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Increased respiratory symptoms following surgery in children exposed to environmental tobacco smoke

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Summary

Objective: The aim of this study was to determine if children exposed to environmental tobacco smoke (ETS) via parental smoking (ETS+) developed more respiratory symptoms resulting in longer recovery times following surgical outpatient procedures compared with children of nonsmoking parents (ETS–).

Methods: One hundred and forty six children (4.9 ± 3 years) undergoing inguinal hernia repair were prospectively studied. Parental smoking behaviour was determined by survey and urine analysis. Seven respiratory symptoms were evaluated during induction and emergence from anaesthesia and during the recovery room (RR) stay.

Results: Fifty-seven (39%) families admitted a smoking history while 89 (61%) denied it. This strongly correlated with the cotinine/creatinine ratio (Pearson correlation coefficient = 0.76; $P = 0.01$). ETS exposure was associated with an increased frequency of RR symptoms (ETS+: 56%; ETS–: 31%; $P = 0.007$).

Conclusions: In children undergoing general anaesthesia for inguinal hernia repair, ETS exposure was associated with an increased frequency of respiratory symptoms during emergence from anaesthesia and during postoperative recovery.

Keywords: environmental tobacco smoke; cotinine; respiratory symptoms

Introduction

Numerous reports have shown that environmental tobacco smoke (ETS), commonly referred to as second-hand smoke, is deleterious to the health of foetuses, infants and children. Passive and active smoking by pregnant mothers has been shown to lower neonatal birth weights (1–3) and result in a higher incidence of neonatal mortality (4). In addition, children of smoking mothers also have a higher incidence of respiratory disorders, reduced rate of lung function development, deficiencies in physical growth, as well as delays in intellectual and

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emotional development (4–9). The onset of childhood asthma has been associated with exposure to passive smoking (10,11); however, other papers argue against this association (12,13). Additionally, second-hand smoke has been shown to act as a major trigger for exacerbation of children's asthma (14–16) and is associated with increased asthma severity in adulthood (17,18). Other papers suggest that *in utero* smoke exposure is associated with wheezing and physician-diagnosed asthma, but not postnatal ETS exposure (19–22). Second-hand smoke increases asthma symptoms (23), bronchial hyperactivity (24), trips to the emergency department (25,26), and medication usage (23,25).

Tobacco smoking is known to pose risks to adult patients who undergo general anaesthesia. These include disruption of myocardial oxygen balance, high carbon monoxide exposure leads to high carboxyhaemoglobin levels which may affect pulse oximetry, and increased postoperative mortality secondary to respiratory complications compared with nonsmokers (27–30). In addition, smokers experience increased length of stay in postanaesthesia care units (PACU), and require longer anaesthetic times (AT) than nonsmokers. All of these effects have been correlated with the number of cigarettes smoked per day (31).

Cotinine, the major metabolite of nicotine, is tobacco specific with a half-life of approximately 24 h, making it a useful marker to assess an individual's recent level of exposure to ETS (32). Cotinine can be measured in serum, saliva or in urine. Importantly, numerous investigators have correlated ETS exposure and levels of urinary cotinine in both adults and children (33–38). Urinary cotinine levels in children correlate with parental smoking as well as with the number of cigarettes consumed per day in the household environment (39,40).

The effects of second-hand smoke on children undergoing general anaesthesia has not been conclusively determined. There is evidence that both pre- and postnatal ETS exposure may impact respiratory function, especially lung development; and, thus, these patients may be more susceptible to adverse side-effects following anaesthesia than nonexposed children (8,9,41,42). We hypothesized that the degree of ETS exposure in children as a result of parental smoking, measured using urinary cotinine as a marker, results in an increase in perioperative respiratory complications following general anaesthesia for inguinal hernia repair, and that these complications result in an increase in total recovery room (RR) time.

