



# Does photobiomodulation therapy improve the postoperative outcomes of tonsillectomy? A systematic review and meta-analysis

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## Abstract

**Introduction:** Postoperative management of patients undergoing tonsillectomy is challenging. Photobiomodulation therapy (PBMT) has emerged as a new tool providing therapeutic benefits. However, the contribution of PBMT to the postoperative outcomes of tonsillectomy is still undefined. This systematic review and meta-analysis evaluated the published literature addressing the effects of PBMT on post-tonsillectomy.

**Methods:** Searches in Scopus, PubMed/MEDLINE, Embase, Web of Science, Cochrane Library, and grey literature were carried out for the identification of randomised controlled trials reported up to August/2021. The risk of bias with the Cochrane Collaboration tool and meta-analysis was performed. Outcomes were assessed with the Kaplan-Meier method and the log-rank test.

**Results:** A total of 1183 articles were retrieved, of which only two were included for qualitative and quantitative analysis. The wavelengths were 685 nm and 980 nm with energy density set at 4 J/cm<sup>2</sup>. The mandibular angle and the surgical wound were the sites of laser irradiation. Individuals who had not undergone PBMT after tonsillectomy were more likely to report pain and odynophagia in the first 24 hours after surgery than individuals who had undergone PBMT after tonsillectomy ( $P < 0.001$ ). Children who received PBMT after tonsillectomy were equally affected by pain and odynophagia in the first seven days after surgery compared to children who had not undergone PBMT after tonsillectomy ( $P > 0.05$ ). However, both studies found a significant association of PBMT with reduced analgesic consumption.

**Conclusion:** Although PBMT seems promising for the management of individuals undergoing tonsillectomy, a limited number of studies are available in the literature.

**Keywords:** Complementary therapies; Low-level light therapy; Photobiomodulation therapy; Systematic review; Tonsillectomy.

## Introduction

Tonsillectomy is at the top of the list of commonly executed surgical procedures in the paediatric population.<sup>1</sup> In the UK, the incidence of evidence-based indications of tonsillectomy is 4.2 per 1000 individuals in a year. From April 2016 to March 2017, approximately 37 000 childhood tonsillectomies were performed at an estimated cost of £42 million.<sup>2</sup> In 2010, nearly 290 000 surgeries

for the removal of tonsils were conducted in American individuals under 15 years of age.<sup>3</sup> The American Academy of Otolaryngology - Head and Neck Surgery (AAOHNH) has issued protocols for tonsillectomy in children.<sup>4</sup> Current indications for surgical procedures encompass recurrent tonsillitis and obstructive sleep apnoea, which may considerably affect the child's health and quality of life.<sup>4</sup> Moreover, tonsillectomy may be

necessary to treat breathing, halitosis, and other conditions related to enlarged tonsils.<sup>4,5</sup> In clinical practice, these recommendations are often generalized to adults, even though the body of evidence endorsing tonsillectomy for adults is less robust.<sup>5</sup>

Intense pain is one of the most critical postoperative complaints after tonsillectomy because it is an invasive procedure and pain continues to be poorly addressed in the medical routine.<sup>6,7</sup> In addition to the healing wound that is exposed to the pharynx movements during swallowing, the risk of haemorrhage and the issues of the prescription of medications, in particular for young subjects, contribute to the impasse.<sup>8</sup> Although previous guidelines for managing pain shortly after tonsillectomy have been documented elsewhere, they differ from one another.<sup>4,8,9</sup> Combinations of non-steroidal anti-inflammatory drugs and paracetamol prescribed preoperatively, intraoperatively, and postoperatively are strongly recommended unless there are absolute contraindications.<sup>8</sup> The use of codeine and opioids for the surgical management of pain is also an alternative, but prescription of these medications involves clinical challenges due to the concerns about side effects, including life-threatening respiratory depression. This is particularly true for paediatric individuals with a history of respiratory obstruction and sleep-disordered breathing.<sup>10</sup> In this respect, a treatment plan that includes pain control strategies is highly desirable.

