

Intubating conditions following four different doses of propofol in children

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Background: Day case surgery offers advantages to the patient, the family and the performing institution. Children are excellent candidates since they are generally healthy and often require brief surgical interventions. Day case surgery requires rapid emergence from anaesthesia, minimal delay in recovery and rapid readiness for discharge from the ward. The ideal anaesthetic agents should have rapid onset, short duration, minimal side effects and minimal residual effects. The pharmacodynamics and -kinetics of propofol and alfentanil are well suited for day case surgery and may obviate the need for muscle relaxants. The purpose of our study was to determine the optimal dosing schedules for intubation following propofol combined with alfentanil and sevoflurane anaesthesia while maintaining haemodynamic stability as these dosing schedules still warrant refinement.

Methods: We conducted a randomised prospective blinded study in which fifty-nine children (aged 3–10 years) presenting for dental extractions were induced with sevoflurane (in 50% oxygen/nitrous oxide), then received propofol (0.5, 1, 1.5 or 2 mg/kg) and alfentanil (10 µg/kg) to aid intubation. For each dose of propofol, the ease of intubation (assessed by the Helbo-Hansen score) was correlated with blood pressure and pulse rate (prior, during and after intubation) to determine the optimal propofol dosage allowing adequate intubation conditions with the least haemodynamic effects.

Results: Overall adequacy of intubating conditions improved significantly ($p = 0.0079$) as propofol dose increased. Similarly, decrease in vocal cord movement ($p = 0.0341$), incidence of coughing ($p = 0.0379$) and limb movement ($p = 0.0165$) was observed. Ease of laryngoscopy and jaw relaxation did not improve significantly ($p = 0.1319$ and 0.1971 respectively). Changes in systolic, diastolic and mean arterial pressure as propofol dose increased were not statistically significant.

Conclusion: Propofol in a dose of 1.5 to 2 mg/kg (when used in conjunction with alfentanil 10 µg/kg, after sevoflurane induction) allowed adequate intubating conditions whilst maintaining cardiovascular stability. The decrease in blood pressure, although not statistically significant, may become clinically relevant in children with underlying cardiovascular disease. This drug combination seems to be a reasonable means for avoiding the need for muscle relaxation for children who require tracheal intubation for brief surgical procedures.

Keywords: day case surgery, propofol, intubation, paediatrics, anaesthesia

Background

The popularity and safety of day case surgery has increased due to advances in surgical techniques and technology, analgesia, anaesthesia and changing parental and societal expectations.¹⁻³ It is associated with fewer behavioural disturbances and the psychological stress of overnight hospital admission is avoided. It also reduces the exposure to hospital acquired infections, causes less disruption to normal family routine and high parental and child satisfaction is noted.^{4,5} Children requiring surgical procedures rarely have major comorbid conditions, making them ideal candidates for minor or intermediate surgery of short duration.^{6,7}

The use of muscle relaxants to facilitate endotracheal intubation is considered the gold standard, since it improves tracheal intubating conditions while decreasing laryngeal morbidity (post intubation hoarseness and pain).⁸⁻¹⁰ However, for brief procedures that mandate tracheal intubation, a technique that avoids muscle relaxants that may exceed the duration of the procedure would be desirable.^{4,11-15} The purpose of our study was to examine the dose response for providing adequate conditions for tracheal intubation using a combination of increasing doses of propofol combined with 10 µg/kg of alfentanil^{11,16} under sevoflurane anaesthesia while maintaining haemodynamic stability.

Methods

Participants were recruited from the paediatric population that presented for elective dental extractions or restorative work. Consent was obtained from the parents of eligible children to be included in the study. If the patient was older than 7 years, assent was also obtained from the patient. Subsequently the participants were randomly assigned to one of four groups by drawing a dose from a sealed envelope. Randomisation of the propofol dose, administration of IV agent and data collection was done by the same researcher (TdP). The second researcher (JMD) performed the laryngoscopy, intubation and assessment thereof with the Helbo-Hansen scoring system whilst remaining blinded to the propofol dose used.

Baseline blood pressure, pulse and weight were measured in the preoperative area. No premedication was administered. Parents accompanied children in theatre until loss of consciousness. Once priming of the breathing circuit with sevoflurane 8% (in 50% oxygen/nitrous oxide mixture) was achieved, anaesthetic induction proceeded until loss of consciousness (loss of eyelid reflex).

