EJA

Eur J Anaesthesiol 2019; **36:**206–214

ORIGINAL ARTICLE

Bupivacaine infiltration in children for postoperative analgesia after tonsillectomy

A randomised controlled study

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BACKGROUND Adenotonsillectomy is a frequently performed procedure in paediatric day-case surgery. Postoperative pain can be significant and standard analgesia protocols are often insufficient.

OBJECTIVE Our primary objective was to investigate if infiltration of the peritonsillar space with bupivacaine would reduce the need for postoperative opioids compared with pre-emptive intravenous tramadol.

DESIGN A double-blind, randomised controlled trial.

SETTING Ambulatory surgical day care centre, University Hospitals of Leuven, Belgium, from January 2012 to September 2016.

PATIENTS Two hundred children, between 4 and 10 years old, undergoing elective adenotonsillectomy were included in the study.

INTERVENTION Children were randomly allocated to receive either a bolus of 3 mg kg^{-1} intravenous tramadol or infiltration of the tonsillar lodge with 5-ml bupivacaine 0.25%. Reasons for exclusion were American Society of Anesthesiologists classification greater than 2, allergies to the investigated products, psychomotor retardation, bleeding disorders and lack of proficiency in Flemish.

MAIN OUTCOME MEASURES The primary endpoint was the number of children in need of piritramide postoperatively. Secondary outcomes included the cumulative dose of postoperative piritramide, pain scores and the incidence of postoperative nausea and vomiting during the first 24 postoperative hours, time to discharge and adverse effects.

RESULTS The proportion of children in need of postoperative piritramide was significantly lower in the tramadol group than in children with peritonsillar infiltration (57 vs. 81%, $P < 0.001$). When in need of postoperative piritramide, the tramadol-group required a significantly lower dose (median [IQR] 0.7 [0.6 to 1] vs. 1 [0.6 to 1.5] mg, $P < 0.007$) and had lower pain scores during the first 60 min after surgery. There were no statistically significant differences in postoperative nausea and vomiting incidence, need for antiemetics or complications.

CONCLUSION Compared with peritonsillar infiltration, preemptive intravenous tramadol decreases the need for postoperative opioids after tonsillectomy in children without increasing the incidence of side effects.

TRIAL REGISTRATION EudraCT 2011-005467-25.

Published online 10 January 2019

Introduction

Tonsillectomy in children is often performed on an outpatient basis. Despite the comparably minor surgical trauma, analgesia in the postoperative period frequently remains insufficient. Effective postoperative analgesia is required for comfort, to encourage oral intake for the maintenance of normal hydration and to minimise crying, as the latter enhances the risk of postoperative bleeding.[1] NSAIDs and paracetamol are frequently used for pain relief after tonsillectomy, but their analgesic effect is often inadequate.[1] The use of NSAIDs is controversial

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DOI:10.1097/EJA.0000000000000950

due to a possible increased risk of postoperative bleeding.[2] Opioids provide effective analgesia but can cause sedation and have pro-emetogenic effects, which can delay time to discharge in day-case surgery.[3] Emetogenesis is of particular concern because after tonsillectomy children already carry a high risk for postoperative nausea and vomiting (PONV).[4]

Tramadol is a centrally acting analgesic and an agonist for the opiate μ receptor. Due to its relatively weak potency, tramadol has been traditionally considered as unlikely to induce hypoventilation and cause significant sedation.[5] It has proven its effectiveness in posttonsillectomy pain.[6] Although the evidence for its emetogenic effects in children is controversial,[7,8] this possible side effect makes tramadol at best a suboptimal option for the management of posttonsillectomy pain.

Local infiltration analgesia (LIA) has proven its effectiveness after different types of surgery, decreasing the need for opioids postoperatively and also the risk of PONV.[9] Numerous trials have already evaluated the efficacy of LIA in the reduction of posttonsillectomy pain.[10] Notably, these studies employed different local anaesthetics, various infiltration techniques[11] and included only relatively few patients, making a comparison difficult. Moreover, in the setting of tonsillectomy, the efficacy of LIA has only been tested against placebo, and not against a standard analgesic regimen with intra-operative opioids.[12]

Given the well known benefits of LIA in other surgical procedures and the encouraging results of LIA against placebo, we hypothesised that – in comparison with intra-operative pre-emptive intravenous tramadol – a peritonsillar infiltration with bupivacaine would result in better pain relief and decrease the need for opioids in the early postoperative period.