The use of photobiomodulation therapy (PBMT) as a new method for pain management has been expanded since it reduces pain and has no side effects.<sup>11-13</sup> PBMT has been outlined as the deployment of nonionizing types of light, including light-emitting diodes, lasers, and broadband light in order to boost physiological targets and therapeutic advantages.<sup>12</sup> Solid proof emerging from laboratory, animal, and clinical studies indicates that PBMT is a safe and feasible adjunct therapy that reduces inflammation and accelerates healing.<sup>12,14-16</sup> PBMT drives cellular biostimulation through the stimulation of intracellular chromophores such as endogenous porphyrins, mitochondrial and membrane cytochromes, as well as flavoproteins.<sup>11,15</sup> Hence, the effects of PBMT on tissues depend on the amount of irradiation and the therapeutic parameters.<sup>11</sup> Although PBMT is used in clinical practice, its effects on the postsurgical outcomes of tonsillectomy have not yet been summarized.

Although there is a body of literature, which has provided a basis for the development of guidelines, significant gaps in knowledge about the postoperative care of individuals undergoing tonsillectomy still exist.<sup>4</sup> Therefore, in order to carry out a comprehensive analysis, the purpose of this systematic review and meta-analysis was to gather information from the literature regarding the influence of PBMT over the postoperative outcomes of tonsillectomy. Our hypothesis was that PBMT reduces postoperative

pain and medication rescue, thus improving the quality of care of individuals who undergo tonsillectomy.

## Materials and Methods

### *Recording of a Priori Protocol*

This study was recorded under the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).<sup>17</sup> PROSPERO (the International Prospective Register of Systematic Reviews) was the database where a priori protocol was recorded (PROSPERO; No. CRD42020201237).

### *Eligibility Criteria*

Inclusion criteria were randomized controlled trials (RCTs) in which PBMT was carried out during the postoperative period in individuals who had undergone tonsillectomy. Restrictions on the publication date, language, or geographic region were not placed. Reviews, reports of a case or series of cases, letters sent to journals' editors, expert opinions, and conference/meeting abstracts were excluded. The PICO research question was depicted as appended below:

P (Participants): subjects who had undergone tonsillectomy.

I (Intervention): PBMT during the postoperative period.

C (Comparison): no use of PBMT during the postoperative period.

O (Outcome): any outcome.

### *The Strategy Employed in Databases*

Searches across the electronic databases PubMed/MEDLINE, Embase, Cochrane Library, Scopus, and Web of Science were performed. The time period included references that had been published from the databases' inception date until September 2020. An update took place in August 2021.

The search strategy used was as follows: (photostimulation OR photoirradiation OR photoactivation OR photobiomodulation OR PBMT OR PBM OR LLLT OR laser OR "light emitting diode" OR "red laser therapy" OR "red laser therapies" OR "infra-red laser therapy" OR "infra-red laser therapies" OR "low intensity laser therapy" OR "low intensity laser therapies" OR "low-intensity laser therapy" OR "low-intensity laser therapies" OR "low level laser therapy" OR "low level laser therapies" OR "low-level laser therapy" OR "low-level laser therapies" OR "low level light therapy" OR "low level light therapies" OR "low-level light therapy" OR "low-level light therapies" OR "low power laser therapy" OR "low power laser therapies" OR "low-power laser therapy" OR "low-power laser therapies" OR "low power laser irradiation" OR "low-power laser irradiation" OR "photobiomodulation therapy" OR "photobiomodulation therapies" OR "laser biostimulation" OR "laser

phototherapy” OR “laser phototherapies”) AND (tonsillectomy OR tonsillectomies). Moreover, the reference lists of the articles selected were assessed. Google Scholar and the grey literature (OpenGrey and Proquest) were also evaluated. For these three databases, the first 200 hits were analysed,<sup>18</sup> being the references in Google Scholar and Proquest arranged in relevance order. In OpenGrey, after running the search, the word “Otorhinolaryngology” was used to refine the references retrieved. References that were duplicated across databases were found and eliminated with a command of the software EndNote (End Note® Online, Clarivate Analytics, Canada).

