

# Continuous Infusion of Lidocaine in Pediatric Colonoscopy: A Randomized Placebo-Controlled Study

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## Research article

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## Abstract

**Background:** To investigate the effect of intravenous lidocaine on perioperative propofol and sufentanil dosage, pulse oxygen saturation, postoperative pain score and recovery time during pediatric colonoscopy.

**Methods:** We designed a randomized placebo-controlled study and enrolled 80 children aged from 3 to 10 years old who were received colonoscopy. After titration of propofol to achieve unconsciousness, patients were given intravenous lidocaine ( $1.5 \text{ mg kg}^{-1}$  then  $2 \text{ mg kg}^{-1} \text{ h}^{-1}$ ) or the same volume of saline. Sedation was standardized and combined propofol with sufentanil. The primary outcome variables were intraoperative propofol and sufentanil requirements and number of oxygen desaturation episodes. Secondary outcome variables were recovery time after colonoscopy and post-colonoscopy pain.

**Results:** Lidocaine infusion resulted in a significant reduction in propofol requirements: mean (SD) 44.3 (9.9) vs 74.5 (12.0) mg, respectively;  $P<0.001$ ) and sufentanil requirements: mean (SD) 1.5 (0.3) vs 2.6 (0.6) ug respectively;  $p<0.001$ ). The number of subjects who experienced oxygen desaturation below 95% in the lidocaine group was also significantly less than that in the control group: 2 vs 8 ( $P=0.04$ ). The mean (SD) recovery time was significantly shorter in lidocaine group: 19.2 (2.6) vs 13.3 (2.6) min respectively;  $p<0.001$ ). There were no significant difference regarding post-colonoscopy pain.

**Conclusions:** Continuous infusion of lidocaine resulted in reduction of propofol and sufentanil dose, recovery time and risk of hypoxemia during pediatric colonoscopy.

**Trial Registration:** Chinese Clinical Trials Registry, ChiCTR2000028927, 8 January, 2020, prospectively registered.

## Background

With the development of medical technology, colonoscopy is commonly conducted in infants and children for the diagnosis and treatment of abdominal pain, diarrhea, weight loss, unexplained iron deficiency anemia, or unexplained hematochezia <sup>1,2</sup>. Colonoscopy has developed into a diagnostic and therapeutic tool for pediatric patients <sup>3</sup>. Anesthesiologists are increasingly involved in providing procedural sedation and analgesia for pediatric colonoscopy due to the lack of cooperation. Midazolam, propofol and opioids are the most commonly anesthetics used for procedural sedation and analgesia during pediatric colonoscopy <sup>4,5</sup>. However, each of these anesthetics causes respiratory depression and combining midazolam or propofol with opioids may further increasing the risk for hypoxemia and apnoea during pediatric colonoscopy <sup>6</sup>. In order to decrease the incidence and frequency of complications during pediatric endoscopy, different methods have been tried previously. Propofol-ketamine combinations are associated with fewer cardiopulmonary adverse effects than with propofol alone according to previous reports.<sup>7-9</sup> C. Forster et al<sup>10</sup> reported that intravenous (i.v.) lidocaine was another adjunct to propofol sedation during adult colonoscopy and concluded that i.v. lidocaine resulted

in a 50% reduction of propofol dose requirements. However, the application of lidocaine in pediatric colonoscopy has not been reported yet. We therefore conducted a clinical study to investigate whether i.v. lidocaine reduces propofol requirements and improves post-colonoscopy recovery during pediatric colonoscopy.

## Methods

To address the research purpose, we designed and implemented a randomized placebo-controlled double blind trial in the operating room of Guangdong Women and Children Hospital, China. This study was approved by the ethics committee of Guangdong Women and Children Hospital in December 30, 2019 (identifier number 201901164) and registered with the Chinese Clinical Trials Registry ([www.chictr.org.cn](http://www.chictr.org.cn), identifier number ChiCTR2000028927, 8 January 2020, prospectively registered). After obtaining written informed consent, 80 American Society of Anesthesiologists (ASA) grade 1–2 aged from 3 to 10 children undergoing colonoscopy under sedation were included in this randomized placebo-controlled double blind study from 9 January 2020 to June 30, 2020 (see Fig. 1 for CONSolidated Standards Of Reporting Trials (CONSORT) trial profile). Inclusion criteria: aged from 3 to 10 with normal electrocardiogram (ECG) result. Exclusion criteria were: age > 10 year or < 3 year, liver insufficiency, major cardiac arrhythmia, and allergy to lidocaine.

