Humidification reduces coughing and breath-holding during inhalation induction with isoflurane in children

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Purpose: *Inhalation induction using isoflurane is associated with airway irritability, coughing, breath-holding and laryngospasm. These complications are more common in children. This study was designed to determine if humidification of isoflurane in oxygen/nitrous oxide would reduce respiratory complications and hypoxic episodes at induction.*

Methods: *Fifty-nine unpremedicated children, aged three months to 12 yr, were enrolled in the study and randomised to receive either humidified isoflurane (n = 27, Group A), or non-humidified isoflurane (n = 32, Group B). All inductions of anaesthesia were with isoflurane 4% in 50% oxygen/nitrous oxide. Subjects were observed for the occurrence of breath-holding, coughing, laryngospasm, bronchospasm, secretions, and hiccoughs. The severity of each complication was graded on a scale of 0–3. The need to administer 100% oxygen and/or succinylcholine was also identified.*

Results: *Coughing (33% vs 53%) was more frequent in Group B ($P < 0.05$). Coughing severity scores (13 vs 36) and breath-holding severity scores (8 vs 19) were also greater in Group B ($P < 0.05$). A change in FiO_2 was required more frequently in Group B (4% vs 16%). Although there was a high incidence of laryngospasm in both groups (52% vs 59%), no other differences were identified, breath-holding (26% vs 31%), secretions (30% vs 31%), hiccough (11% vs 12.5%) ($P > 0.05$).*

Conclusion: *Humidification of inspired isoflurane reduces the frequency and severity of coughing, the severity of breath-holding, and the need to increase supplemental inspired oxygen concentration, when isoflurane is used for inhalation induction of anaesthesia in children. Humidification has no effect, however, on the frequency and severity of laryngospasm, or on the frequency of occurrence of arterial oxygen desaturation.*

Objectif: *L'induction par inhalation d'isoflurane est associée à l'irritabilité des voies aériennes, à la toux, à l'apnée et au laryngospasme. Ces complications surviennent surtout chez les enfants. Cette étude visait à déterminer si l'humidification de l'isoflurane en oxygène/protoxyde d'azote pouvait diminuer l'incidence des complications respiratoires et les épisodes d'hypoxie à l'induction.*

Méthodes: *Cinquante enfants non prémédiqués, âgés de trois mois à 12 ans ont été assignés à cette étude aléatoirement pour recevoir soit de l'isoflurane humidifié (n = 27, groupe A), soit de l'isoflurane non humidifié (n = 32, groupe B). L'induction a toujours été réalisée à l'isoflurane dans un mélange oxygène/N_2O 50:50. On recherchait spécifiquement l'apnée, la toux, le laryngospasame, les sécrétions et le hoquet. Un score de gravité de 0–3 était assigné à chacune de ces complications. La nécessité d'administrer de l'oxygène à 100% et/ou de la succinylcholine était aussi notée.*

Résultats: *La toux (33% vs 53%) a été plus fréquente dans le groupe B ($P < 0,05$). Les scores de gravité pour la toux (13 vs 36) et l'apnée (8 vs 19) étaient aussi plus élevés dans le groupe B ($P < 0,05$). Il a fallu changer la FiO_2 plus fréquemment dans le groupe B (4% vs 16%). Bien que l'incidence du laryngospasme ait été élevée dans les deux groupes (52% vs 59%), on n'a pas noté d'autres différences: apnée (26% vs 32%), sécrétions (30% vs 31%), hoquet, (11% vs 12,5%) ($P > 0,05$).*

Conclusion: *L'humidification de l'isoflurane inspiré diminue la fréquence et la gravité de la toux, de l'apnée et le besoin d'oxygène inspiré supplémentaire lorsqu'on utilise l'isoflurane comme agent d'induction inhalatoire chez les enfants. Toutefois, l'humidification n'a aucun effet sur la fréquence et*

Key words

ANAESTHESIA: paediatric;
ANAESTHETIC TECHNIQUE: induction, inhalation;
ANAESTHETIC: volatile, isoflurane, humidification;
COMPLICATIONS: breath-holding, coughing, laryngospasm, secretions, hypoxia.

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la gravité du laryngospasme ni sur l'incidence de la désaturation artérielle en oxygène.

Isoflurane is known to be associated with an increased frequency of coughing, breath-holding and laryngospasm when used for inhalation induction of anaesthesia.[1] Its pungent odour is irritant to the airway, contributing to the high incidence of respiratory complications and episodes of arterial oxygen desaturation.