### **Selection of Studies and Data Extraction**

Independent examiners (JAAA; ACVPS) assessed titles and abstracts, and the articles were selected in two independent phases. In phase 1, the titles and abstracts meeting the inclusion/exclusion criteria were selected for analyses of the full texts. Phase 2, during which the full texts were assessed, was performed shortly thereafter. The full text of the articles without sufficient information in the titles/abstracts was retrieved to assist the two authors in the decision to include or exclude. Those meeting the eligibility criteria were included. Disagreements between the two authors in any stage were settled by consulting a third author (RAM) until a consensus was reached.

The data were obtained from each article as follows: authors' name and year of publication, countries where the research was conducted, demographic characteristics (participants' sex and age), technique or instrumentation employed for tonsillectomy, complications, and results of the studies regarding each outcome assessed. As regards the parameters of the laser device, when available, we extracted the items based on the guidelines of the World Association for Laser Therapy (WALT): manufacturer, wavelength, operation mode, power, power density, energy density, total energy, spot area, and treatment standards (time of irradiation, frequency of irradiation, irradiation done in contact/distance).<sup>11</sup> Also, information on the sources of financial or nonfinancial support for the studies was collected. An author (ACVPS) extracted all the data from the included studies, and a second author (JAAA) double-checked these data. If the authors disagreed, they discussed solving the disagreement. For cases not resolved, another author (RAM) was consulted.

### **Outcome Measurements**

The primary and secondary outcomes were defined on the basis of continuous and dichotomous data. The presence and intensity of pain were evaluated with the visual analogue scale (VAS). The need for and quantity of analgesics taken within the follow-up and the participants' diet acceptance/odynophagia were assessed using appropriate questionnaires. The data

were reported as mean/median and standard deviation, number of individuals with outcomes and total number of individuals assessed. A threshold of 0.05 for the *P* value indicated statistical significance.

### **Data Analyses**

#### **Meta-analysis**

Studies displaying methodological uniformity were incorporated into meta-analyses, which were undertaken for the postoperative pain and odynophagia/acceptance of diet outcomes assessed 24 hours after tonsillectomy. Subgroup analyses with evaluations of children and adults were also performed. Dichotomous data (the number of individuals affected by pain or odynophagia/acceptance of diet assessed 24 hours after tonsillectomy and the total number of individuals) were used. Version 5.4.1 of RevMan (Review Manager, The Cochrane Collaboration, 2020) was used. The results were reported as odds ratio (OR) and confidence intervals (CI). Statistical heterogeneity was estimated using the  $I^2$  test. The random effect model or fixed effect model could be used after the analysis of the  $I^2$  and the clinical data heterogeneity.<sup>19</sup>

#### **Analysis of the Likelihood of Reporting Pain and Odynophagia**

The comparison of pain and odynophagia/acceptance of diet during the postoperative period (first 24 hours and first seven days) between individuals who had undergone PBMT after tonsillectomy and those who had not undergone PBMT after tonsillectomy was carried out with the Kaplan-Meier method and the log-rank test. Statistical analysis was run with MedCalc (MedCalc, Ostend, Belgium). For all analyses, the level of significance was  $P < 0.05$ .

#### **Assessment of Risk of Bias**

The risk-of-bias assessment within RCTs incorporated in this systematic review and meta-analysis was assessed using the Cochrane risk of bias tool.<sup>20</sup> Two authors (LFS; JAAA) performed the risk-of-bias assessment. This tool evaluates bias of selection (random sequence generation and allocation concealment), bias of performance (whether participants and personnel were blinded), bias of detection (whether the assessor of the outcome was blinded), bias regarding attrition (incompleteness of data of the outcome), bias of reporting (whether the reporting was selective), and any other bias. A third author (LGA) resolved the discrepancies.

### **Results**

#### **Study Selection**

Electronic searches yielded 1183 articles. Of these, 236 were from PubMed/MEDLINE, 259 were retrieved from Web of Science, 397 from Scopus, 216 from Embase, and 75 from the Cochrane Library. After the withdrawal of

635 duplicates, eligibility criteria were directly applied to 548 hits and two studies were selected for this systematic review and meta-analysis.<sup>21,22</sup> No reference meeting the inclusion/exclusion criteria was found in the reference lists of the selected articles or in the databases where grey literature was reviewed. Figure 1 depicts the process of article selection.