## Study design and intervention

Once the participants entered the operating room, ECG and oxygen saturation ( $\text{SpO}_2$ ) were routinely monitored. All children were sedated with i.v. bolus injection of propofol (Lipofen, B.Braun Melsungen AG, specifications: 20ml: 100 mg, batch number: 17515033)  $1.5 \text{ mg kg}^{-1}$  by the same anesthesiologist (C. Y.) who was blinded to patient allocation group. A dose of sufentanil (Sufentanil citrate injection, EuroCept BV, specifications: 1ml: 75 ug, batch number: 180262)  $0.05 \text{ ug kg}^{-1}$  was administered i.v. after loss of consciousness. Then, children were randomly and double blindly assigned to group saline (group S) and group lidocaine (group L) using sealed envelopes by W.H. The group L was given an i.v. bolus of lidocaine  $1.5 \text{ mg kg}^{-1}$  followed by a continuous infusion of  $2 \text{ mg kg}^{-1} \text{ h}^{-1}$  and group S was given the same volume of saline.<sup>11</sup> Study medications were prepared by the same anesthesiologist (J.W.) involved neither in patient sedation nor in collecting study data. In order to avoid interference with blinding, study medications were infused after loss of consciousness in two groups as the initial bolus of lidocaine may result in specific reaction. I.V. boluses of propofol 10–20 mg were administered in response to abdominal discomfort expressed by the children or evidenced by irritability or haemodynamic changes (increase in heart rate  $\geq 20 \text{ beats min}^{-1}$ ) during colonoscopy. Sufentanil  $0.05 \text{ ug kg}^{-1}$  was added if propofol was insufficiently effective. All children breathed spontaneously and received oxygen  $4 \text{ L min}^{-1}$  through a nasal catheter in order to maintaining oxygen saturation  $> 90\%$  during colonoscopy. Mask control breathing or tracheal intubation mechanical ventilation was given if the children arised respiratory depression or respiratory arrest.

## Outcome variables

The primary outcome variables were intraoperative propofol and sufentanil requirements and number of oxygen desaturation episodes (defined as peripheral capillary oxygen desaturation ( $\text{SpO}_2$ ) less than 95% and 90%). Secondary outcome variables were recovery time in the postanesthesia care unit (PACU) (time between end of colonoscopy and ability for the children to blink) and post-colonoscopy pain. Pain scores were recorded using Wong-Baker FACES Pain Rating Scale after recovery in the PACU 15 and 30 min later. Researcher involved in the assessment of these variables were blinded to patient allocation group.

## Statistical analysis

The sample size was calculated on the basis of local pilot study. The mean propofol requirements during pediatric colonoscopy was  $120 \pm 28$  mg. To detect a 30% decrease in propofol needs between groups, power estimation analysis suggested that 13 patients per group would be required to achieve a power of 90%, when considering a bilateral type I error of 0.05. In view of a dropout rate of 10%, we decided to recruit 40 children in each group finally. All statistical analyses were performed using IBM SPSS Statistics for Windows (version 23.0, IBM Corp, Chicago, IL, USA). Quantitative variables were presented as mean  $\pm$  standard deviation (SD) or median with interquartile range. Categorical data were reported as frequencies. Enumeration data and categorical variables were analyzed using Chi square test or Fisher's exact tests as appropriate. Continuous variables were tested with Student's *t* test or Mann Whitney U test depending on the distribution of the data. Mixed model analysis of variance (ANOVA) was used to compare postoperative pain score. A value of  $P < 0.05$  was considered statistically significant.

## Results

A total of 120 children were screened and evaluated from 9 January 2020 to June 30, 2020 in the operating room, Guangdong Women and Children Hospital. Among them, 23 children did not consent and 3 children had exclusion criteria (major cardiac arrhythmia), 14 children withdrawn because colonoscopy combined with gastroscopy. At last, 80 ASA 1–2 aged from 3 to 10 children undergoing colonoscopy under sedation were included in this randomized placebo-controlled double blind study (Fig. 1). There was no significant difference in age, gender, weight, height, BMI, ASA physical status Hb, iron, hs-CRP, reasons for colonoscopy and duration of colonoscopy between two groups (Table 1). It revealed that the data sets of two groups were comparable in equilibrium.