Methods

The current double-blind, randomised controlled trial was approved by the ethics committee of the University Hospitals of the KU Leuven (EC S 53718, 20 December 2011) and the Belgian Government. It was registered in the publicly accessible study register of the European Medicines Agency (EUDRACT 2011-005467-25) and reported according to the CONSORT statement (Supplementary data). Children undergoing elective (adeno)-tonsillectomy in an ambulatory setting were enrolled between January 2012 and September 2016. Children aged between 4 and 10 years with American Society of Anesthesiologists physical status 1 or 2 were included. Exclusion criteria were allergies to the investigated products, psychomotor retardation, bleeding disorders and lack of proficiency in Flemish.

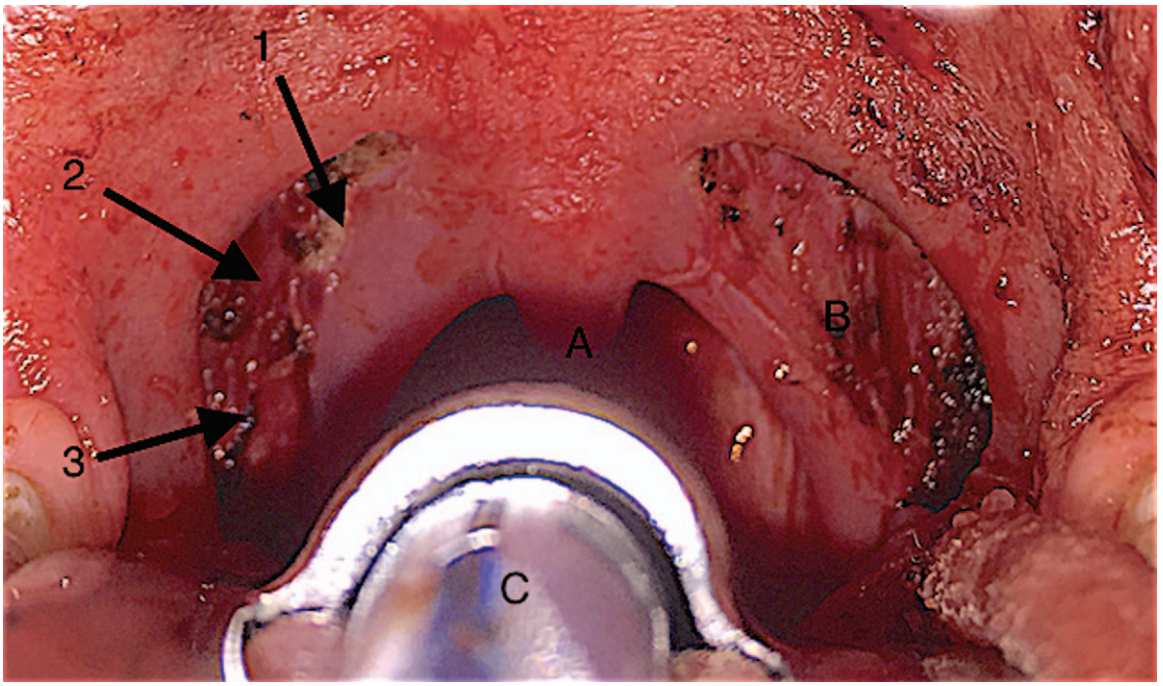
Following parental written informed consent children were randomly allocated on an intention-to-treat basis to receive either LIA or pre-operative intravenous analgesia, using a computer-generated random table (Graphpad Software Inc., La Jolla, California, USA). Allocation concealment was ensured by enclosing assignments in sealed, opaque, sequentially numbered envelopes, which were opened only after the arrival of the child in the operating theatre. The study medication was prepared by a consultant staff member of the Department of Anaesthesiology who was not further involved with peri-operative care, nor in data gathering and study visits. The study medication was handed over to the investigators in an unlabelled syringe. Surgeons, anaesthesiologists and nurses responsible for the further follow-up were also blinded.

Patients in the LIA-group received a bilateral peritonsillar infiltration with 2.5-ml bupivacaine 0.25% (Marcaine; Astra Zeneca, Ukkel, Belgium) using the posttonsillectomy three-point wound infiltration technique[11] (Fig. 1) and 5 ml of 0.9% saline placebo intravenously after induction of anaesthesia. After induction of anaesthesia each child in the tramadol (Contramal; Grünenthal, Aachen, Germany) group (T-group) received a bolus of intravenous 3 mg kg^{-1} tramadol diluted with 0.9% saline to obtain a volume of 5 ml, and a bilateral posttonsillectomy infiltration with 2.5 ml of 0.9% saline placebo. Peritonsillar infiltration was performed by the surgeon.