Materials and methods

Following approval from University of Michigan's Institutional Review Board and written informed parental consent, 146 children (4.9 ± 3.2 years) undergoing elective inguinal hernia repair under general anaesthesia (GA) between 1997 and 1999 were prospectively studied. Children scheduled for elective inguinal hernia repair from 3 months to 13 years of age were eligible for entry into the study. Exclusion criteria included children with a history of renal failure, diabetes insipidus, diabetes mellitus, cyanotic heart disease, incarcerated hernias or children less than 37 weeks of gestational age at birth. Urine samples were obtained from parents and patients for measurement of cotinine and creatinine levels. In addition, data regarding the method of anaesthetic delivery, surgical duration, adverse respiratory events during induction and emergence from anaesthesia and during the recovery room stay, duration of the postanaesthesia care unit stay, intra- and postoperative pain medications, parental smoking habits (by survey) and physiological criteria for patient discharge were collected.

All patients underwent general anaesthesia according to the following protocol: children were premedicated with midazolam intranasally (0.2 $mg \cdot kg^{-1}$) or orally (0.5 $mg \cdot kg^{-1}$). Following an inhalation induction of anaesthesia with halothane, an intravenous catheter was placed followed by administration of atracurium (0.5 $mg \cdot kg^{-1}$). Anaesthesia was maintained with 0.5–1.0 MAC isoflurane in 70% nitrous oxide and 30% oxygen. Following induction and prior to skin incision, acetaminophen (20 $mg \cdot kg^{-1}$) was administered. At this time, additional analgesic measures included either an ilioinguinal nerve block using 0.25% bupivacaine (0.25 $ml \cdot kg^{-1}$, maximum 5 ml) or a caudal block using 0.25% bupivacaine (0.5–0.75 $ml \cdot kg^{-1}$, maximum 15 ml) with 1 : 200 000 epinephrine (0.75 $ml \cdot kg^{-1}$, maximum 15 ml). In addition, prior to skin closure, the wound was infiltrated with 0.25% bupivacaine. In the RR, patients received incremental doses of morphine sulphate for breakthrough pain (up to a maximum of 0.1 $mg \cdot kg^{-1}$) intravenously. Ondansetron

(0.15 $mg \cdot kg^{-1}$, maximum 4 mg) was administered to treat postoperative nausea and vomiting.

On the day of surgery, a urine sample was obtained from the child and both parents. The urine sample was then frozen and stored in a −70°C freezer for later analysis of cotinine, nicotine and creatinine. Parental cotinine was measured by a spectrophotometric assay previously described and was able to accurately discriminate smokers from nonsmokers (43). Patient cotinine and nicotine levels were measured by a more sensitive method using high-pressure liquid chromatography (44). Parental and patient creatinine levels were measured spectrophotometrically by a standard diagnostic kit (Sigma 555). Concentrations of cotinine were expressed as nanogram urine cotinine/mg urine creatinine, termed the cotinine–creatinine ratio (CCR).

Parents were asked to fill out a questionnaire designed to elicit information on their smoking habits and the exposure of their children to second-hand smoke. Neither the anaesthesiologists nor the RR nurses were aware of parental smoking status. The anaesthesiologist evaluated the child during induction of and emergence from GA for seven airway and cardiopulmonary criteria including: coughing (>15 s), laryngospasm (active glottic closure requiring intervention), inspiratory or expiratory stridor, excessive salivation, breath holding (>10 s), bradycardia (50% reduction of baseline heart rate) and wheezing. The RR nurses also monitored these same parameters until the patient was transferred to the step-down RR or discharged. An additional recovery room survey instrument measured the time that the patient achieved physiological readiness to be transferred from the main RR to the step-down RR; that time was recorded and designated as the recovery room stay. This was carried out in order to remove 'noise' inherent in the system which delays patient discharge such as nurse staffing problems, physician availability in signing discharge orders or parental delay in obtaining and understanding discharge instructions.

Data were analysed using an SPSS statistical package with a *P*-value of <0.05 considered significant. Student's *t*-test was used to compare the continuous data and the chi-square test was used to evaluate categorical data. Logistic regression with multivariable analysis of the study parameters was utilized to identify predictive variables. Data are represented as mean ± SD, median and range, unless otherwise noted.

Results

Analysis of smoke exposed (ETS+) and nonexposed (ETS−) patient demographics are presented in Table 1. There was no significant difference in mean patient age, mean total operative time or the mean total time the patients spent in the PACU. Patient weight was significantly different between the two groups ($P = 0.001$). There was no significant difference between the percentage of males and females who were smoke exposed by survey ($P = 0.68$). Likewise, there were no significant differences in type of anaesthetic regimen employed between the two groups ($P = 0.46$).