After loss of eyelid reflex (LER), the IV line was inserted, and sevoflurane concentration decreased to 4%. Alfentanil was administered as soon as the end-tidal sevoflurane concentration

measured 4%. The predetermined dose of propofol followed 15 seconds later. Endotracheal intubation was attempted 45–60 seconds after propofol administration.

The Helbo-Hansen scoring system was used to grade intubating conditions; for every parameter, a score of one or two was considered adequate and a score of three to four inadequate (Table I).

Table I: Helbo Hansen intubating conditions score

	1	2	3	4
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe
Jaw relaxation	Complete	Slight	Stiff	Rigid
Limb movements	None	Slight	Moderate	Severe (jerky)

Blood pressure (SBP, DBP and MAP) was measured using the standard anaesthetic monitor in theatre (Datex Ohmeda ADU S5[®], Datex Engstrom, Bromma, Sweden) at predefined intervals: 1 – pre-induction (baseline), 2 – at LER, 3 – after alfentanil and propofol administration, 4 – during intubation, and 5 – 60 seconds after intubation. Data collection ended once the fifth observation was recorded. The presence or absence of apnoea after intubation was also recorded.

Data were recorded in a Microsoft Excel[®] (Microsoft Corp 2010, USA) spreadsheet. Analysis was done in conjunction with a biostatistician using Stata/IC 14.0 for Windows (copyright StataCorp LP 1985–2015, Texas, USA).

Sample size determination considered a contrast between means associated with a linear trend. A sample size of 11 children per group (total sample = 44) had a 90% power to detect a contrast of 19.1 mmHg (contrast -2, -1, 1, 2 and expected means of 2, 3.5, 6 and 10.3 mmHg) and a common standard deviation of 5.8 mmHg (sqrt 2*4.1). The biostatistician advised that groups

should consist of a minimum of 11 patients but that 15 patients per group would be advisable.

Relative to the minimum dose (0.5 mg/kg) overall ease of laryngoscopy, vocal cord position, jaw relaxation, risk of coughing and limb movement, total scores and incidence of apnoea for higher doses (1.0, 1.5 and 2.0 mg/kg) were assessed using odds ratio along with 95% confidence interval. The trend in odds ratio over dose was tested for $p < 0.05$ level of significance.

SBP, DBP and MAP data were summarised by dose group using descriptive statistics, mean and standard deviation. When adjusted for baseline mean, the 95% confidence interval was employed. Following a one-way analysis of co-variance for change in SBP, DBP and MAP, the contrast with coefficients (-2, -1, 1, 2) was tested to assess the trend over dose. The data obtained for SBP, DBP and MAP were displayed graphically for all doses as predictive margins in a mixed effect likelihood (ML) regression.

Results

Sixty-eight children were assessed for eligibility and fifty-nine were enrolled for the study; of the nine excluded patients, seven did not meet the inclusion criteria and in two cases the parents refused consent (Figure 1). The age, gender and weight distribution did not differ between groups. No adverse events occurred during the course of the study and all children were intubated successfully.

Intubating conditions

Laryngoscopy

In the 0.5 mg/kg group laryngoscopy was adequate (easy/fair) in 93% of cases and inadequate (difficult/impossible) in 7% (Table II). The other treatment groups (1.0, 1.5 and 2.0 mg/kg) had an adequate score in all participants. The difference in ease of laryngoscopy between the different dosages was not statistically significant ($p = 0.1319$).