The anaesthetic management was standardised for all patients. Standard monitoring was applied. Anaesthesia was induced by inhalation of sevoflurane 8% in 100% oxygen. After induction, an intravenous cannula was inserted and connected to a paediatric crystalloid infusion, consisting of a combination of saline 0.3% and glucose 3.3%, which was administered using the 4-2-1-rule. Before tracheal intubation, children received a bolus of intravenous propofol (2 mg kg^{-1}) and fentanyl (1 μg kg^{-1}). No neuromuscular blocking agents were administered. General anaesthesia was maintained with sevoflurane 2% in 40% oxygen using pressure-controlled ventilation. All children underwent tonsillectomy using the traditional blunt dissection technique. Intra-operatively, all patients received the routine postoperative pain protocol for this procedure in use at that time consisting of an intravenous loading dose of 30 mg kg^{-1} paracetamol and 0.5 mg kg^{-1} ketorolac.

Postoperatively the intensity of pain was registered using the Wong-Baker Faces Pain Rating Scale (WB-FPRS).[13] The WB-FPRS was scored upon arrival at the postanaesthesia care unit (PACU) and every 15 min during the first hour, followed by every hour until discharge and at 24 h at home. The decision to receive pain medication was left to the discretion of the child who decided at which pain score pain medication should be given (self-determined pain medication threshold). Analgesics were administered when the child indicated that the chosen face represented a pain level above his individual pain treatment threshold.[14] The pain treatment scheme consisted of increments of intravenous piritramide

Fig. 1



Peritonsillar infiltration technique. The figure shows the anatomical site after tonsillectomy: Uvula (a). Bare muscle fibres of the tonsillar lodge (b). Kilner Retractor (c). The arrowheads point at the three infiltration points in which a total of 2.5 ml of study medication were injected at each side.

0.03 mg kg^{-1} until comfort was achieved, according to our standard hospital protocol in the PACU, intravenous paracetamol 15 mg kg^{-1} to be repeated every 6 h if necessary, and ibuprofen syrup 10 mg kg^{-1} to be repeated every 8 h if necessary in the day care ward. At home, paracetamol syrup or suppository (dose according to weight class) was given every 6 h and ibuprofen syrup every 8 h if needed.

The incidence of nausea and vomiting was evaluated in a dichotomous way (yes/no).

Nausea or vomiting was treated rigorously, according to our standard guidelines by the attending nurse in the PACU, who was blind to the treatment allocation. PONV was first treated with intravenous ondansetron 0.1 mg kg^{-1} and then with intravenous dexamethasone 0.1 mg kg^{-1}. If the child was still complaining of nausea or vomiting was still present, intravenous alizapride 1 mg kg^{-1} or oral domperidone 10 mg was added, depending on whether the intravenous cannula was still present or not. The incidence of PONV or the need for treatment of PONV was noted using the same schedule as the pain assessment.

Study outcomes

The primary outcome was the number who needed intravenous piritramide in the PACU, triggered by the face on the WB-FPRS representing the individual child's pain treatment score.

Secondary outcomes included: the cumulative dose of postoperatively administered piritramide, the postoperative need for paracetamol and ibuprofen, the time course of the WB-FPRS-score, the incidence of PONV, the need for treatment of PONV, discharge times and the rate of unplanned admissions to the hospital.

Safety outcomes

All children were closely monitored by the study nurse for adverse events caused by the infiltration technique, such as upper airway obstruction or vocal cord paralysis,[15] until postoperative day 1. The study was to be stopped if the incidence of these infiltration-related complications was significantly higher than 3% (using a one-sided 5% LanDeMets stopping boundary for continuous safety monitoring), in both groups combined or in one group separately. The incidence of early and late posttonsillectomy haemorrhage (PTH) and need for observation or surgical re-intervention were registered for a total time period of 14 postoperative days by checking the electronic files.

All data were collected by qualified research personnel, who were blinded to the treatment allocation.

Sample size calculation

The sample size was calculated to compare the proportion of children who needed piritramide postoperatively and was based on a χ^2 test (two-sided with alpha = 5%). To detect a clinically meaningful reduction in the proportion needing piritramide from 50 to 30%, 93 in each group were needed to achieve 80% power. The proportion of 50% in need of postoperative piritramide was based on unpublished observations in children undergoing tonsillectomy in our department who received an intra-operative bolus of 3 mg kg^{-1} tramadol. To compensate for dropouts, we aimed for 200 recruits.