Inhalation induction of anaesthesia is commonly used in children and, as reflex airway responses are more pronounced in children than in adults, the incidence of airway complications is more frequent in the paediatric population.[2] Several studies have shown that the use of isoflurane for inhalation induction of anaesthesia in children is associated with a high incidence of upper airway problems.[1,3–6] Premedication has been shown to reduce the frequency of these complications.[7]

Humidification of anaesthetic gases has previously been shown to decrease the incidence of respiratory complications occurring during inhalation induction with isoflurane.[9] This study was in a predominantly adult population. The effect of humidification on inhalation induction with isoflurane in a group of premedicated children found no benefit of humidification on the incidence of respiratory complications.[2]

Since a large proportion of children presenting for anaesthesia and surgery today are unpremedicated and scheduled for elective day-case surgery, inhalation induction using isoflurane in this patient population has the potential to result in a high incidence of coughing, breath-holding and laryngospasm. Our intention in this study was to determine whether the addition of humidification to inspired anaesthetic gases would reduce airway complications, in unpremedicated children using a standard style of inhalation induction with isoflurane.

Methods

With Hospital Ethics Committee approval and informed parental consent, 59 children, ASA class I–II, aged three months to 12 yr, scheduled to undergo minor elective day-case surgical procedures were enrolled in a randomised double-blind study protocol. Exclusion criteria included a history of asthma, cardiac, renal or hepatic disease, oesophageal reflux, difficult airway, a history of malignant hyperthermia or any adverse response to previous anaesthetics.

The children were randomised to receive an inhalation induction using either humidified (Group A) or non humidified (Group B) isoflurane. In Group A, general anaesthesia was induced using isoflurane 4% in 50% oxygen/nitrous oxide, inspired gases passing through a hot water humidifier, distal to the common gas outlet of the anaesthetic machine. The humidifier was heated to 60°C, giving a temperature of 27°C at the patient end. Children in Group B, received an inhalation induction using isoflurane 4% in 50% oxygen/nitrous oxide, inspired gases passing through a non-functioning humidifier.

A standardised anaesthetic technique was used for all subjects. Children were unpremedicated and anaesthesia was induced using an Ayre's T-piece with Jackson-Rees' modification (weight < 25 kg), or a Bain breathing system (Mapleson's Type D) (weight > 25 kg), using a fresh gas flow, 2.5 times the patient's minute ventilation, to prevent rebreathing. Initially, the gases were administered with the aid of a cupped hand held over the child's nose and mouth. Consequently, the initial inspired concentrations of isoflurane and nitrous oxide were less than 4% and 50% respectively. With loss of the eyelash reflex, signifying loss of consciousness (LOC), an appropriate sized anaesthetic face mask was introduced. Deep anaesthesia was evidenced by unconsciousness, regular breathing, eyes fixed and central and pupils constricted. All inductions were performed by one of two anaesthetists, blinded as to whether or not the humidifier was in use.

The following standardised measurements were conducted on all subjects and recorded every 30 sec: heart rate, respiratory rate, arterial oxygen saturation. All measurements were made by an independent observer. The incidence of breath-holding, coughing, laryngospasm, bronchospasm, secretions, hiccough, were recorded. The severity of each complication was graded on a scale 0–3 (Table I) and the total severity score for a particular complication in each group was calculated and compared between groups. The total severity score for a complication e.g., coughing, was the sum of the individual severity scores for each child, 0 = no coughing, 1 = 1–2 coughs, 2 = >2 coughs (no laryngospasm), 3 = >2 coughs (laryngospasm). Mild and severe episodes of arterial oxygen desaturation (SaO_2 < 96%, SaO_2 < 90%) were recorded. The need to change to 100% oxygen and/or to administer succinylcholine to a child due to severe respiratory compromise was recorded.

Statistical analysis

Demographic data were compared using Students t test. Time to loss of consciousness and deep anaesthesia, incidence and severity of respiratory complications, episodes of arterial oxygen desaturation and change to 100% oxygen – were analysed using Mann-Whitney U test and Chi-squared analysis. Statistical significance was a $P < 0.05$.

