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The effect of premedication on oxygen saturation during the post-premedication period in 20 Chinese children undergoing elective surgery

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Summary

Peri-operative continuous pulse oximetric data were studied in healthy Chinese children randomly allocated to receive either pethidine 1 mg kg $^{-1}$ and atropine 0.02 mg kg^{-1} intramuscularly 90 min prior to surgery (n=10), or midazolam 0.5 mg kg^{-1} and atropine 0.02 mg kg^{-1} orally, 120 min before surgery (n=10). Data were collected during the night before surgery, after premedication and for 8 h post-operatively. The pulse oximeter (Nellcor N-200E) output was retrospectively evaluated using Satmaster ™, a computer programme which permits storage, retrieval, signal evaluation and compilation of oximetric data. There was no significant difference in the frequency, duration, or magnitude ofde-saturation episodes recorded during the post-premedication period compared to the desaturation episodes which occurred in the same child during normal sleep, on the night before surgery. Furthermore, there was no significant difference in the desaturation data between the two premedicant regimens. No child recorded a genuine desaturation less than 80% for longer than 15 s at any time during the study. Neither regimen significantly depressed saturation in otherwise healthy children presenting for minor surgical procedures.

Keywords: ANAESTHESIA, paediatric; PREMEDICATION, atropine, midazolam, pethidine; MEASUREMENT TECHNIQUES, pulse oximetry.

Introduction

The pulse oximeter has become a vital instrument in the detection of peri-operative hypoxaemia [1]. Previous studies of the effect of premedication on arterial oxygenation using intermittent blood gas sampling have reported conflicting results [2–4] and few workers have employed continuous pulse oximetry to examine the pre-operative period [5,6]. Continuous oximetrc data acquisition should overcome the limitations of intermittent data sampling and permit a more accurate comparison of the effect on blood oxygenation of premedicant drug regimens. However, our previous work suggests that retrospective evaluation of peri-operative desaturation data, employing the computer Satmaster™ [7], is necessary before inferences can be drawn from the results [8].

The aim of this study was to compare the effect of two premedication regimens on arterial oxygen saturation in the post-premedication period and the influence, if any, of premedication on the episodic desaturation incidence during the first post-operative 8-h period, employing evaluated, continuous, pulse oximetry in children undergoing minor surgery.

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Methods

Twenty ASA grade I, Chinese children aged 1–8 years undergoing elective orthopaedic or a minor general surgical procedure were investigated. The study was approved

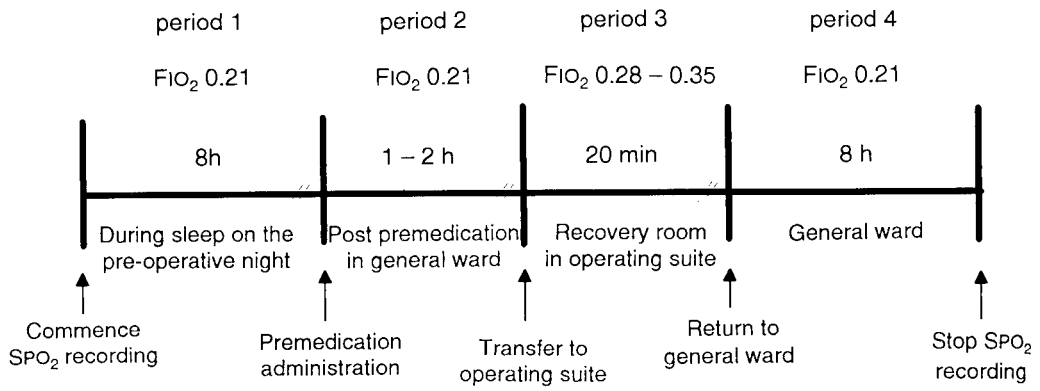

Fig. 1. Plan of the study, showing periods of recording and inspired O_2 concentrations.

by the Faculty of Medicine Ethics Committee (The University of Hong Kong) and written informed consent was obtained from the parents. Children were excluded from the study if there was a history of asthma or allergies, previous adverse anaesthetic experience, hepatic, renal, respiratory, cardiac or haematological disease, mental retardation or the predicted operation time was less than half an hour or greater than 2 h.

Oximetry data were recorded continuously during four time periods: whilst asleep, on the night before surgery; the period after the premedicant was administered and before transfer to the operating suite; post-operatively in the recovery room; and for a further 7 h after the child had returned to the general ward (Fig. 1). A Nellcor D-20/250 Oxisensor™ probe was attached to the great toe of each child and the same Nellcor N-200E oximeter was connected to each patient throughout the study. Proper function of the oximeter was checked by activating the oximeter's 'self-check' routine and prior attachment of the instrument to one of the investigators. The serial communication port of the oximeter was connected to an Amstrad 386DX laptop computer. Oximetry, (SPO_2), pulse rate and signal amplitude data were sampled 60 times min^{-1} and displayed by Satmaster™ (EMG Scientific) on the computer screen. On completion of the study the data were downloaded to disk for subsequent analysis. Satmaster was programmed to invalidate zero signal strength data occurring with probe disconnection. Each oximetry profile was examined by one of the authors who applied a previously described method to discard artefactual desaturation episodes attributed to probe movement, before compilation of the data [8]. An acute desaturation episode for the purpose of this study was defined as a decrease in oxygen saturation of more than 2% to less than 95% for more than 15 s duration.