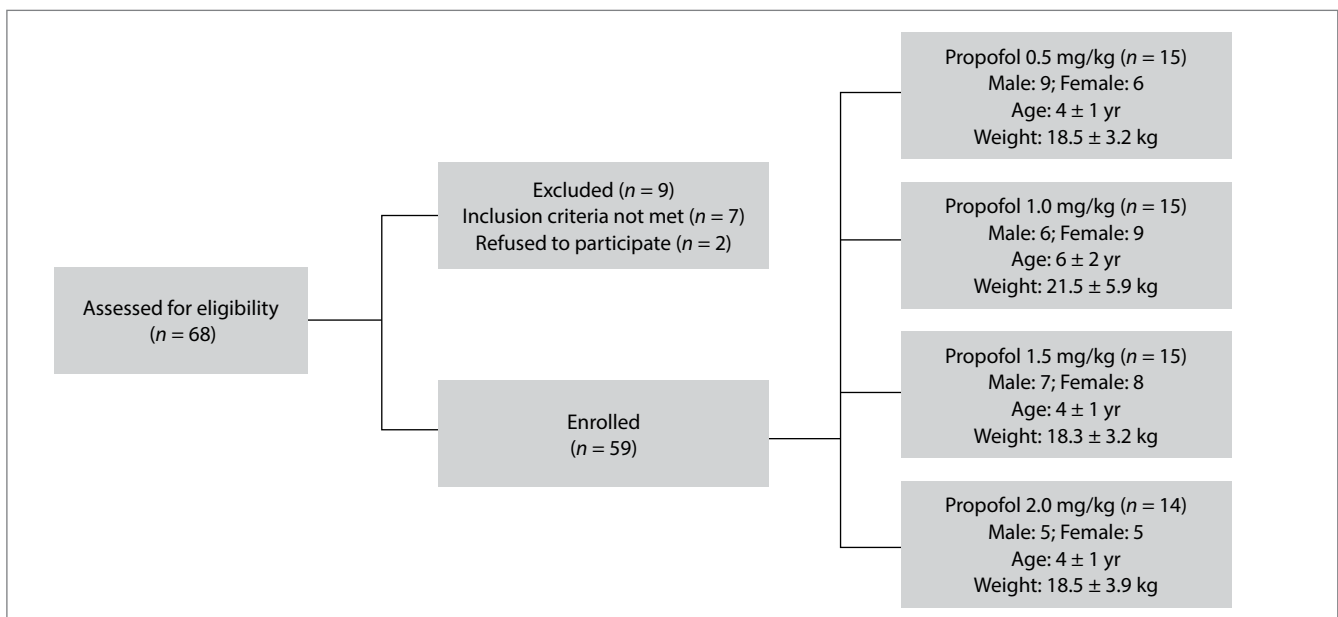


Figure 1: Flowchart patient distribution

Table II: Laryngoscopy (LAR)

Dose mg/kg	Adequate (1–2)	Inadequate (3–4)	Odds ratio	Chi ²	<i>p</i> > Chi ²	95% confidence interval
0.5	14 (93%)	1 (7%)	1			
1.0	15 (100%)	0	0.5	1.00	0.3173	
1.5	15 (100%)	0	0.5	1.00	0.3173	
2.0	14 (100%)	0	0	0.93	0.3340	
Score test trend of odds: <i>p</i> = 0.1319						

Table III: Vocal cord movement (CORD)

Dose mg/kg	Adequate (1–2)	Inadequate (3–4)	Odds ratio	Chi ²	<i>p</i> > Chi ²	95% confidence interval
0.5	10 (66%)	5 (33%)	1			
1.0	12 (80%)	3 (20%)	0.5	0.66	0.4169	0.0906–2.7564
1.5	12 (80%)	3 (20%)	0.5	0.66	0.4169	0.0906–2.7564
2.0	14 (100%)	0 (0%)	0	5.44	0.0196	
Score test trend of odds: <i>p</i> = 0.0341						

Table IV: Coughing (COUGH)

Dose mg/kg	Adequate (1–2)	Inadequate (3–4)	Odds ratio	Chi ²	<i>p</i> > Chi ²	95% confidence interval
0.5	9 (60%)	6 (40%)	1			
1.0	11 (73%)	4 (27%)	0.54	0.58	0.4463	0.1119–2.6585
1.5	12 (80%)	3 (20%)	0.37	1.38	0.2399	0.0683–2.0573
2.0	13 (92%)	1 (8%)	0.11	4.12	0.0423	0.0093–1.4255
Score test trend of odds: <i>p</i> = 0.0379						

Table V: Jaw relaxation (JAW)

Dose mg/kg	Adequate (1–2)	Inadequate (3–4)	Odds ratio	Chi ²	<i>p</i> > Chi ²	95% confidence interval
0.5	13 (87%)	2 (13%)	1			
1.0	13 (87%)	2 (13%)	1	0.00	1.0000	0.1174–8.5107
1.5	14 (93%)	1 (7%)	0.46	0.36	0.5496	0.0353–6.0986
2.0	14 (100%)	0 (0%)	0	1.94	0.1641	
Score test trend of odds: <i>p</i> = 0.1971						