Parent demographic data are presented in Table 2. Correlation between survey results and parental urine CCR analysis was highly significant (Pearson correlation coefficient = 0.76; $P < 0.01$). Fathers who smoked comprized 34% ($n = 49$) of the population studied and were younger, but not significantly, than nonsmoking fathers (34.6 ± 8.6 years vs 36.8 ± 7.0 years old; $P = 0.085$). By survey, fathers

Table 1
Patient population details

Variable	*Nonexposed* (n, %)	*Smoke exposed* (n, %)	P-*value*
Sex			
Males	69 (60%)	46 (40%)	
Females	20 (65.5%)	11 (35.5%)	0.68
Anaesthetic regimen			
Caudal block	65 (63%)	38 (37%)	
Inguinal block	24 (56%)	19 (44%)	0.46
Patient age (years)			
Mean ± SD	4.9 ± 3.1	4.9 ± 3.5	0.29
Median	4.4	4.1	
Range	0.28–12.59	0.25–13	
Patient weight (kg)			
Mean ± SD	19.2 ± 8.4	22.6 ± 16.1	0.001
Median	18	18.9	
Range	5.8–51	4.8–79	
Total operative time (min)			
Mean ± SD	43.4 ± 16.2	47.2 ± 24.1	0.30
Median	39	42	
Range	21–103	20–178	
Total recovery room time (min)			
Mean ± SD	116 ± 52	111 ± 48	0.66
Median	102	100	
Range	45–367	57–335	

Table 2
Parent population demographics

Variable	*Nonsmokers* (n, %)	*Smokers* (n, %)	P-*value*
Father (*n*, %)	93 (66%)	49 (34%)	0.001
Mother (*n*, %)	104 (72%)	41 (28%)	0.001
Either parent (*n*, %)	89 (61%)	57 (39%)	0.001
Father age (years)			
Mean ± SD	36.8 ± 7.0	34.6 ± 8.6	0.085
Median (range)	36 (22–57)	34 (18–59)	
Mother age (years)			
Mean ± SD	34.8 ± 6.2	30.9 ± 6.5	0.001
Median (range)	35 (20–52)	31 (17–50)	
Father cotinine–creatinine ratio (CCR) (ng·mg^{-1})			
Mean ± SD	1566 ± 1369	13 858 ± 7464	0.001
Median (range)	1135 (304–7655)	13 992 (1264–29 708)	
Mother CCR (ng·mg^{-1})			
Mean ± SD	1966 ± 1541	13 230 ± 10 538	0.001
Median	1535 (57–9441)	11 366 (824–42 947)	
Father (cigarettes per day; survey)			
Mean ± SD	0	17.7 ± 12.0	0.001
Median (range)	0 (0)	20 (0.5–60)	
Mother (cigarettes per day; survey)			
Mean ± SD	0	11.8 ± 9.6	0.001
Median (range)	0 (0)	10 (0.5–30)	
Total parent CCR (ng·mg^{-1})			
Mean ± SD	1797 ± 1398	13 680 ± 7832	0.001
Median (range)	1513 (204–8000)	12 320 (1264–31 695)	
Total parent (cigarettes per day)			
Mean ± SD	0	27.2 ± 18.4	0.001
Median (range)	0 (0)	25 (0.5–80)	

smoked an average of 17.7 ± 12.0 cigarettes per day, and they had mean urine CCR of 13 858 ± 7464 (nanogram cotinine/mg creatinine), which was significantly higher than the CCR of fathers who were nonsmokers (1566 ± 1369 ng·mg^{-1}); $P = 0.001$). Mothers who smoked comprised 28% ($n = 41$) of the population studied, however, in contrast with fathers, were significantly younger (30.9 ± 6.5 years old) compared with nonsmoking mothers (34.8 ± 6.2 years old; $P = 0.001$). Mothers smoked an average of 11.8 ± 9.6 cigarettes per day, and had significantly increased mean urine CCR of 13 230 ± 10 538 ng·mg^{-1}; $P = 0.001$) compared with nonsmoking mothers (1966 ± 1541 ng·mg^{-1}. When either or both parents smoked, the children were designated as smoke exposed (ETS+) and consisted of 39% ($n = 57$) of the population studied. The mean urine CCR of the tobacco smoking parental group was 13 680 ± 7832 ng·mg^{-1} (vs 1797 ± 1398 ng·mg^{-1} in nonsmoking households; $P = 0.001$) and the mean number of cigarettes smoked was 27.2 ± 18.4 per day.