Data analysis

All statistical analyses were performed using R version 3.3.1 (2016-06-21) [Team RC. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria (software) 2016.]

The Fisher's exact test was used for the comparison of all categorical variables, while the Mann–Whitney *U* test was used to compare continuous data between both groups. A linear model for repeated measurements was used to compare the evolution over time for the WB-FPRS. Bonferroni–Holm adjustments were used to correct for multiple comparisons performed at each time point. All tests were performed two-sided with an alpha = 5%.

No correction for multiple testing for the set of secondary outcomes was applied, implying that a strong claim can only be made for the primary outcome and that all other results should be interpreted with caution.

Results

The study flow chart is shown in Fig. 2. Two hundred children were randomised to the treatment with LIA (n=100) or intravenous tramadol (n=100). All received their allocated treatment. All data were analysed until discharge from the hospital but 25 were lost to follow-up after 24 h (LIA-group: n=17; T-group: n=8). The personal characteristics of the children in each group were similar (Table 1) as was the intra-operative medication.

Primary outcome

In the PACU, significantly fewer children in the tramadol group required intravenous piritramide than in the LIA-group (Table 2).

Secondary outcomes

Children in the tramadol group who were still in need of postoperative opioid therapy received not only significantly less piritramide than children in the LIA-group, but also a lower number of doses were given (Table 2). There was no significant difference in the time to the first administration of rescue medication between groups (Table 2).

Both in the day care ward and at home there were no significant differences between the two groups regarding the use of paracetamol or ibuprofen (Table 2).

The LIA-group had a WB-FPRS score that was on average 0.83 (95% CI: 0.47 to 1.2) points higher than in the tramadol group ($P < 0.001$). The interaction term between group and time in the linear model was significant ($P < 0.001$) indicating that the difference between groups differed across time, with a significantly higher WB-FPRS score in the LIA-group during the first postoperative 60 min (Fig. 3) (Table 3).

The incidence of PONV and the need for treatment of PONV was higher in the tramadol group, but these differences were not significant (Table 4).

Likewise, groups were not significantly different with regard to the incidence of unplanned hospitalisation (Table 4). In contrast, the median time until discharge was longer in the tramadol group than in the LIA-group.

Safety outcomes

No patient showed symptoms of airway obstruction. The overall incidence of primary PTH was 3% with only one requiring a surgical re-exploration (Table 4). The other children with early PTH were admitted to the hospital after surgery, and bleeding resolved spontaneously overnight or after administration of tranexamic acid. Readmittance to the hospital for secondary PTH was observed in 8 children (4%) with two needing surgical re-intervention, at 3 and 6 days postoperatively (Table 4).