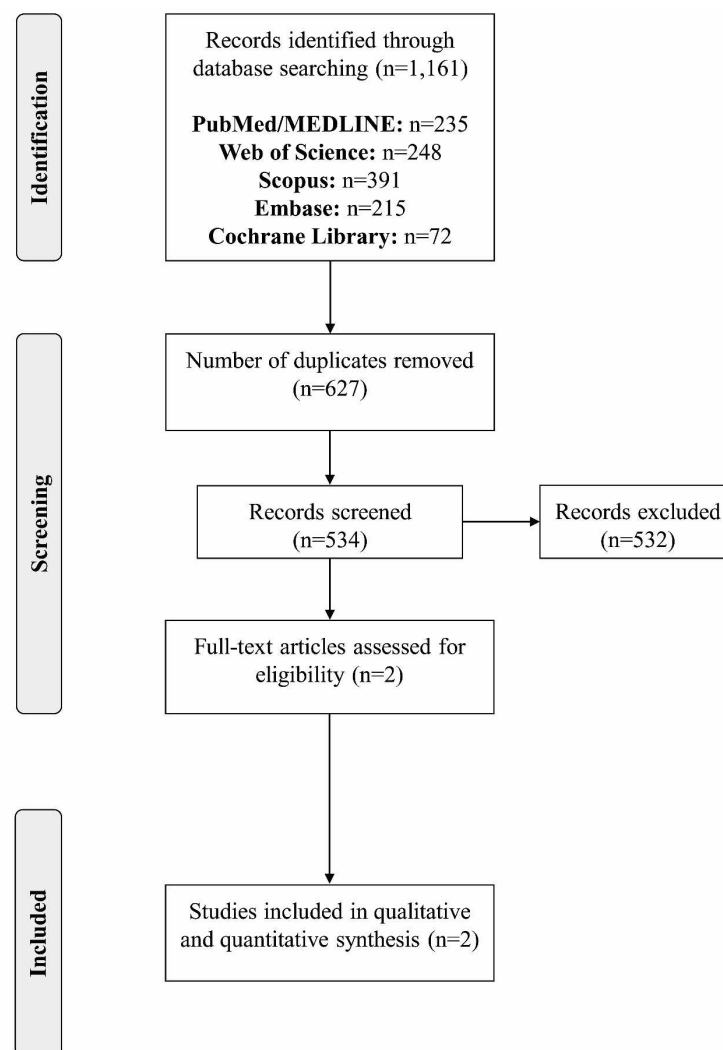
### Study Characteristics

The two studies evaluated, during the postoperative period of tonsillectomy, a total of 39 individuals submitted to PBMT and 39 individuals allocated to the control group who did not undergo PBMT. Both articles were published in English; one in 2010<sup>21</sup> and the other in 2013.<sup>22</sup> One study was conducted in Brazil<sup>21</sup> and the other in Iran.<sup>22</sup> The first study<sup>21</sup> included children and adolescents of both sexes, whose age ranged from 5 to 15 years (a mean of 8.5 years). Of these, individuals aged 5 to 15 years (a mean of 8.6 years) had been assigned to the control group and individuals aged 6 to 13 years (a mean of 8.3 years) had been assigned to the PBMT group. The

second study<sup>22</sup> comprised adults of both sexes, who were aged 20 to 40 years.<sup>22</sup> Individuals assigned to the control group were those with a mean age of  $20.53 \pm 6.83$ , while individuals assigned to the PBMT group were those with a mean age of  $24.15 \pm 7.5$ . Details of the distribution of individuals are depicted in Table 1.