Patients were randomly allocated to receive either pethidine 1 mg kg^{-1} and atropine 0.02 mg kg^{-1} intramuscularly (i.m.) 1.5 h before surgery (n=10), or midazolam 0.5 mg kg^{-1} and atropine 0.02 mg kg^{-1} orally (p.o.) 2 h before surgery (n=10). EMLA cream 2 g (lignocaine 25 mg g^{-1} and prilocaine 25 mg g^{-1}) was also applied to the dorsum of the hand at the same time. In the operating suite a standard anaesthetic technique was used in both groups of patients. Induction was with fentanyl 1 μg kg^{-1} and propofol 2 mg kg^{-1}, the patient was paralysed with atracurium 0.5 mg kg^{-1}, the trachea intubated and the lungs ventilated to normocapnia. A subjective assessment of tonsillar size and a graded view of glottal exposure were noted during direct laryngoscopy [9]. Thereafter, anaesthesia was maintained with 67% nitrous oxide and 1.0–1.5% isoflurane in oxygen, with additional increments of fentanyl 1 μg kg^{-1} h^{-1} and atracurium 0.2 mg kg^{-1} every 30 min, administered as required. At the completion of surgery the relaxant was reversed with neostigmine 0.05 mg kg^{-1} and atropine 0.04 mg kg^{-1} and the patients were extubated 'awake' observing the usual clinical criteria for adequate neuromuscular function [10], transferred to the recovery room and given oxygen (FIO_2 0.28–0.35) via a Hudson mask until discharge.

Statistical significance ($P<0.05$) was determined for interval scale data by unpaired t-test, nominal scale data by the Fisher exact probability test, ordinal scale data were analysed by the Mann-Whitney rank-sum test and the Wilcoxon signed-rank test was employed for before and after premedication comparison of data in the same patient.

Table 1. Patient-related data

	Pethidine group (n=10)	Midazolam group (n=10)
Age (years)	3.8 (1.8)	4.6 (2.6)
Weight (kg)	16.3 (5.7)	16.3 (2.3)
Anaesthetic time (min)	63.5 (39.9)	58.0 (21.4)
Sex (M/F)	9/1	6/4
Operative procedure: orthopaedic/general surgical	4/6	6/4

Interval scale data are mean (±SD).

Results

Both groups were comparable for age, weight, sex, anaesthetic time and operative procedure (Table 1). At direct laryngoscopy all children were found to be Cormack and Lehane grade 1 [9] and no child had tonsillar tissue projecting beyond the palatopharyngeal and palatoglossal arches into the oropharynx.

A total of 335 h of oximetric data was collected from 20 children. The total raw data time recorded with a saturation less than 95% in all children was 951.5 min, which, after evaluation with the template, resulted in a total of 228 min of valid desaturation time during the four study periods ($P<0.001$). The raw desaturation time in the period after premedication before operation was 132.5 min which, after evaluation, resulted in 33.5 min of valid desaturation time ($P<0.03$).

There was no difference in mean oxygen saturation between the two groups during the four periods under investigation, nor the mean percentage of time the oxygen saturation was less than 95% (Table 2). Within-group comparison of the percentage of time recorded with an oxygen saturation $<95\%$ during the pre-operative night and during the period after premedication, prior to transfer to the operating suite, revealed no significant difference (Table 3). Furthermore, a between-group comparison in the post-premedication period of the incidence of desaturation episodes per hour below 95% and of greater than 15 s duration, revealed no significant difference ($P=0.8$), nor was the patients' post-premedication incidence of desaturation episodes significantly different from the pre-operative incidence (Table 3). Twenty-four (65%) of the 37 valid post-premedication desaturation episodes occurred 45–105 min after administration of premedication.

Only two patients (one from each group) recorded five or more desaturation episodes per hour with an SPO_2 $<95\%$ and >15 s duration, following premedication, and no patient recorded a genuine desaturation less than 80% for longer than 15 s at any time during the study. The minimum SPO_2 recorded after premedication in either group was 85% and the longest duration of a particular episode was 75 s to a lowest saturation of 91%.