Table 3
Urinary nicotine, cotinine and cotinine–creatinine ratio (CCR) levels in patients

Variable	*ETS+*	*ETS–*	P-*value*
Nicotine (ng·ml^{-1})			
Mean ± SD	16.2 ± 34.6	6.4 ± 10.6	0.022
Median	3.4	0.0	
Range	0–197	0–54	
Cotinine (ng·ml^{-1})			
Mean ± SD	11.7 ± 21.0	1.0. ± 5.2	0.001
Median	0.0	0.0	
Range	0–94	0–38	
CCR (ng·mg^{-1})			
Mean ± SD	17.6 ± 29.4	1.5 ± 7.4	0.001
Median	0.0	0.0	
Range	0–128	0–49	

Table 4
Frequency of respiratory events in patients during induction and emergence from anaesthesia and in the recovery room (RR)

Patient group	*Induction percentage* (n)	*Emergence percentage* (n)	*RR percentage* (n)
All patients	14 (20)	42 (58)	41 (54)
ETS+	13 (7)	44 (25)	56 (30)*
ETS–	16 (13)	40 (33)	31 (24)

*$P < 0.01$ compared with ETS–.

Mean nicotine level was 16.2 ± 34.6 ng·ml^{-1} in the smoke exposed children vs. 6.4 ± 10.6 ng·ml^{-1} in those children whose parents did not smoke ($P = 0.022$). Likewise, the mean level of the nicotine metabolite, cotinine, in smoke exposed children was significantly elevated compared with children whose parents did not smoke (11.7 ± 21.0 vs 1.0 ± 5.2 ng·ml^{-1}, respectively) ($P = 0.001$). The mean CCR was also significantly elevated (17.6 ± 29.4 ng·mg^{-1} vs 1.5 ± 7.4 ng·mg^{-1}) ($P = 0.001$) in smoke exposed children (Table 3).

The frequency of respiratory symptoms is presented in Table 4. For all patients in the study, the frequency of any respiratory symptom occurring during induction, emergence and in the recovery room was 14.3%, 41.7% and 40.9%, respectively. There was a significant increase in the frequency of recovery room symptoms in the ETS+ children (56%) compared with those not exposed (31%; $P < 0.01$). Recovery room time between ETS exposed children and nonexposed children was not significantly different (ETS+ 111 ± 48 min vs ETS– 116 ± 52 min; $P = 0.53$).

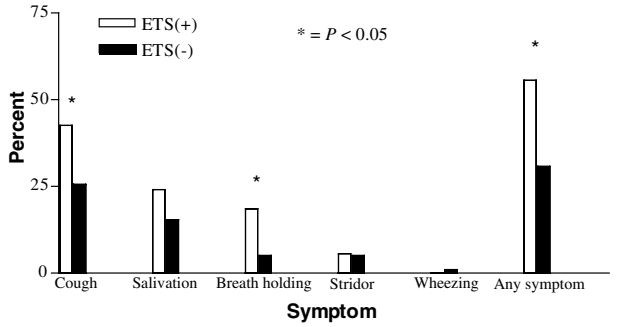

Figure 1
Distribution of recovery room symptoms in environmental tobacco smoke (ETS+) and ETS− children postoperatively. There was a significant difference in the frequency of breath holding and coughing, as well as differences in the frequency of exhibiting any respiratory symptom in the recovery room between smoke exposed and nonsmoke exposed children.

The frequency of specific symptoms found in the recovery room between ETS+ and ETS− children is presented in Figure 1. Coughing (42.6 vs 25.6%) and breath holding (18.5 vs 5.1%) in the RR was significantly increased in ETS+ children compared with the ETS− children ($P < 0.05$). All of the other individual variables evaluated trended higher in ETS+ patients compared with ETS− patients, but the differences were not statistically significant. However, the prevalence of having any recovery room respiratory symptom was significantly higher in the ETS+ patients (56%) compared with ETS− patients (31%; $P = 0.007$).