### Surgical Procedures

Neiva et al<sup>21</sup> adopted blunt dissection using the graspers/suction dissector. The other study did not provide any surgical details.<sup>22</sup> The premedication of children and adolescents was oral midazolam 0.3 mg/kg. Sevoflurane supplemented with IV fentanyl 3 mcg/kg, propofol 5 mg/kg, and rocuronium 0.6 mg/kg rocuronium was used in anesthesia, which was maintained with isoflurane 0.5% to 2.0%, nitrous oxide 50%, and oxygen 50%.<sup>21</sup> The premedication used in adults was fentanyl (1 µg/kg) along with midazolam (30 µg/kg). Propofol (2 mg/kg) and atracurium (0.5 mg/kg) were used in induction. Anesthesia consisted of the TIVA (Total intravenous anesthesia) technique combining propofol and



**Figure 1.** Flow Chart Showing the Results of the Search Process.

**Table 1.** Summary of the Study Characteristics and Results of the Included Studies

Variables	Neiva et al <sup>21</sup>			Aghamohammadi et al <sup>22</sup>		
Country	Brazil			Iran		
Groups	PBMT, n=9			PBMT, n=30		
	Control, n=9			Control, n=30		
Gender	Male, n=12			Male, n=21		
	Female, n=6			Female, n=39		
Mean age	PBMT, 8.3 years			PBMT, 24.15 years		
	Control, 8.6 years			Control, 20.53 years		
PBMT protocol	50 mW			NI		
	685 nm			980 nm		
	3 minutes and 20 seconds			NI		
	4 J/cm <sup>2</sup>			4 J/cm <sup>2</sup>		
	Surgical wound			Mandibular angle		
Time of PBMT application	Intraoperatively and on the first postoperative day			End of surgery		
Postoperative evaluation	Seven days			24 hours		
Pain assessment		PBMT Group (Median)	Control Group (Median)	Period of Evaluation	PBMT Group (mean $\pm$ SD)	Control Group (mean $\pm$ SD)
	1 <sup>st</sup> day	3	5	0 h	1.84 $\pm$ 0.80	2.77 $\pm$ 0.57
	2 <sup>nd</sup> day	3	5	2 h	1.55 $\pm$ 0.74	2.7 $\pm$ 0.60
	3 <sup>rd</sup> day	3	3	4 h	1.43 $\pm$ 0.68	2.41 $\pm$ 0.63
	4 <sup>th</sup> day	2	3	6 h	1.38 $\pm$ 0.96	2.21 $\pm$ 0.73
	5 <sup>th</sup> day	2	3	8 h	1.59 $\pm$ 1.00	2.00 $\pm$ 0.63
	6 <sup>th</sup> day	1	2	12 h	1.5 $\pm$ 0.71	1.5 $\pm$ 0.59
	7 <sup>th</sup> day	0	1	24 h	1.00 $\pm$ 0.00	1.19 $\pm$ 0.40
Drug administration		PBMT Group (Number of Individuals)	Control Group (Number of Individuals)	Use of Analgesics	PBMT Group (Number of Individuals)	Control Group (Number of Individuals)
	1 <sup>st</sup> day	None: 5 (55%)	2 doses: 6 (66%)	No	28	20
				Yes	2	10
	2 <sup>nd</sup> day	None: 4 (44%)	None: 2 (22%)			
		1 dose: 4 (44%)	2 doses: 2 (22%)			
		-	3 doses: 2 (22%)			
	3 <sup>rd</sup> day	None: 6 (66%)	1 dose: 6 (66%)			
	4 <sup>th</sup> day	None: 7 (77%)	None: 5 (55%)			
	5 <sup>th</sup> day	None: 6 (66%)	None: 8 (88%)			
Acceptance of diet/odynophagia	6 <sup>th</sup> day	None: 8 (88%)	None: 9 (100%)			
	7 <sup>th</sup> day	None: 8 (88%)	None: 9 (100%)			
		PBMT Group (Number of Individuals)	Control Group (Number of Individuals)	Period of Evaluation	PBMT Group (Mean $\pm$ SD)	Control Group (Mean $\pm$ SD)
	1 <sup>st</sup> day	Average: 5 (55%)	Good: 4 (44%)	0 h	1.64 $\pm$ 0.74	2.82 $\pm$ 0.39
				2 h	1.48 $\pm$ 0.67	2.63 $\pm$ 0.61
				4 h	1.35 $\pm$ 0.61	2.45 $\pm$ 0.63
	2 <sup>nd</sup> day	Good: 4 (44%)	Average: 4 (44%)	6 h	1.45 $\pm$ 1.04	2.07 $\pm$ 0.7
				8 h	1.61 $\pm$ 1.30	1.8 $\pm$ 0.69
				12 h	1.50 $\pm$ 0.71	1.52 $\pm$ 0.59
				24 h	1.00 $\pm$ 1.00	1.21 $\pm$ 0.43
	3 <sup>rd</sup> day	Good: 4 (44%)	Good: 6 (66%)			
		Average: 4 (44%)	-			
	4 <sup>th</sup> day	Good: 6 (66%)	Good: 7 (77%)			
	5 <sup>th</sup> day	Good: 6 (66%)	Good: 7 (77%)			
	6 <sup>th</sup> day	Good: 9 (100%)	Good: 9 (100%)			
	7 <sup>th</sup> day	Good: 9 (100%)	Good: 9 (100%)			