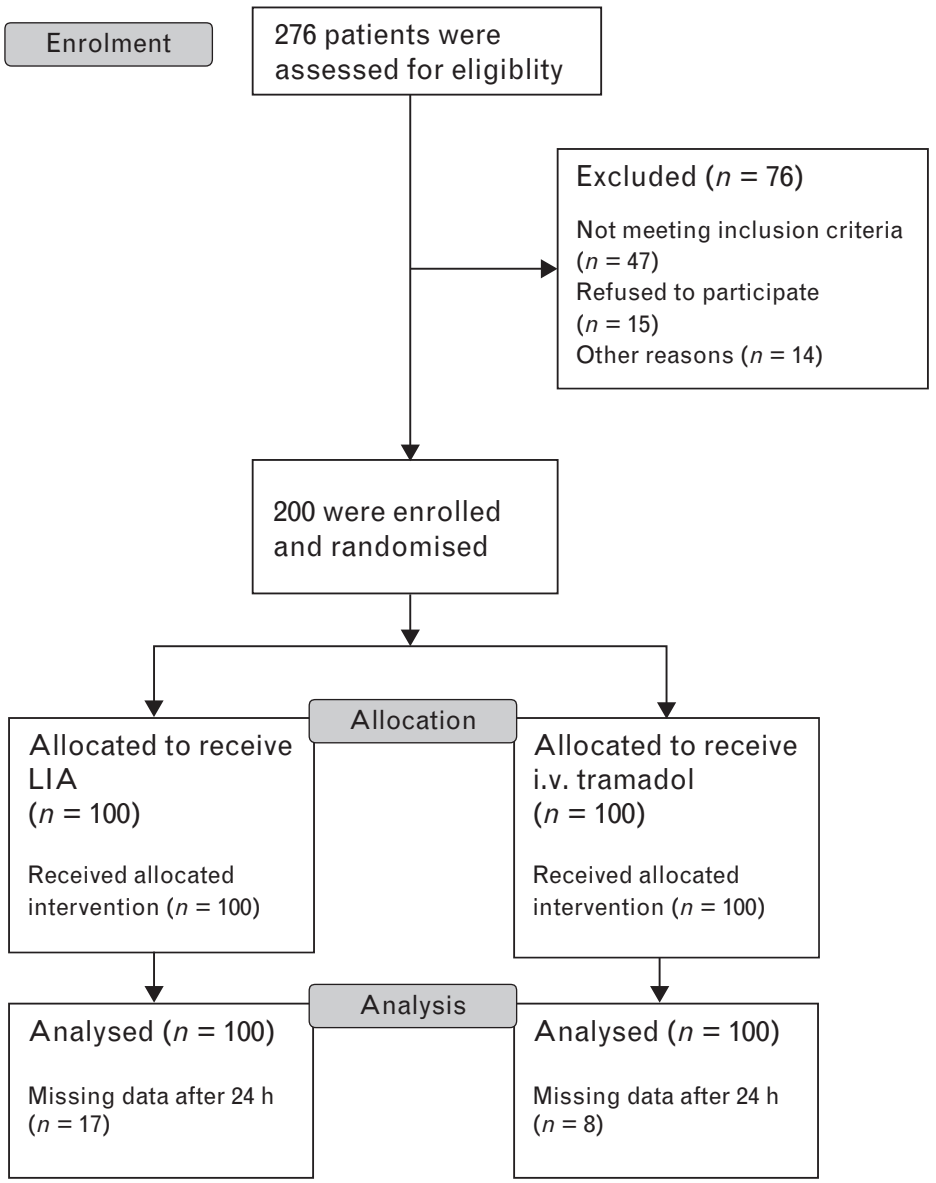
Discussion

We had to refute our hypothesis that peritonsillar infiltration would decrease the need for postoperative opioids compared with the intra-operative administration of tramadol. We unexpectedly found the opposite. Our results suggest that peritonsillar infiltration with bupivacaine in comparison with intravenous tramadol increases the number needing piritramide in the PACU after (adeno)-tonsillectomy. In addition, the cumulative postoperative piritramide doses and pain scores were lower in the tramadol group. No significant differences in the incidence of PONV or other adverse events were observed.

Various factors could have contributed to finding that LIA is inferior in comparison with intravenous tramadol.

First, while other investigators demonstrated superior analgesic efficacy for ropivacaine infiltration when compared with a relatively low dose of intravenous tramadol (1 mg kg^{-1}) or saline,[16] our trial is the first to compare posttonsillectomy infiltration with a high dose of tramadol (3 mg kg^{-1}). This dose has already proven its efficacy and safety when compared with placebo in a previous retrospective analysis in our day care centre in which the standard analgesic regimen (paracetamol + ketorolac) was compared with the standard regimen combined with

Fig. 2



Flow diagram according to the CONSORT statement.

tramadol.[8] The effectiveness of tramadol has also been demonstrated in a meta-analysis of postoperative pain treatment in children when tramadol was compared with a placebo, revealing a reduced need for rescue analgesics.[6] The studies included in this meta-analysis were mainly (12/20) evaluating pain after adenotonsillectomy, but included only small studies in which different doses were used and different methodological problems occurred.

Second, our results show significantly lower pain scores in the tramadol group compared with the bupivacaine group during the first 60 min. This early postoperative difference could be due to the fact that, unlike tramadol that was administered after induction of anaesthesia, LIA was performed at the end of surgery. It is likely that bupivacaine, which is known to have a slow onset time, had not yet reached its peak effect when the child reached the PACU. Of note, the timing of LIA in adenotonsillectomy is a controversial issue. Some authors recommend pre-emptive infiltration (prior to resection) to prevent sensitisation of the central nervous system, whilst others argue that pre-emptive infiltration results in the waste of local anaesthetic in the resected tonsil.[17,18] In a direct comparison of pre- vs. postresection infiltration, the latter was found to be superior with regard to postoperative pain scores.[11] This was the reason why we opted for post-tonsillectomy infiltration in our patients. Nevertheless, future studies are warranted to assess the efficacy of

Table 1 Patient characteristics

	Tramadol, *n*=100	LIA, *n*=100
Age (years)	5 [4 to 6] 5 (± 2)	5 [4 to 7] 6 (± 2)
Weight (kg)	19 [17 to 21.5] 20 (± 6)	20.5 [17.1 to 25] 22 (± 7)
ASA		
ASA 1, *n*	93 (93)	94 (94)
ASA 2, *n*	7 (7)	6 (6)
Sex		
Female, *n*	42 (42)	48 (48)
Male, *n*	58 (58)	52 (52)
Operation type		
Tonsillectomy, *n*	43 (43)	48 (48)
Adenotonsillectomy, *n*	57 (57)	52 (52)

Data are presented as median [IQR] and mean (± SD) or as frequency (percentage). ASA, American Society of Anesthesiologists physical status; LIA, local infiltration analgesia.

posttonsillectomy LIA using local anaesthetics with fast onset times.