Table VI: Limb movements (LIMB)

Dose mg/kg	Adequate (1–2)	Inadequate (3–4)	Odds ratio	Chi ²	<i>p</i> > Chi ²	95% confidence interval
0.5	12 (80%)	3 (20%)	1			
1.0	14 (93%)	1 (7%)	0.28	1.12	0.2909	0.0239–3.4115
1.5	15 (100%)	0 (0%)	0	3.22	0.0726	
2.0	14 (100%)	0 (0%)	0	3.02	0.0825	
Score test trend of odds: <i>p</i> = 0.0165						

Movement of vocal cords

In the 0.5 mg/kg group, 66% of cases were judged adequate (open/moving) and 34% inadequate (closing/closed) (Table III). The 1.0 and 1.5 mg/kg group had 80% adequate and 20% inadequate movement of vocal cords. The 2.0 mg/kg group had absence of vocal cord movement in all participants. The improvement in the groups from 0.5 to 2.0 mg/kg was statistically significant (*p* = 0.0341).

Coughing

In the 0.5 mg/kg group 60% scored adequate (none/slight) and 40% inadequate (moderate/severe). The 1.0 mg/kg group scored 73% adequate and 27% inadequate, the 1.5 mg/kg group 80% adequate and 20% inadequate and the 2.0 mg/kg group 92% adequate and 8% inadequate (Table IV). The decreased incidence

of coughing as the dose increased was statistically significant (*p* = 0.0379).

Jaw relaxation

Both the 0.5 and 1.0 mg/kg group scored 87% adequate (complete/slight) and 13% inadequate (stiff/rigid) (Table V), while the 1.5 mg/kg group scored 93% adequate and 7% inadequate and the 2.0 mg/kg group adequate conditions for all participants. Scores between the groups did not differ significantly (*p* = 0.1971).

Lack of limb movement

The 0.5 mg/kg group scored 80% adequate with regards to lack of limb movements (none/slight) and 20% inadequate (moderate/severe) (Table VI). In the 1.0 mg/kg group 93% scored adequate

Table VII: Total scores (TOTAL)

Dose mg/kg	Adequate (1–2)	Inadequate (3–4)	Odds ratio	Chi ²	<i>p</i> > Chi ²	95% confidence interval
0.5	7 (47%)	8 (53%)	1			
1.0	11 (73%)	4 (27%)	0.32	2.15	0.1427	0.0632–1.6020
1.5	11 (73%)	4 (27%)	0.32	2.15	0.1427	0.0632–1.6020
2.0	13 (93%)	1 (7%)	0.07	6.97	0.0083	0.0047–0.9710

Score test trend of odds: *p* = 0.0079

Table VIII: Apnoea

Dose mg/kg	Adequate (1–2)	Inadequate (3–4)	Odds ratio	Chi ²	<i>p</i> > Chi ²	95% confidence interval
0.5	6 (40%)	9 (60%)	1			
1.0	10 (67%)	5 (33%)	0.33	2.07	0.1501	0.0617–1.6061
1.5	8 (53%)	7 (47%)	0.58	0.52	0.4718	0.1320–2.5775
2.0	8 (57%)	6 (43%)	0.5	0.82	0.3643	0.1085–2.3040

Score test trend of odds: *p* = 0.3842

Table IX: Diastolic blood pressure changes from baseline

Dosage (mg/kg)	Loss of eyelid reflex (LER)	Post propofol/alfentanil (Post meds)	Intubation	After 60 seconds (60 sec)
0.5	10.425 [4.502–16.349]	16.238 [12.166–20.309]	2.838 [-3.848–9.524]	4.616 [-0.547–9.780]
1.0	3.439 [-2.469–9.348]	17.667 [13.605–21.728]	4.773 [-1.896–11.443]	10.928 [5.777–16.079]
1.5	9.724 [3.811–15.638]	20.933 [16.869–24.998]	9.509 [2.834–16.184]	11.879 [6.724–17.035]
2.0	8.940 [2.818–15.062]	21.103 [16.895–25.310]	6.871 [-0.039–13.781]	9.760 [4.423–15.097]
<i>p</i> -value	0.3305	0.2559	0.5369	0.2053
Linear regression		0.0514		