TABLE I Respiratory Complications (Grading Scale)

		Grade
Breath-holding		
None		0
Mild	<15 sec	1
Moderate	>15 <60 sec	2
Severe	>60 sec	3
Coughing		
None		0
Mild	1–2 Coughs	1
Moderate	>2 coughs (no laryngospasm)	2
Severe	>2 coughs (larnygospasm)	3
Laryngospasm		
None		0
Mild	>5 sec phonation	1
Moderate	>5 sec phonation, <10 sec transient, complete obstruction	2
Severe	>10 sec complete obstruction	3
Bronchospasm		
None		0
Mild	Wheeze end-expiration	1
Moderate	Wheeze (throughout expiration) – adequate ventilation	2
Severe	Wheeze (throughout expiration) – impaired ventilation	3
Secretions		
None		0
Mild	Present, no suction required	1
Moderate	Suction 1–2	2
Severe	Suctioning >2	3

TABLE II Demographic data and group characteristics. Age and weight expressed as mean (range). LOC and deep anaesthesia expressed as mean (SD)

	Humidified isoflurane (Group A) n = 27	*Non-humidified isoflurane (Group B) n = 32*
Age (yr)	3.3 (0.2–12.4)	4.5 (0.21–12.5)
Weight (kg)	15.0 (6.5–26)	18.1 (7.8–34)
Sex (M/F)	17/10	23/9
LOC (min)	1.1 ± 0.45	1.1 ± 0.48
Deep anaesthesia (min)	4.3 ± 1.06	4.8 ± 1.21

TABLE III Incidence and severity of respiratory complications occurring during inhalation induction of anaesthesia using isoflurane

	Humidified isoflurane (Group A) n = 27	*Non-humidified isoflurane (Group B) n = 32*
Incidence		
Coughing	9 (33%)	17 (53 %)*
Breath-holding	7 (26%)	10 (31%)
Laryngospasm	14 (52%)	19 (59%)
Hiccough	3 (11%)	4 (12.5%)
Bronchospasm	0	0
Severity score		
Coughing	13	36*
Breath-holding	8	19*
Laryngospasm	20	30
Secretions	10	13
Desaturation		
SaO_2 < 96%	8 (29%)	9 (28%)
SaO_2 < 90%	4 (14.5%)	5 (15.5%)
Change FiO_2	1 (4%)	4 (16%)*

Statistical significance *$P < 0.05$.

Results

There were no demographic differences between groups (Table II). Time to loss of consciousness (LOC) was 1.1 ± 0.45 min in Group A and 1.1 ± 0.48 min in Group B. Time to deep (surgical) anaesthesia was 4.3 ± 1.06 min in Group A and 4.8 ± 1.21 min in Group B. These times were not different between groups.

The incidence and severity of respiratory complications occurring at induction are recorded in Table III. The incidence and severity of coughing were greater in Group B (non-humidified) ($P < 0.05$). In Group A (humidified isoflurane) 33% of children (9/27) coughed at induction, compared with 53% of children (17/32) in Group B (non-humidified). Individual coughing severity score of 2 or 3 was recorded in 7% children (Group A), and 34% children (Group B). Coughing severity score of 3 occurred in 7% children (Group A), and 25% children (Group B). Episodes of breath-holding were longer in Group B (non-humidified) ($P < 0.05$). Moderate breath-holding (15–60 sec) and severe breath-holding (>60 sec) (severity score of 2 or 3) occurred with only one child in Group A, compared with 25% children in Group B. A higher incidence of respiratory complications necessitating change to 100% oxygen occurred in Group B (non-humidified), with 4% of children in Group A (humidified), and 16% of children in Group B (non-humidified) requiring change to 100% oxygen ($P < 0.05$).

There were no differences between groups (Group A vs Group B) with regard to the incidence of breath-holding (26% vs 31%), laryngospasm (52% vs 59%), secretions (30% vs 31%), hiccough (11% vs 12.5%) ($P > 0.05$). There was a high incidence of laryngospasm in both groups, Group A (humidified) 52% of children (14/27), Group B (non-humidified) 59% of children (19/32) ($P > 0.05$). Episodes of arterial oxygen desaturation that occurred in both groups were not different ($P >$

0.05). Oxygen saturation <96% occurred in 29% of children (8/27) (Group A), and 28% of children (9/32) (Group B). Oxygen saturation <90% occurred in 14.5% of children (4/27) (Group A), and 15.5% of children (5/32) (Group B). In this study no child required the administration of succinylcholine. For all measured variables, no differences were found between groups.