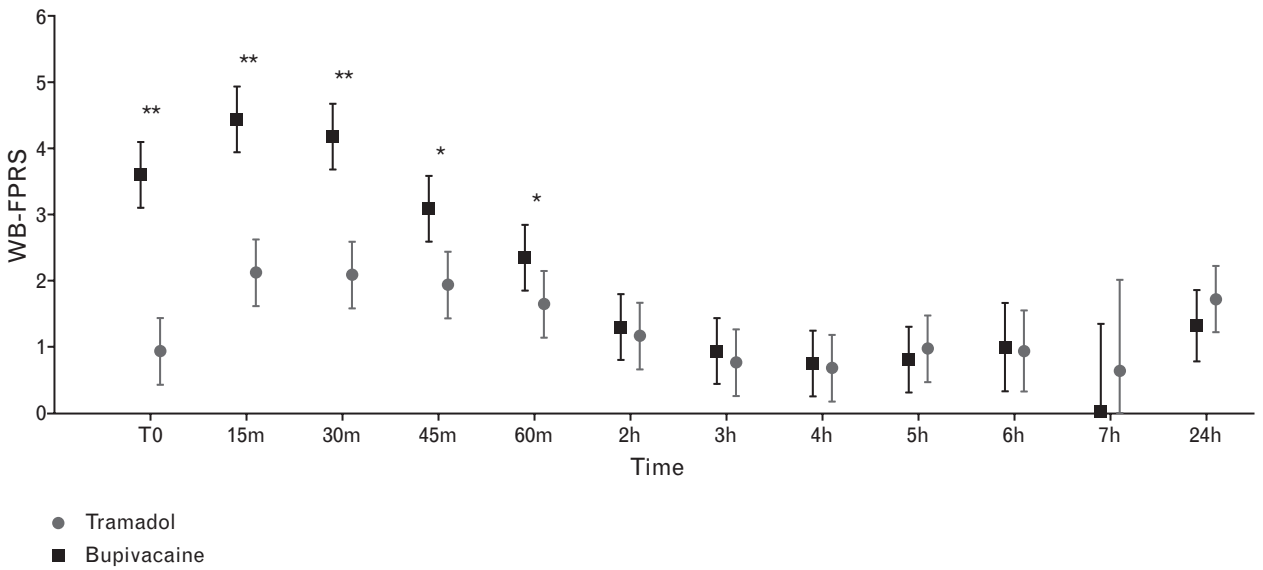
Opioids, including tramadol, are well known triggers for PONV,[7] which is frequently observed in paediatric anaesthesia, in particular after tonsillectomy. To evaluate the influence of tramadol on PONV in an unmasked way, we chose to administer no prophylactic medication. This strategy was justified by findings that PONV-incidences are not increased when tramadol is compared with placebo.[7,16] Also we did not observe a statistically significantly increased incidence of PONV or need for antiemetic medication in the tramadol group even though a high dose of tramadol was used, albeit acknowledging that there was a positive trend towards a higher incidence of PONV after tramadol. Our findings are in contrast with

Table 2 Postoperative analgesia

In hospital		Tramadol *n*=100	LIA *n*=100	*P* value
Piritramide	Number of patients, *n*	57 (57)	81 (81)	**<0.001**
	Dose[a] (mg)	0.7 [0.6 to 1]	1 [0.6 to 1.5]	**0.007**
	Number of doses, *n*	0.5 (± 0.5)	1.0 (± 0.8)	**<0.0001**
	1	36 (63)	35 (43)	0.364
	2	20 (35)	32 (40)	
	3	1 (2)	12 (15)	
	4	0	2 (2)	
	Time to first dose (min)	24 [0 to 45] 29 (± 33)	25.5 [14 to 41.75] 30 (± 30)	
Paracetamol	Number of patients, *n*	44 (44)	30 (30)	0.057
	Dose[a] (mg)	200 [150 to 300] 308 (± 324)	300 [180 to 357] 302 (± 124)	0.068
At home		***n*=92**	***n*=83**	
Paracetamol	Number of patients, *n*	89 (97)	81 (98)	1.00
Ibuprofen	Number of patients, *n*	89 (97)	81 (98)	1.00

Data are presented as median [IQR], mean (± SD) or frequency (percentage). LIA, local infiltration analgesia. [a] Dose within the group of patients receiving analgesia.Bold values indicate a *P*-value < 0.05.