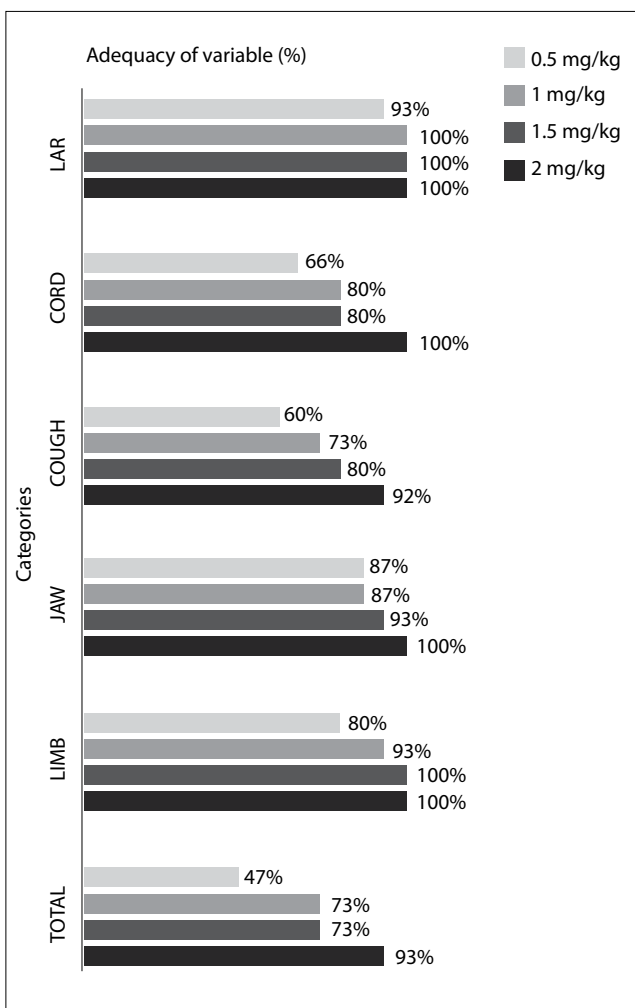


Figure 2: Helbo-Hansen Intubation score

and 7% inadequate. Limb movement was absent in 100% of the participants in the 1.5 and 2.0 mg/kg groups. The adequacy with increasing dose was statistically significant (*p* = 0.0165).

Total scores

Combining the scores for assessment of overall intubating conditions, the adequacy improved with increase in propofol dosage in a statistically significant manner (*p* = 0.0079) (Table VII). Adequacy of variables assessed with the Helbo-Hansen scoring system in the different groups is summarised in Figure 2.

Apnoea

The incidence of apnoea was recorded and did not show a statistically significant increase with an increase in propofol dose (*p* = 0.3842) (Table VIII).

Blood pressure fluctuations

Following the trend noted in similar studies, SBP, DBP and MAP all decreased from baseline value after the propofol/alfentanil administration in a near linear manner as the dosage of the propofol increased. Intubation attenuated this response with the blood pressure almost returning to baseline 60 seconds later. The deviation of the components of blood pressure from baseline as the propofol dose increased was not statistically significant (SBP: *p* = 0.1925, DBP: *p* = 0.0514 [Figure 3; Table IX], MAP: *p* = 0.616). Figures 4 and 5 and Tables X and XI depicting changes in SBP and MAP are included in the Appendix.