Table 1  
Characteristic data and duration of colonoscopy. Data are mean (standard deviation), or number.

	Group S (n = 40)	Group L (n = 40)	P
Age (yr)	6.40 ± 2.06	6.70 ± 2.17	0.53
Gender (M/F)	21/19	18/22	0.50
Weight (kg)	24.80 ± 5.61	25.20 ± 7.27	0.78
Height (cm)	1.16 ± 0.14	1.15 ± 0.14	0.75
BMI (kg m <sup>-2</sup> )	21.25 ± 3.02	21.59 ± 4.21	0.68
hs-CRP	3.97 ± 1.31	4.01 ± 1.36	0.89
Hb	122.4 ± 11.6	120.8 ± 11.7	0.55
Iron	15.34 ± 5.74	15.99 ± 6.12	0.63
Reason for colonoscopy:			
Hematochezia	9	12	0.45
Intestinal polyps	16	14	0.64
Inflammatory bowel disease	15	14	0.82
ASA physical status (1/2)	19/21	23/17	0.37
Duration of colonoscopy (min)	12.40 ± 1.65	12.35 ± 1.79	0.90

Abbreviations: BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein; Hb, hemoglobin; ASA, American Society of Anesthesiologists.

The propofol and sufentanil consumption in group L showed a significant reduction compared with group S ( $P < 0.001$ ; Table 2). The recovery time of group L was shorter than that of group S ( $P < 0.001$ ; Table 2). The number of subjects who experienced oxygen desaturation below 95% in the lidocaine group was also significantly less than that in the control group: 2 vs 8 ( $P = 0.04$ ; Table 2). The number of children who experienced oxygen desaturation below 90% (1 vs 2 subjects in the group L and group S, respectively) was similar in two groups ( $P = 0.56$ ; Table 2). No tracheal intubation and apnea occurred in both groups. Pain scores after colonoscopy were also similar in two groups [ANOVA: drug effect (df = 1, F = 3.7):  $P = 0.06$ ; time effect (df = 1, F = 74.4):  $P < 0.001$ ; interaction (df = 1, F = 3.3):  $P = 0.071$ ] (Fig. 2).

Table 2  
Result variables. Data are mean (standard deviation) or number.

	Group S (n = 40)	Group L (n = 40)	<i>P</i>
Propofol: total dose (mg)	$112.8 \pm 20.5$	$82.4 \pm 19.6$	$< 0.001$
Propofol: induction of sedation (mg)	$38.3 \pm 8.7$	$38.1 \pm 10.4$	0.94
Propofol: during infusion of study medications (mg)	$74.5 \pm 12.0$	$44.3 \pm 9.9$	$< 0.001$
Sufentanil (ug)	$2.6 \pm 0.6$	$1.5 \pm 0.3$	$< 0.001$
Lidocaine (mg)	—	$39.8 \pm 10.9$	—
Recovery time (min)	$19.2 \pm 2.6$	$13.3 \pm 2.6$	$< 0.001$
$\text{SpO}_2 < 95\%$ (n)	8	2	0.04
$\text{SpO}_2 < 90\%$ (n)	2	1	0.56

## Discussion

Colonoscopy has developed into a diagnostic and therapeutic tool for pediatric patients. Discomfort associated to pediatric colonoscopy leading to lack of cooperation results mainly from visceral nociception secondary to colonic distension and tractions. However, experimental studies demonstrated that i.v. lidocaine was an efficient method in alleviating visceral pain.<sup>12,13</sup> Forster et al<sup>10</sup> already reported that intravenous (i.v.) lidocaine was an efficient choice to alleviate visceral pain during adult colonoscopy and concluded that i.v. lidocaine resulted in a 50% reduction of propofol dose requirements. However, the application of lidocaine in pediatric colonoscopy has not been reported yet. We therefore conducted a clinical study to investigate whether i.v. lidocaine reduces propofol requirements and improves post-colonoscopy recovery during pediatric colonoscopy. Our study demonstrates that adding i.v. lidocaine can significantly reduce the propofol and sufentanil needs for pediatric colonoscopy, at the same time, shorten the recovery time.