Fig. 3



Postoperative time course of the Wong-Baker Faces Pain Rating Scale in both groups. Mean Wong-Baker Faces Pain Rating Scale profiles over time for both conditions with 95% confidence intervals. *P value <0.05, **P value <0.001.

Table 3 Postoperative Wong-Baker Faces Pain Rating Scale: evolution over time for both groups

Timepoint Group	T0	15 min	30 min	45 min	60 min	2 h	3 h	4 h	5 h	6 h	7 h	24 h
Tramadol												
Mean score (± SD)	**0.95** (± 2.46)	**2.12** (± 2.91)	**2.09** (± 2.73)	**1.94** (± 2.83)	**1.65** (± 2.27)	1.17 (± 2.08)	0.77 (± 1.43)	0.68 (± 1.19)	0.97 (± 1.74)	0.92 (± 1.87)	0.45 (± 0.82)	1.72 (± 2.19)
LIA												
Mean score (± SD)	**3.56** (± 4.26)	**4.42** (± 3.88)	**4.18** (± 3.53)	**3.09** (± 3.12)	**2.35** (± 2.54)	1.30 (± 2.02)	0.94 (± 1.63)	0.75 (± 1.47)	0.88 (± 1.62)	1.06 (± 1.69)	0.67 (± 1.30)	1.36 (± 2.02)
P value	**<0.001**	**<0.001**	**<0.001**	**0.003**	**0.022**	0.37	0.388	0.931	0.696	0.548	0.936	0.133

Data are presented as mean (± SD). Bold values indicate a significant difference between groups with a *P* value less than 0.05. LIA, local infiltration analgesia; T0, arrival at PACU; WB-FPRS, Wong-Baker Faces Pain Rating Scale.

Cocelli *et al.*[16] who measured a higher incidence of PONV when comparing tramadol with LIA. However, it is difficult to compare both studies because Cocelli *et al.* used an anaesthetic technique that included nitrous oxide and neostigmine. In awake patients, PONV triggered by tramadol has been attributed to high plasma peak concentrations immediately after intravenous administration.[19] In our study, peak plasma concentrations were reached while the patients were still under anaesthesia, which may explain why this regimen was not associated with a statistically significant increase in the PONV incidence.

Only recently there have been increasing concerns about the risk for respiratory depression in children treated with tramadol,[20] which might be of particular concern in children undergoing adenotonsillectomy who frequently exhibit an obstructive sleep apnoea (OSA) pattern preoperatively.[21] Recurrent hypoxia associated with OSA alters the central opioid responsiveness and makes children suffering from OSA more sensitive to the effects of opioids. As a consequence, several authors have advised limiting the use of tramadol to monitored settings.[22] The US Food and Drug Administration has even issued a warning that tramadol is contra-indicated in pain management in children younger than 12 years, and for treating pain after removal of tonsils and/or adenoids in adolescents between 12 and 18 years (US Food and Drug Administration, 2017. Safety announcement: FDA restricts use of prescription codeine pain and cough medicines and tramadol pain medicines in children; recommends against use in breastfeeding women. Available at: https://www.fda.gov:80/FDAgov/Drugs/DrugSafety/ucm549679.htm.). Notably, this statement has not had the agreement of the European Medicine Agency.[23] Notwithstanding, no event of respiratory depression was noted in our study.

Table 4 Postoperative outcomes

	Tramadol, *n*=100	LIA, *n*=100	*P* value
PONV incidence, *n*	61 (61)	47 (47)	0.065
Use of antiemetics, *n*	23 (23)	15 (15)	0.207
Ondansetron, *n*	23 (23)	14 (14)	0.144
Dexamethasone, *n*	1 (1)	1 (1)	1.00
Alizapride, *n*	1 (1)	0 (0)	1.00
Domperidone, *n*	1 (1)	1 (1)	1.00
Discharge time, min	370 [352 to 390] 372 (± 54)	358 [344 to 376] 358 (± 61)	**0.013**
Unplanned hospitalisation, *n*	10 (10)	7 (7)	0.447
PTH, *n*			
Early PTH			
Incidence	4 (4)	2 (2)	0.683
Re-intervention	1 (1)	0 (0)	1.00
Late PTH			
Incidence	4 (4)	4 (4)	1.00
Re-intervention	2 (2)	0 (0)	0.497

Data are presented as median [IQR], mean (± SD) or absolute number (percentage of the whole). LIA, local infiltration analgesia; PONV, postoperative nausea and vomiting; PTH, posttonsillectomy haemorrhage. Bold values indicate a *P*-value < 0.05.