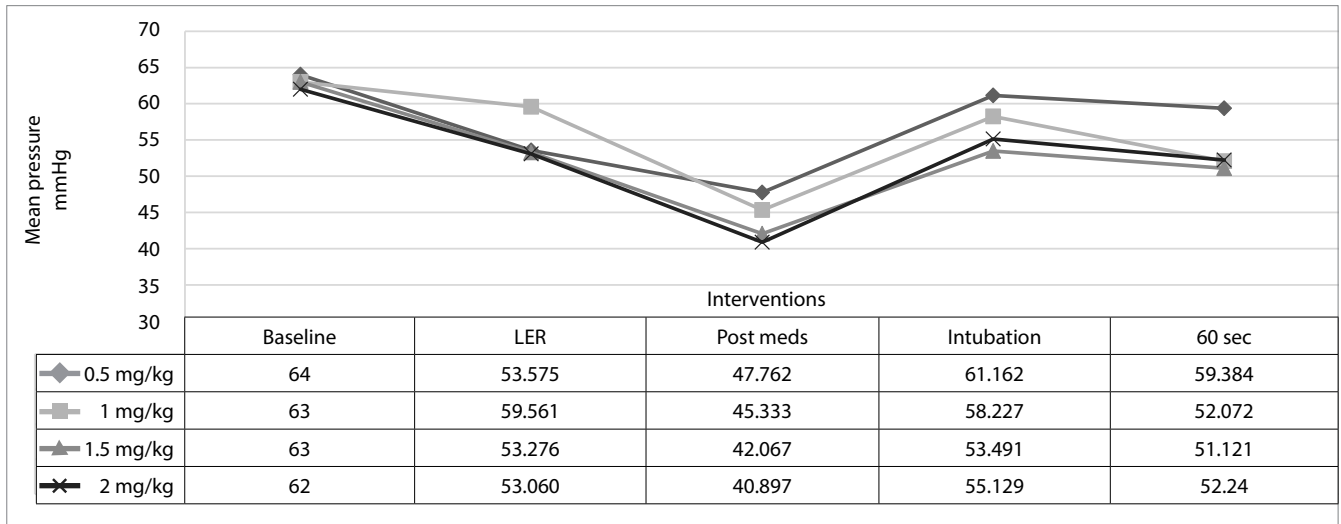


Figure 3: Diastolic blood pressure variation

Discussion

This study aimed to determine the optimal dose of propofol (in combination with sevoflurane and alfentanil) that offers the best intubating conditions while causing the least fluctuations in blood pressure.

Improvement in intubating conditions with increasing doses of propofol was found to be statistically significant when considering the total scores ($p = 0.0079$), correlating with findings from Lerman et al.¹² who compared intubating conditions with propofol doses between 0 mg/kg and 3 mg/kg. Ease of laryngoscopy and jaw relaxation did not show statistically significant improvement with increasing propofol doses. It is noteworthy that laryngoscopy was adequate in 93% of patients in the 0.5 mg/kg group and 100% in the 1.0, 1.5 and 2.0 mg/kg groups. Jaw relaxation was adequate in 87% of patients in the 0.5 and 1.0 mg/kg groups, 93% in the 1.5 mg/kg group and 100% in the 2.0 mg/kg group. All dosage groups had a high percentage of acceptable conditions with these two variables.

Individually, vocal cord movement ($p = 0.0341$), coughing ($p = 0.0379$) and limb movement ($p = 0.0165$) showed statistically significant improvement. Acceptable vocal cord movement was 66% in the 0.5 mg/kg group, 80% in the 1.0 and 1.5 mg/kg group and 100% in the 2.0 mg/kg group. With regards to coughing, the effect of propofol was much more pronounced with acceptable conditions seen in 60% of the 0.5 mg/kg group, 73% of the 1.0 mg/kg group, 80% of the 1.5 mg/kg group and 92% of the 2.0 mg/kg group. Limb movement also showed high acceptable percentages with 80% for 0.5 mg/kg, 93% for 1.0 mg/kg and 100% for the 1.5 and 2.0 mg/kg groups. The improvement seen with vocal cord movement and coughing is attributed to the depression of the upper airway reflexes seen with propofol. All variables showed acceptable conditions in 80% or more of the study participants in the 1.5 and 2.0 mg/kg groups.

Our results mirrored those of Bartolek et al.¹⁷ They compared intubation conditions with propofol 2.0, 2.5 and 3 mg/kg (with 20 µg/kg alfentanil) and 0.45 mg/kg rocuronium. They found

clinically acceptable intubating conditions in 94% in the 2.0 mg/kg group, 95% in the 2.5 mg/kg group and 98% in the 3.0 mg/kg group, similar to our results. The improvement found across the dose range was not statistically significant. Siddik-Sayyid et al.¹⁸ compared the effects of propofol 1–2 mg/kg in combination with sevoflurane 8%. They found clinically acceptable intubation conditions in 70% of the 1 mg/kg group and 94% of the 2 mg/kg group, closely resembling our findings (73% in the 1 mg/kg group, 94% in the 2 mg/kg group).