In our study, despite the propofol and sufentanil requirement in the lidocaine group was significantly less, endoscopists' working conditions were not affected and all children successfully completed colonoscopy. In addition, postoperative pain after colorectal surgery was similar in both groups, and no tracheal intubation and apnoea occurred in both groups. Hypoxia and apnoea secondary to respiratory depression and airway obstruction are the most frequent cardiopulmonary complication of sedation for pediatric colonoscopy. One of the aims to administer an adjunct to propofol and sufentanil is to reduce their needs and consequently the incidence of their adverse effects. In our study, the number of subjects who experienced oxygen desaturation below 95% in the lidocaine group was significantly less than that in the control group, but there was no significant difference in age, gender, weight, height, BMI, ASA physical status Hb, iron, hs-CRP, reasons for colonoscopy and duration of colonoscopy between two groups, thus

we believed that continuous infusion of lidocaine can reduce the risk of hypoxemia by reducing the use of propofol and sufentanil. Although the duration of colonoscopy in two groups were similar, the recovery time was also shortened when adding i.v. lidocaine, which may also be related to reducing the dosage of propofol and sufentanil.

Nonetheless, several limitations of this study should be addressed. For example, recording of the blood pressure might further help detect differences of adverse events associated with propofol. Endoscopists' working conditions were not quantified for better comparison, and they can be quantified using visual analog scores. Finally, This study is a single-center clinical trial, and the sample size is relatively small, a multi-center clinical study should be carried out to further confirm it in the future.

In conclusion, adding i.v. lidocaine can significant reduce the propofol and sufentanil needs and risk of hypoxemia for pediatric colonoscopy, at the same time, shorten the recovery time without impacting working conditions for the endoscopists.

## Declarations

### *Ethics approval and consent to participate*

This study was approved by the ethics committee of Guangdong Women and Children Hospital in December 30, 2019 (identifier number 201901164). The written informed consent was obtained from a guardian for participates.

### *Consent for publication*

Not applicable.

### *Availability of data and materials*

Deidentified individual participant data (including data dictionaries) will be made available, in addition to study protocols, the statistical analysis plan, and the informed consent form. The data will be made available upon publication to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal. Proposals should be submitted to [mzkhrong@163.com](mailto:mzkhrong@163.com).

### *Competing interests*

The authors declare that they have no competing interests.

### *Funding*

Not applicable.

### *Authors' contributions*

CY and CW conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. JW, NG, KL, YL, XH and WH designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. ZH conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Not applicable.

## **References**

1. Friedt M, Welsch S. An update on pediatric endoscopy. *Eur J Med Res.* 2013;18:24.
2. Schreiber-Dietrich DG, Hocke M, Gottschalk U, et al. [Update in pediatric endoscopy]. *Z Gastroenterol.* 2017;55(5):490-500.
3. Lightdale JR, Acosta R, Shergill AK, et al. Modifications in endoscopic practice for pediatric patients. *Gastrointest Endosc.* 2014;79(5):699-710.
4. Cohen S, Glatstein MM, Scolnik D, et al. Propofol for pediatric colonoscopy: the experience of a large, tertiary care pediatric hospital. *Am J Ther.* 2014;21(6):509-511.
5. Amornyotin S, Aanpreung P, Prakarnrattana U, et al. Experience of intravenous sedation for pediatric gastrointestinal endoscopy in a large tertiary referral center in a developing country. *Pediatr Anesth.* 2009;19(8):784-791.
6. Nieuwenhuijs DJ, Olofsen E, Romberg RR, et al. Response surface modeling of remifentanil-propofol interaction on cardiorespiratory control and bispectral index. *Anesthesiology.* 2003;98(2):312-322.
7. Jalili M, Bahreini M, Doosti-Irani A, et al. Ketamine-propofol combination (ketofol) vs propofol for procedural sedation and analgesia: systematic review and meta-analysis. *Am J Emerg Med.* 2016;34(3):558-569.
8. Hu Y, Xu W, Cao F. A meta-analysis of randomized controlled trials: combination of ketamine and propofol versus ketamine alone for procedural sedation and analgesia in children. *Intern Emerg Med.* 2019;14(7):1159-1165.
9. Yan JW, McLeod SL, Iansavitchene A. Ketamine-Propofol Versus Propofol Alone for Procedural Sedation in the Emergency Department: A Systematic Review and Meta-analysis. *Acad Emerg Med.* 2015;22(9):1003-1013.
10. Forster C, Vanhaudenhuyse A, Gast P, et al. Intravenous infusion of lidocaine significantly reduces propofol dose for colonoscopy: a randomized placebo-controlled study. *Brit J Anaesth.* 2018;121(5):1059-1064.
11. Hans GA, Lauwick SM, Kaba A, et al. Intravenous lidocaine infusion reduces bispectral index-guided requirements of propofol only during surgical stimulation. *Brit J Anaesth.* 2010;105(4):471-479.