The incidence of PTH observed in the current study is within the reported range.[24] All our patients received ketorolac intra-operatively, and most of them ibuprofen postoperatively, as the use of NSAIDs in tonsillectomy has been shown to reduce the incidence of PONV, most probably due to opioid-sparing effects.[2,25] Of note, there is an ongoing discussion on the safety of NSAIDs after tonsillectomy, as the incidence of postoperative bleeding might be increased due to the inhibition of platelet function. A recent Cochrane review remained inconclusive with respect to the bleeding risk, while another systematic review considered the use of NSAIDs after tonsillectomy to be safe.[2,26]

Strengths of our trial include the very large patient population and the blinding of all investigators including the surgeon performing LIA and the anaesthesiologist. Other studies on LIA in adenotonsillectomy included only small patient numbers and suffered from a lack of blinding.[12]

Nevertheless, we acknowledge that our study is subject to several limitations. First, the objective assessment of pain remains notoriously difficult, particularly in children.[27] In our study, pain intensity was evaluated using the WB-FPRS, which is a standard for paediatric anaesthesia research.[13] This scale is based on the children's self-report of pain intensity. The recommended age for this type of scale is 4 up to 12 years which is in accordance with the age of our cohort.[14]

Second, the decision to receive pain medication was left at the discretion of the child who decided at which pain

score pain medication should be given (self-determined pain medication threshold).[28] These threshold scores varied highly among the children (from 2 to 10) and did not necessarily correlate with other evaluations of pain. It could be argued that the decision to treat pain should not only be triggered by the child and his or her self-reported pain scale but also by parents' reports, nurse evaluations, clinical data and observation of the behaviour of the child.[14]

Third, we acknowledge that the high loading dose of paracetamol 30 mg kg^{-1} might be a point of discussion because it is twice the dose, which is nowadays recommended.[29] This dose was part of the standard analgesic protocol in our hospital at that time and was extrapolated from evidence in adults in which a loading dose of 2 g was found to have superior efficacy in treating postoperative pain.[30–32] Notably, despite the high loading dose, the recommended maximum daily dose of 75 mg kg^{-1} was never exceeded in our patients. In the meantime (but after completion of the current study), we have reduced the standard paracetamol-dose in our patients to 15 mg kg^{-1}.

Fourth, our study focused on the early postoperative period although pain after tonsillectomy may be present for several days postoperatively due to inflammation at the surgical site. Pain scores were only measured until postoperative day 1 and the effectiveness of our pain treatment protocol after discharge was not evaluated because this long-term follow-up was not the purpose of our study.

Fifth, the evaluation of nausea and vomiting was only analysed in a dichotomous way because a validated and reliable rating scale for measuring nausea is only available for older children.[33] The decision to treat PONV was made only by the nurse. Although the indication for treatment lacked standardisation, it is important to note that the attending nurses were blinded to the treatment allocation.

Sixth, our findings with respect to postoperative analgesia could not be translated into an improvement of 'hard' outcomes. Despite experiencing more pain (during the first 45 min after surgery), patients in the LIA-group were discharged from the hospital even earlier than patients with pre-emptive tramadol. Although this difference was statistically significant, it lacked clinical relevance (11 min in relation to a discharge time of approximately 6 h).

Lastly, our findings demonstrate that LIA with bupivacaine is insufficient as the sole analgesic strategy. However, this does not preclude that LIA might have benefits when combined with the pre-emptive administration of opioids and this should be evaluated in further studies.

It should be noted that the present trial was powered only for the primary outcome. All other results of secondary endpoints should therefore be interpreted with caution.

In conclusion, the results of this randomised, double-blind controlled trial indicate that peritonsillar infiltration with bupivacaine does not decrease the need for postoperative opioids, the incidence of PONV or complications compared with a prophylactic intravenous bolus of tramadol of 3 mg kg^{-1}.

Acknowledgements relating to this article

Assistance with the study: we would like to express our appreciation to our research nurse Christel Huygens and her team for their valuable assistance.

Financial support and sponsorship: none.

Conflicts of interest: none.

Presentation: part of this work was presented as a poster at the Euroanaesthesia meeting, June 2017, Geneva, Switzerland.

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