The changes in systolic, diastolic and mean arterial blood pressures compared with baseline after propofol/alfentanil administration during intubation and 60 seconds after intubation were not statistically significant although up to a 15% reduction in systolic pressure was noted in some patients. A similar decrease in MAP (12%) was found in the study by Bartolek et al.¹⁷

Lerman et al.¹² found a dose dependent increase in the incidence of apnoea. The incidence of apnoea was 21% with 0 mg/kg; 25% with 0.5 mg/kg; 38% with 1 mg/kg; 45% with 2 mg/kg and increased to 80% with 3 mg/kg. Our findings were similar with the incidence of apnoea following propofol doses of 0.5 mg/kg (40%) to 2.0 mg/kg (57%), although not statistically significant.

Conclusion

Intubating conditions improved as the dose of propofol increased from 0.5 to 2.0 mg/kg in a statistically significant manner. The decrease in blood pressure when increasing the propofol dosage from 0.5 to 2.0 mg/kg was not statistically significant but may be clinically important for select patients. In clinically healthy children, we recommend a dose of 1.5–2.0 mg/kg of propofol in combination with alfentanil 10 µg/kg and sevoflurane (in a 50% nitrous oxide and oxygen mixture) to allow adequate intubation conditions whilst maintaining a favourable haemodynamic profile.

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Conflict of interest

No conflict of interest was reported by the authors.

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Ethical approval

The institutional ethics review board (UP approval number 238/2015).

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Appendix:

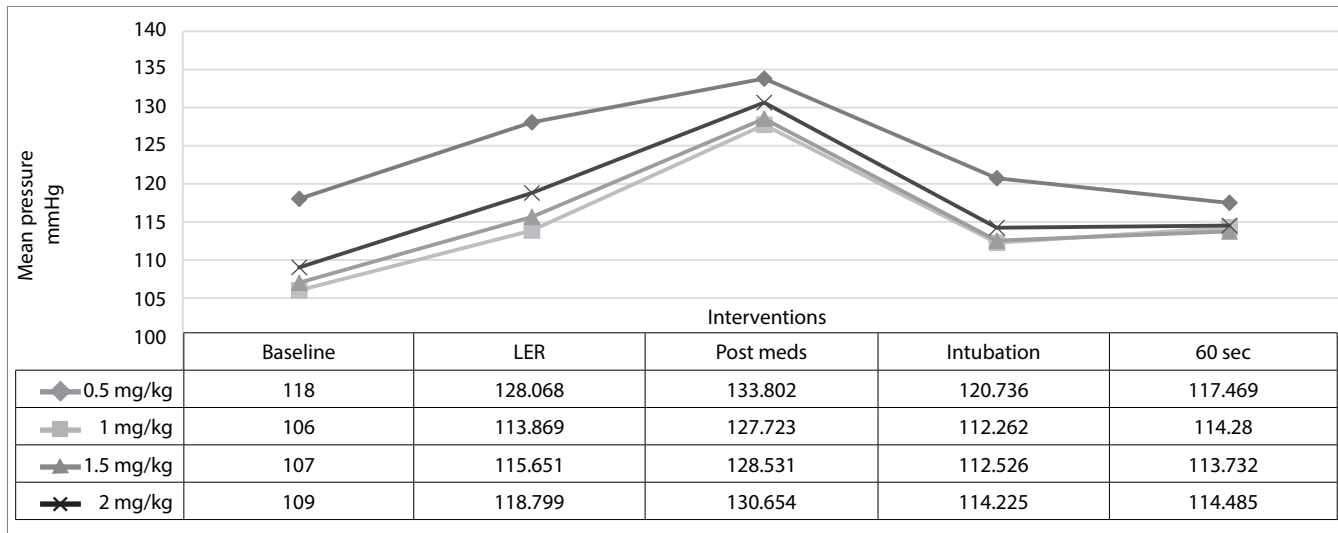


Figure 4: Systolic blood pressure variation

Table X: Systolic blood pressure changes from baseline

Dosage (mg/kg)	Loss of eyelid reflex (LER)	Post propofol/alfentanil (Post meds)	Intubation	After 60 seconds (60 sec)
0.5	10.068 [3.857–16.279]	15.802 [10.367–21.237]	2.736 [-4.888–10.359]	-0.531 [-8.060–6.998]
1.0	7.869 [1.611–14.126]	21.723 [16.247–21.198]	6.262 [-1.418–13.942]	8.280 [0.694–15.865]
1.5	8.651 [2.402–14.900]	21.531 [16.063–27.000]	5.526 [-2.144–13.195]	6.732 [-0.843–14.307]
2.0	9.799 [3.369–16.229]	21.654 [16.028–27.280]	5.225 [-2.667–13.116]	5.485 [-2.309–13.279]
p-value	0.9553	0.3367	0.9216	0.3770
Linear regression		0.1925		

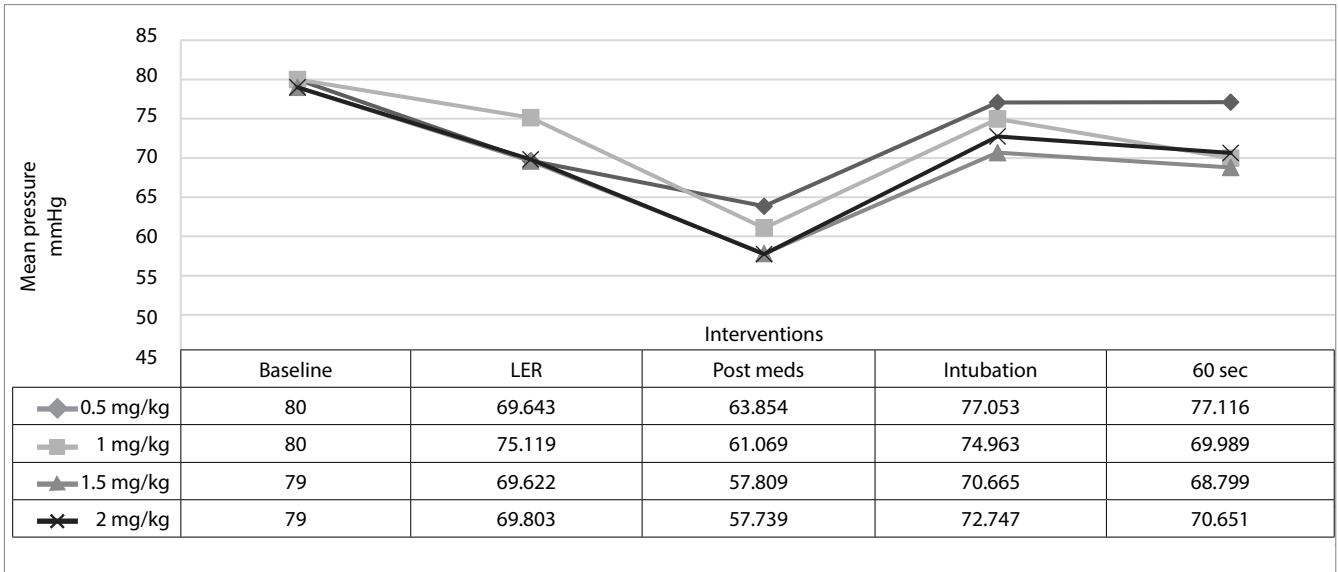


Figure 5: Mean blood pressure variation

Table XI: Mean blood pressure changes from baseline

Dosage (mg/kg)	Loss of eyelid reflex (LER)	Post propofol/alfentanil (Post meds)	Intubation	After 60 seconds (60 sec)
0.5	10.357 [4.683–16.031]	16.146 [12.068–20.223]	2.947 [-3.637–9.532]	2.884 [-2.458–8.226]
1.0	4.881 [0.795–10.557]	18.931 [14.852–23.010]	5.037 [-1.550–11.625]	10.011 [4.667–15.356]
1.5	9.378 [3.697–15.059]	21.191 [17.108–25.274]	8.335 [1.741–14.928]	10.201 [4.852–15.550]
2.0	9.197 [3.328–15.067]	21.261 [17.043–25.479]	6.253 [-0.559–13.065]	8.349 [2.822–13.876]
p-value	0.5333	0.2584	0.7064	0.1893
Linear regression		0.0616		