12. Ness TJ. Intravenous lidocaine inhibits visceral nociceptive reflexes and spinal neurons in the rat. *Anesthesiology*. 2000;92(6):1685-1691.
13. Ness TJ, Randich A. Which spinal cutaneous nociceptive neurons are inhibited by intravenous lidocaine in the rat? *Reg Anesth Pain Med*. 2006;31(3):248-253.

## Figures

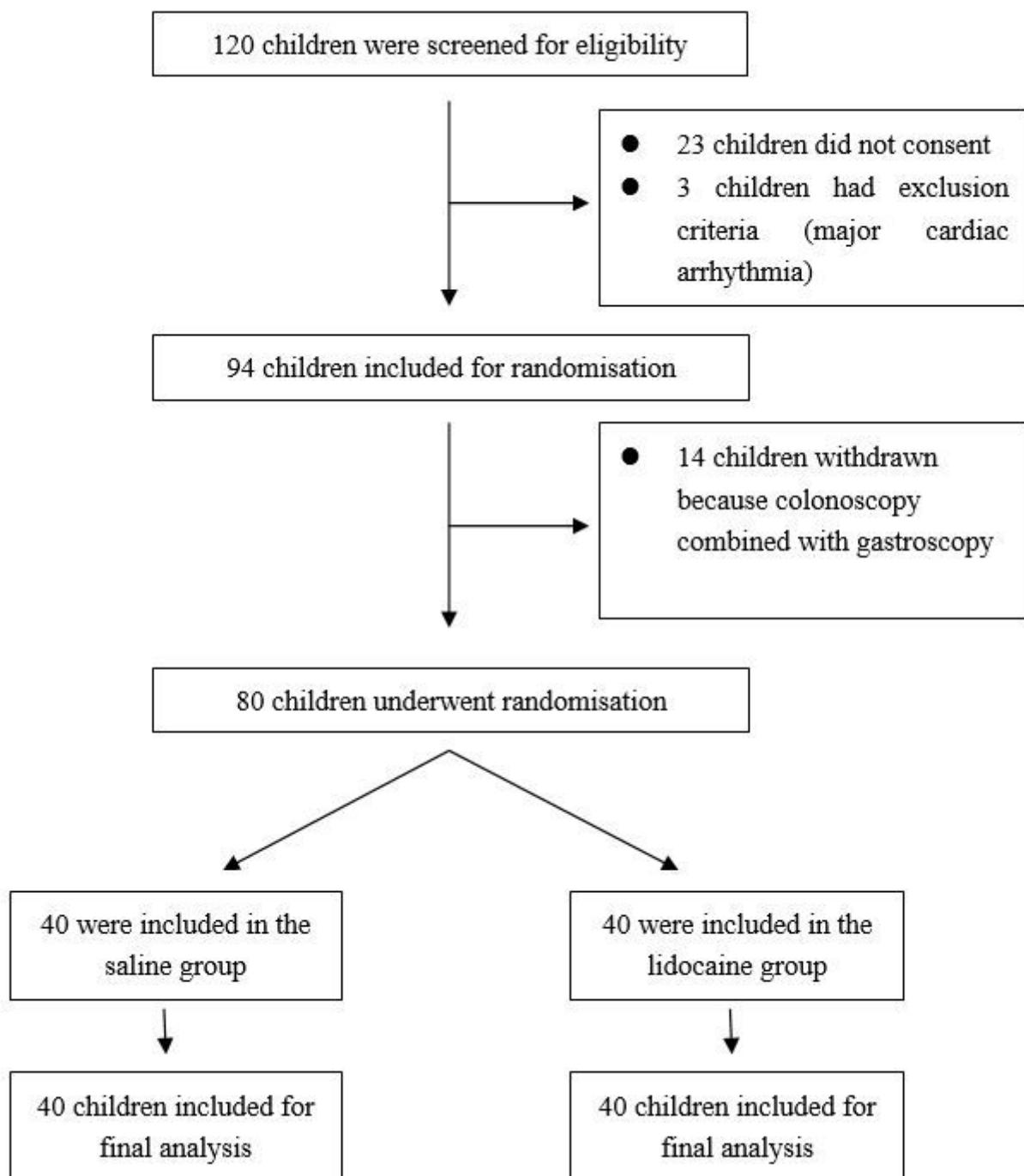
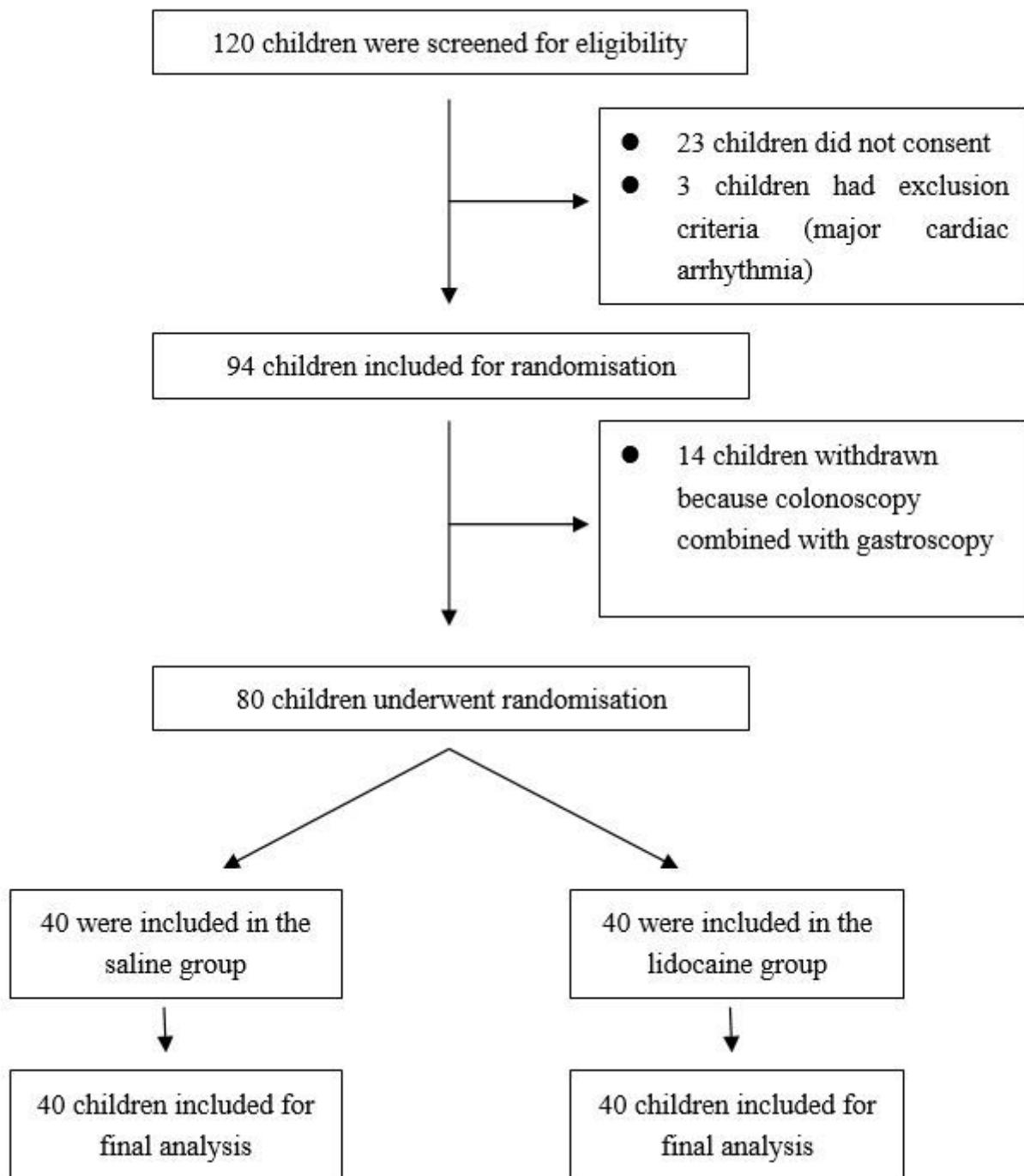


