence of fever in patients

treated with anticholinergic drugs than those in the placebo group.

The definition of fever used in the present study was a tympanic temperature of 37.8 degree C. Fever is generally defined as a rectal temperature of >38 degree C, but the routine use of a rectal thermometer is challenging and tympanic thermometers are preferred. Temperatures measured using tympanic thermometers have been reported to be 0.1–0.2 degree C lower than those measured using a rectal thermometer.15,16

As expected, the quantity of oral secretions was significantly lower in the anticholinergic-treated group than the placebo group, although there were no secretion-associated complications observed in any patient. The increased amount of suction required to deal with the greater volume of oral secretions in the placebo group did not increase the duration of the procedure. The total volume of administered fluid was higher in the anticholinergic-treated group compared with the placebo group, due to the increase in infusion of fluids when fever was present.

The effectiveness of adjunctive anticholinergics prior to sedation is unclear, and routine administration of anticholinergics in procedures such as bronchoscopy has been viewed skeptically.17,18 Some recommend the avoidance of adjunctive anticholinergics in paediatric patients,19 because of their limited effect on suppressing salivation while increasing the risk of enhancing the adverse effects of ketamine.20 Adjunctive anticholinergics are recommended for the suppression of hypersalivation and for their antiemetic effect in ketamine sedation.21 To our knowledge, the only report of the relationship between adjunctive anticholinergics and fever is a study applying atropine to eyes prior to ophthalmic examination.22 Our present findings suggest that routine premedication with adjunctive anticholinergics should not be recommended in paediatric patients receiving ketamine sedation, because the increase in body temperature outweighs any advantages gained from suppression of oral secretions during surgery.

There were several limitations to our study. Various surgical procedures were included and there was no evaluation of the surgical difficulties caused by oral secretions. More informative data could be collected if procedures that are sensitive to the amount of oral secretion are studied, and if any surgical difficulties are evaluated by the surgeon.

In conclusion, routine premedication with adjunctive anticholinergics should not be considered in paediatric patients receiving ketamine sedation due to the increased risk of fever. Use of anticholinergics should be limited to procedures that require a high level of secretion suppression.

Tables:

TABLE 1: The patient characteristics:
Data presented as n, or mean ± SD.

NS, not statistically significant (P ≥ 0.05); VAS, visual analogue scale (mm).
A Independent t-test.
B Temperature ≥ 37.8 degree C at more than one time point.

Characteristic	Glycopyrrolate group *n* = 42	Control group *n* = 42	Statistical significance
Sex, male/female	22/20	23/19	NS
Age, years	3.5 ± 1.6	3.7 ± 2.2	NS
Weight, kg	16.7 ± 3.8	17.7 ± 6.8	NS
Duration of surgery, min	6.7 ± 3.1	7.6 ± 4.0	NS
Ketamine dose, mg/kg	3.1 ± 0.6	2.9 ± 0.9	NS
Baseline temperature, °C	37.0 ± 0.3	37.0 ± 0.2	NS
Postoperative fever [b]	14	4	*P* = 0.02
Total intravenous fluid, ml	97.4 ± 44.1	76.1 ± 32.6	*P* = 0.03
Oral secretion volume, VAS	35.3 ± 14.3	44.8 ± 19.5	*P* = 0.02

Figure 1: Consort flow diagram for patient enrolment into a randomized controlled clinical trial to evaluate the fever-causing effects of adjunctive anticholinergics in children under ambulatory anaesthesia using ketamine.

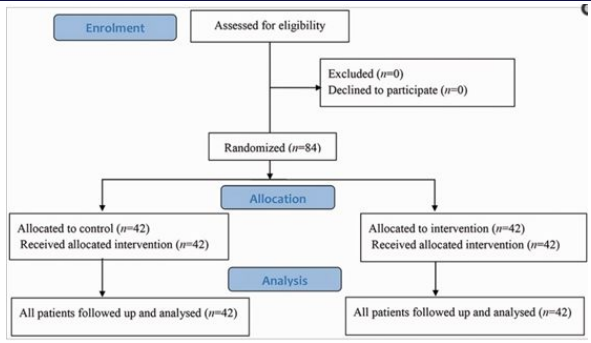
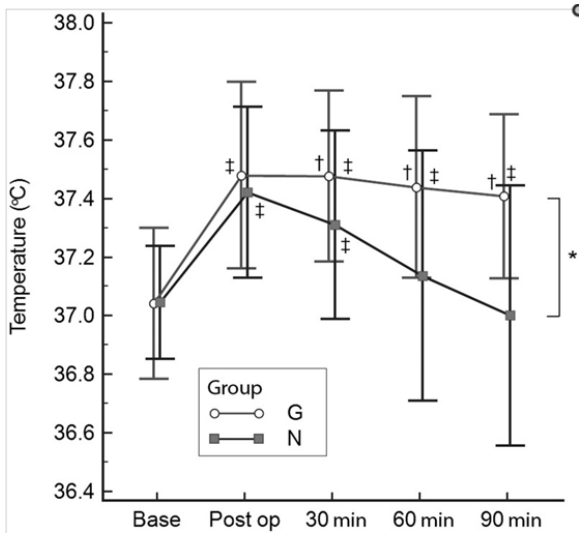


Figure 2:
Body temperature in paediatric patients undergoing ambulatory anaesthesia with ketamine sedation and receiving either 0.005mg/kg glycopyrrolate intravenously (group G, n=42) or the same volume of saline preoperatively (group N, n=42). Body temperature was measured tympanically before surgery (baseline), and at 0, 30, 60 and 90 minutes postsurgery. *P=0.001 between glycopyrrolate and placebo group; † P<0.05 vs control group at same time point; ‡ P<0.05 vs baseline in same group.



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