Discussion

This study demonstrates that in otherwise healthy children, the use of two common premedication regimens employing either pethidine or midazolam, does not significantly depress oxygen saturation. These findings are at variance with previous studies in healthy children, one of which showed that both i.m. and intranasal (i.n.) midazolam (0.2 mg kg^{-1}) caused a significant decrease in arterial oxygen saturation from baseline values [5]. However Rose and colleagues, using i.n. midazolam, demonstrated no change in oxygen saturation levels 15 min after administration [11]. In another study, premedication with rectal midazolam (0.35–0.45 mg kg^{-1}) lowered oxygen saturation 30 min after administration when compared with a placebo [6]. These apparently conflicting results can be explained by our ability to exclude movement-induced artefactual desaturation data before determining the incidence of genuine desaturation episodes [12]. Patient movement resulted in an overestimation of desaturation time by 75% in this study, confirming similar findings in patients following spinal surgery [8].

The route of administration of midazolam in children significantly alters bioavailability and the time to peak serum concentration, making comparison with other studies difficult [13]. Bioequivalence should be present between a 0.2 mg kg^{-1} i.m. dose of midazolam and the 0.5 mg kg^{-1} p.o. dose of midazolam used in this study, from 45 to 120 min after administration [13]. The peak serum concentration of midazolam occurs 15 min after i.m. administration [13] and the onset of sedation, together with the decrease in arterial oxygen saturation from baseline data, was similarly described in the study by de Santos and colleagues [5]. The peak incidence of the recorded minor desaturation episodes in our study occurred 45–105 min after administration of both pethidine and midazolam. It is therefore possible that our premedication regimen was not as sedative as those used in the Spanish study and did not depress respiration to

Table 2. Pulse oximetry data during the four study periods

Data collection periods	Duration of data collection period per patient (h)		Mean SpO_2(%)		*P* value (*t*-test)	Mean percentage of time with an $SpO_2 < 95\%$		*P* value (Mann Whitney *U*-test)
	Pethidine	Midazolam	Pethidine ($n=10$)	Midazolam ($n=10$)		Pethidine ($n=10$)	Midazolam ($n=10$)	
Pre-operative night	11.04 (1.22)	9.63 (0.84)	98.9 (0.57)	98.7 (0.67)	0.48	0.2 (0.63)	1.1 (1.85)	0.08
After premedication	1.29 (0.34)	1.80 (0.31)	98.6 (0.84)	98.7 (0.94)	0.81	1.6 (2.90)	2.8 (5.00)	0.49
Recovery area	0.26 (0.13)	0.35 (0.19)	99.4 (0.70)	99.1 (1.20)	0.50	0.6 (1.30)	5.7 (12.10)	0.35
General ward	7.05 (1.05)	6.52 (1.96)	98.5 (0.70)	98.4 (0.84)	0.78	0.8 (1.30)	1.1 (1.40)	0.60

Data are mean (±SD).

Table 3. A pulse oximetry data before and after premedication

Data collection periods	Pethidine group $n=10$		Midazolam group $n=10$	
	Mean % of time with an $SpO_2 < 95\%$	Desaturation episodes h^{-1} with an $SpO_2 < 95\%$ for >15s	Mean % of time with an $SpO_2 < 95\%$	Desaturation episodes h^{-1} with an $SpO_2 < 95\%$ for >15s
Pre-operative night	0.2 (0.63)	0.36 (0.62)	1.1 (1.85)	0.65 (0.73)
After premedication	1.6 (2.90)	1.48 (2.60)	2.8 (5.00)	1.82 (3.47)
P value (Wilcoxon)	0.11	0.37	0.34	0.51

Data are mean (±SD).

the same degree. Also, our study population may not match those in the other series, but a pharmacokinetic explanation of our oximetry findings is difficult to establish. The small lean body mass of Chinese children should result in a smaller central volume of distribution, higher peak serum concentration of midazolam, a more intense level of sedation of shorter duration, and consequently a higher incidence of episodic desaturation [14]. This was not the case, and, in a separate work, we have found that the serum concentration of midazolam 2 h after oral administration in Chinese children was similar to the serum concentration reported by other workers using a similar dosing regimen in Caucasian children [15]. Furthermore, none of the children in our study had any predisposition to upper airway obstruction or arterial oxygen desaturation and all were ASA class I. Peak respiratory depression in adults is observed within an hour of receiving intramuscular pethidine and there is a return towards baseline values commencing at about 2 h [16]. However pethidine premedication did not depress ventilation in our children to a degree where significant arterial oxygen desaturation occurred, nor to a level that was clinically or statistically significantly different from each child's own sleep SpO_2.

In conclusion, we have shown that neither oral midazolam 0.5 mg kg^{-1}, nor i.m. pethidine 1.0 mg kg^{-1} given as premedicants, significantly depressed SpO_2 in otherwise healthy children presenting for minor surgical procedures. Furthermore, raw oximetry data require careful evaluation and elimination of movement artefact before conclusions regarding the incidence of desaturation can be drawn. If analgesia is not a premedication requirement, then oral midazolam confers the advantage over pethidine of avoiding the pain of an i.m. injection without compromising oxygen saturation.

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