Figure 1

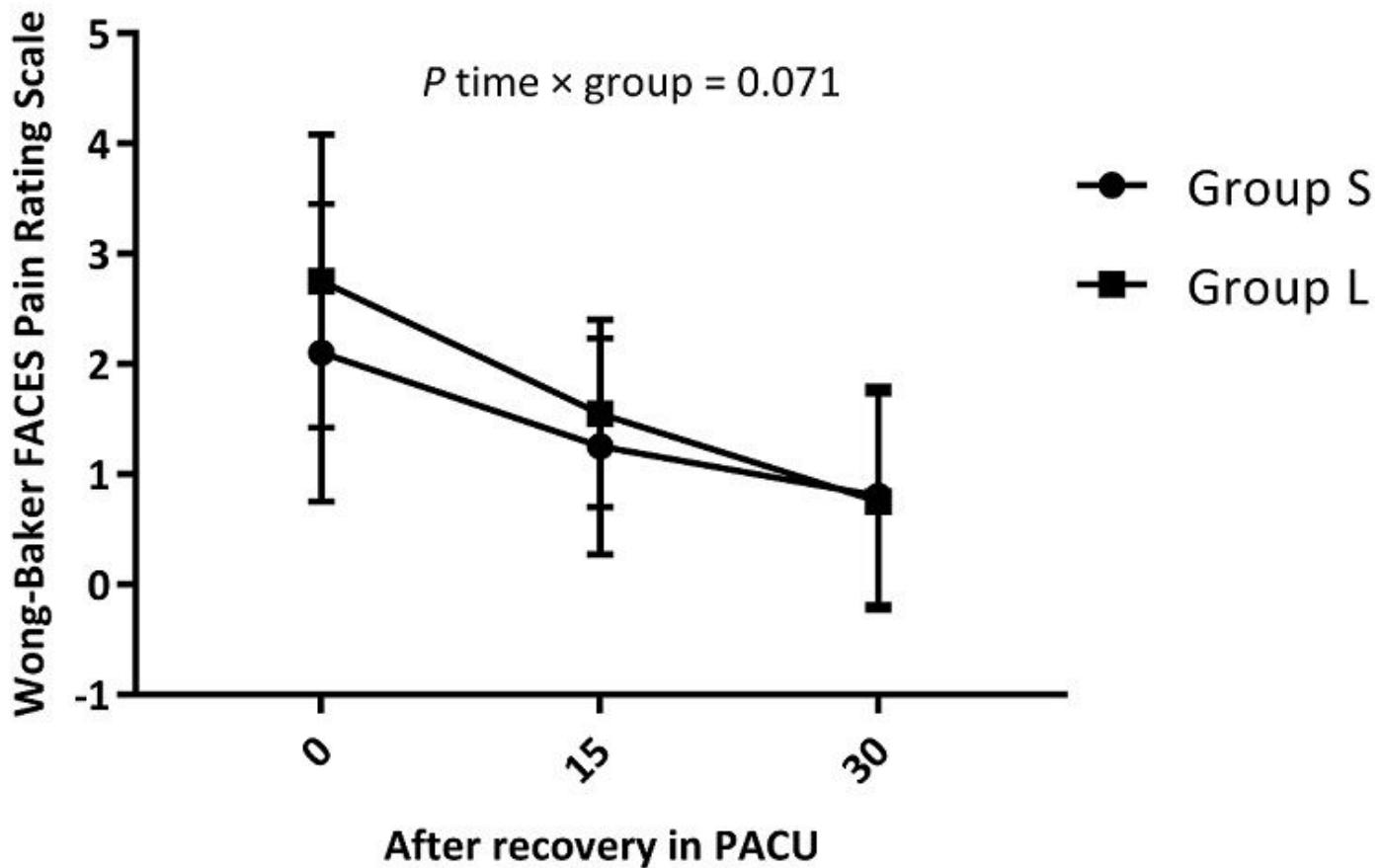
CONSORT 2010 Flow Diagram of this study. A total of 120 children were screened and evaluated from 9 January 2020 to June 30, 2020 in the operating room, Guangdong Women and Children Hospital. Among them, 23 children did not consent and 3 children had exclusion criteria (major cardiac arrhythmia), 14 children withdrawn because colonoscopy combined with gastroscopy. At last, 80 children underwent randomization.