Discussion

Isoflurane has a pungent odour and is irritant to the airways, resulting in coughing, breath-holding, laryngospasm and episodes of arterial oxygen desaturation at induction.[1-6] This problem is more prevalent in the paediatric population,[2-6] especially in unpremedicated children scheduled for elective day-case anaesthesia and surgery.[7] Humidification of inspired gases has been shown to reduce respiratory complications in adults.[9] McAuliffe *et al.*, studied the effects of humidification on inhalation induction with isoflurane in children and found that humidification was of no benefit in reducing respiratory complications.[2]

In our study the inspired gases were humidified, a standard inhalation induction technique with isoflurane was used, and the incidence and severity of respiratory complications occurring during inhalation induction with isoflurane in children were recorded. The incidence and severity of coughing were greater and the duration of breath-holding was longer in the control group, Group B (non-humidified) than in Group A (humidified) ($P < 0.05$). There were no differences between groups regarding the incidence of breath-holding, laryngospasm, secretions and hiccoughs ($P > 0.05$). There was a high incidence of laryngospasm in both groups, 14/27 children in Group A (52%) and 19/32 children in Group B (59%). Humidification did not reduce the incidence of this serious and potentially life threatening complication. Episodes of arterial oxygen desaturation occurred in both groups and were comparable. Respiratory complications necessitating change to 100% oxygen occurred more frequently in the control group (Group B) $P < 0.05$).

Humidification of inspired gases has been shown to reduce respiratory complications.[9] van Heerden *et al.* found that humidification of isoflurane reduced the incidence of coughing, breath-holding and secretions, with a reduction in the incidence of complicated inductions from 45% (control group) to 9% (humidified group). This was a predominantly adult population, the small number of children precluding extrapolation to the paediatric population. McAuliffe *et al.*, studied the effects of humidification on inhalation induction with isoflurane in children and found humidification of no benefit in reducing respiratory complications.[2] They found no difference between groups regarding the incidence of coughing, breath-holding, secretions or laryngospasm, with an incidence of respiratory complications of 25%. In our study the incidence of respiratory complications was higher, 80%, perhaps because we recorded all respiratory complications, mild, moderate and severe on a graded scale. In addition, children in our study were unpremedicated. Children studied by McAuliffe *et al.* were premedicated with 3 $mg \cdot kg^{-1}$ trimeprazine *po*. Premedication has been shown to reduce the incidence of respiratory complications occurring at induction.[7] Interestingly, McAuliffe *et al.* found a higher incidence of restlessness in the humidified group than in the control group (50% vs 20%) and this was ($P < 0.05$). Excessive movement and restlessness have been attributed to the use of nitrous oxide as the carrier gas.[4] They used 67% nitrous oxide in oxygen in that study.[2]

Investigators have used several different techniques to facilitate uneventful inhalation induction of anaesthesia using isoflurane.[12-16] The "single-breath" induction technique or rapid inhalation induction (RII) was first reported by Bourne *et al.* in 1954, in association with cyclopropane, to reduce respiratory complications during inhalation induction.[11] Mackenzie *et al.* studied isoflurane 5% for rapid inhalation induction (RII) of unpremedicated children and concluded that induction was smoother than with conventional isoflurane induction.[13] Applying the technique of rapid inhalation induction (RII), to the paediatric population is technically difficult because of lack of patient understanding and co-operation. A modification of this technique was developed by Warde *et al.* in which anaesthesia was induced using a high initial inspired concentration of isoflurane,[4] rather than with a single-breath. This was compared with the slow "step-up" induction technique, commencing with isoflurane 0.5% and increasing in increments of 0.5% until 4% isoflurane was achieved.[2]

A greater incidence of respiratory complications and a prolonged induction time might be expected when a high inspired isoflurane concentration is used from the outset. Warde *et al.* postulated that airway irritability during inhalation induction is more a reflection of the second stage of anaesthesia than a reaction to the pungency of the agent. They suggested that, if this unpleasant second stage could be shortened by a more rapid uptake of anaesthetic agent, the result might be a reduction in the incidence of respiratory complications during induction.[4] We set out to achieve this using a high initial isoflurane concentration 4% in 50% oxygen/nitrous oxide combined with humidification of the carrier gases.

In this study we recorded the incidence of respiratory complications and graded each complication in accordance with severity (none, mild, moderate, severe).

Other studies have documented the occurrence of respiratory complications, but apart from that by Phillips *et al.* where a grading system was employed,[1] authors did not grade complications according to severity. Thus we feel our results reflect more accurately the occurrence of respiratory complications during inhalation induction using isoflurane.

In conclusion, humidification of isoflurane, in combination with a high initial inspired isoflurane concentration from the outset, resulted in a reduction in the incidence and severity of coughing, the duration of breath-holding and the need to change to 100% oxygen. There was no effect on the incidence of breath-holding, secretions or laryngospasm. We noted a very high incidence of laryngospasm occurring in both groups, presumably related to the pungency of the agent rather than to the inhalation of dry anaesthetic gases. Furthermore, humidification of isoflurane while reducing the incidence and severity of some complications still resulted in an unacceptably high incidence of laryngospasm and arterial oxygen desaturation.

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