The presence of respiratory symptoms in the recovery room was highly correlated with ETS exposure by smoking parents ($P = 0.0039$) and total anaesthetic time ($P = 0.0342$), based on logistic regression. Further logistic regression analysis indicated a significant correlation between parental smoking and their child's CCR levels ($P = 0.0018$). Lastly, patient CCR levels were highly correlated ($P = 0.01$) with the mean number of cigarettes smoked per day by both parents (Pearson correlation = 0.61), mean number of cigarettes smoked per day by the mother (Pearson correlation = 0.557) and the mean number cigarettes smoked per day by the father (Pearson correlation = 0.554).

Discussion

Environmental tobacco smoke is a by-product of cigarette smoking, consisting of sidestream smoke (produced by burning tobacco) and exhaled smoke processed through a primary smokers' lung. Over 3800 compounds have been identified in tobacco smoke (45), and most ETS exposure is from unfiltered sidestream smoke, i.e. that not filtered through the cigarette or processed by a primary smokers' lungs. There is empirical evidence that sidestream smoke (which contains high concentrations of ammonia, benzene, nicotine, carbon monoxide and many carcinogens) is more deleterious to health because it is not filtered through either the cigarette or the smoker (46–57). Cotinine, a nicotine metabolite with a half-life of about 1 day, has been found in hair, saliva, blood and urine of both primary smokers as well as that of nonsmokers exposed to ETS. Smoke exposed children may be more susceptible than adults to the deleterious effects of secondhand smoke because of their smaller size, stage of development and maturation.

In adult patients undergoing general anaesthesia, disruption of myocardial oxygen balance, high carbon monoxide haemoglobin levels, increased postoperative mortality secondary to respiratory complications, increased length of stay in PACU and requirements of longer anaesthetic times (AT) than in nonsmokers have been reported (27–31). These effects correlate with the degree of smoking as well as the number of cigarettes consumed per day. Our study confirmed that there is a significant correlation between the presence and amount of parental cigarette smoking and a child's CCR levels. Significantly higher levels of urinary nicotine and cotinine were observed in children of smoking parents compared with children of nonsmokers. Furthermore, children's CCR levels were most highly correlated with both the mother and father's smoking behaviour. This is similar to a report by Oddoze *et al.*, who analysed urinary cotinine levels, and documented a high correlation between the number of cigarettes smoked, especially by the mother, and children's urinary cotinine levels (58).

Skolnick reported an increase in airway complications of smoke exposed children receiving general anaesthesia (59). These authors stratified patients based upon urine cotinine and noted an association between smoke exposure and airway complications. In our study, the frequency of respiratory complications during anaesthetic induction was comparable in ETS+ vs ETS− patients. However, during emer-

gence from anaesthesia and while the patients were in the recovery room, an increased frequency of respiratory complications was noted in all patients. Our analysis documented a further increase in the frequency of respiratory symptoms during the RR stay in the smoke exposed population (56%) compared with the nonsmoke exposed population (31%; $P < 0.01$). However, the total RR time between ETS+ and ETS− children was similar.

Both pre- and postnatal ETS exposure may have an impact on respiratory function, especially lung development (8,9,41,42). Newborns exposed to prenatal smoke exposure have a higher arousal threshold to auditory stimuli (60). Prenatal smoke exposure has likewise been correlated with an increase in frequency and length of obstructive sleep apnoea (61), and with changes in autonomic nervous system control and subsequent maturation in infants (62). It is unknown whether prenatal or postnatal ETS exposure has a greater effect on subsequent lung growth and respiratory function. Most mothers who smoke during pregnancy continue smoking after their child is born, making studies of this problem difficult to conduct. In addition, mothers who do not smoke prior to and during pregnancy, infrequently take up the habit postdelivery, an important study group for answering questions regarding the impact of prenatal vs postnatal smoke exposure upon respiratory function.

Our study was not designed to discriminate the effects of prenatal vs postnatal smoke exposure. Available evidence suggests a deleterious role by both prenatal and postnatal smoke exposure on lung development and respiratory function. Our study documents a significant association between parental smoking and patient CCR levels, a physiological measure of smoke exposure, and postoperative respiratory symptoms following inguinal hernia surgery in children.

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