**Figure 1**

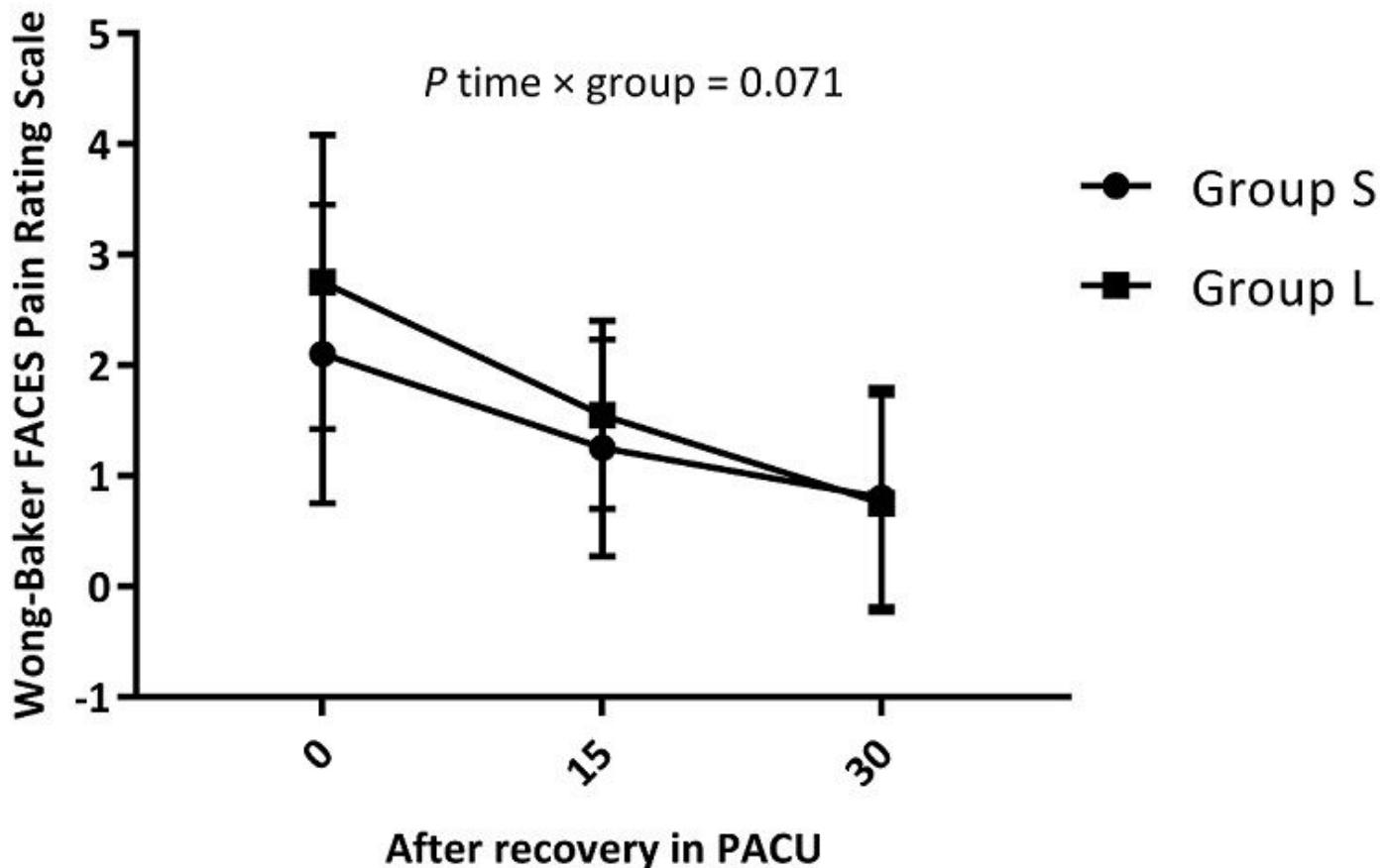
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**Figure 2**

Pain score after colonoscopy. Data are mean (SD). Pain were recorded using Wong-Baker FACES Pain Rating Scale after recovery in the PACU 15 and 30 min later. Pain scores after colonoscopy were similar in two groups (analysis of variance:p=0.071).



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Pain score after colonoscopy. Data are mean (SD). Pain were recorded using Wong-Baker FACES Pain Rating Scale after recovery in the PACU 15 and 30 min later. Pain scores after colonoscopy were similar in two groups (analysis of variance:p=0.071).

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