NI, not informed; PBMT, photobiomodulation therapy; SD, standard deviation.



remifentanyl. Haemostasis and opening of the gag device were carried out.<sup>22</sup> No complications were reported.

### **PBMT: Device Information, Irradiation Parameters, and Treatment Standards**

The Brazilian study used the Dentoflex<sup>®</sup> laser,<sup>21</sup> and the Iranian study did not provide information about the device used.<sup>22</sup> The wavelengths were 685 nm<sup>21</sup> and 980 nm.<sup>22</sup> A power of 50 mW was used by Neiva et al.<sup>21</sup> Total irradiation time was three minutes and 20 seconds in this protocol.<sup>21</sup> The second study did not provide information about irradiation time.<sup>22</sup> The energy density of 4 J/cm<sup>2</sup> was used in both studies. The timing of laser application was at the end of the surgery in one study<sup>22</sup> and at two time points, intraoperatively and on the first postoperative day, in the other.<sup>21</sup> The mandibular angle<sup>22</sup> and the surgical wound<sup>21</sup> were the sites of laser irradiation (Table 1).

### **Pain Assessment, Analgesic Use, and Odynophagia/Acceptance of Diet**

The pain assessment was described from the first to the seventh day by Neiva et al.<sup>21</sup> The median scores of the VAS for the assessment of pain were lower in the group of individuals who had undergone PBMT, with a significant difference on the first postoperative day ( $P=0.01$ ), the second postoperative day ( $P=0.01$ ), the fourth postoperative day ( $P=0.05$ ), and the fifth postoperative day ( $P=0.03$ ). According to Aghamohammad et al.,<sup>22</sup> mean pain severity during recovery was 1.84 among individuals who had undergone PBMT and 2.76 among individuals who had been assigned to the control group ( $P=0.01$ ). At 24 hours after surgery, mean pain was 1.43 among individuals who had undergone PBMT and 2.11 among individuals who had been assigned to the control group ( $P=0.01$ ).

According to Neiva et al.,<sup>21</sup> 55% of the children and adolescents who had undergone PBMT did not use analgesics on the first postoperative day, while all individuals who had been assigned to the control group took a minimum of one dose of dipyrone ( $P=0.01$ ). Regarding the mean doses of dipyrone administered over the seven-day follow-up, individuals in the PBMT group required fewer analgesics than those in the control group ( $P<0.001$ ). On the first postoperative day ( $P<0.01$ ) and the second postoperative day ( $P<0.03$ ), patients in the PBMT group took fewer doses of dipyrone in comparison to those in the control group. In the study by Aghamohammad et al.,<sup>22</sup> the use of 50 mg of tramadol was reported by two patients in the PBMT group, while 28 (93.3%) patients did not receive analgesics. In the control group, in contrast, 10 patients received analgesics and 20 did not receive any painkillers.

The diet acceptance of patients was very much similar in the two groups during the follow-up of seven days in the study of Neiva et al.<sup>21</sup> The mean severity of odynophagia

during recovery was 1.64 for individuals who had undergone PBMT ( $P=0.01$ ) and 2.82 for individuals who had been assigned to the control group. Within the first 24 hours after surgery, the mean values were 1.35 for individuals who had undergone PBMT and 2.12 for individuals who had been assigned to the control group ( $P=0.01$ ).<sup>22</sup>

### **Statistical Analyses**

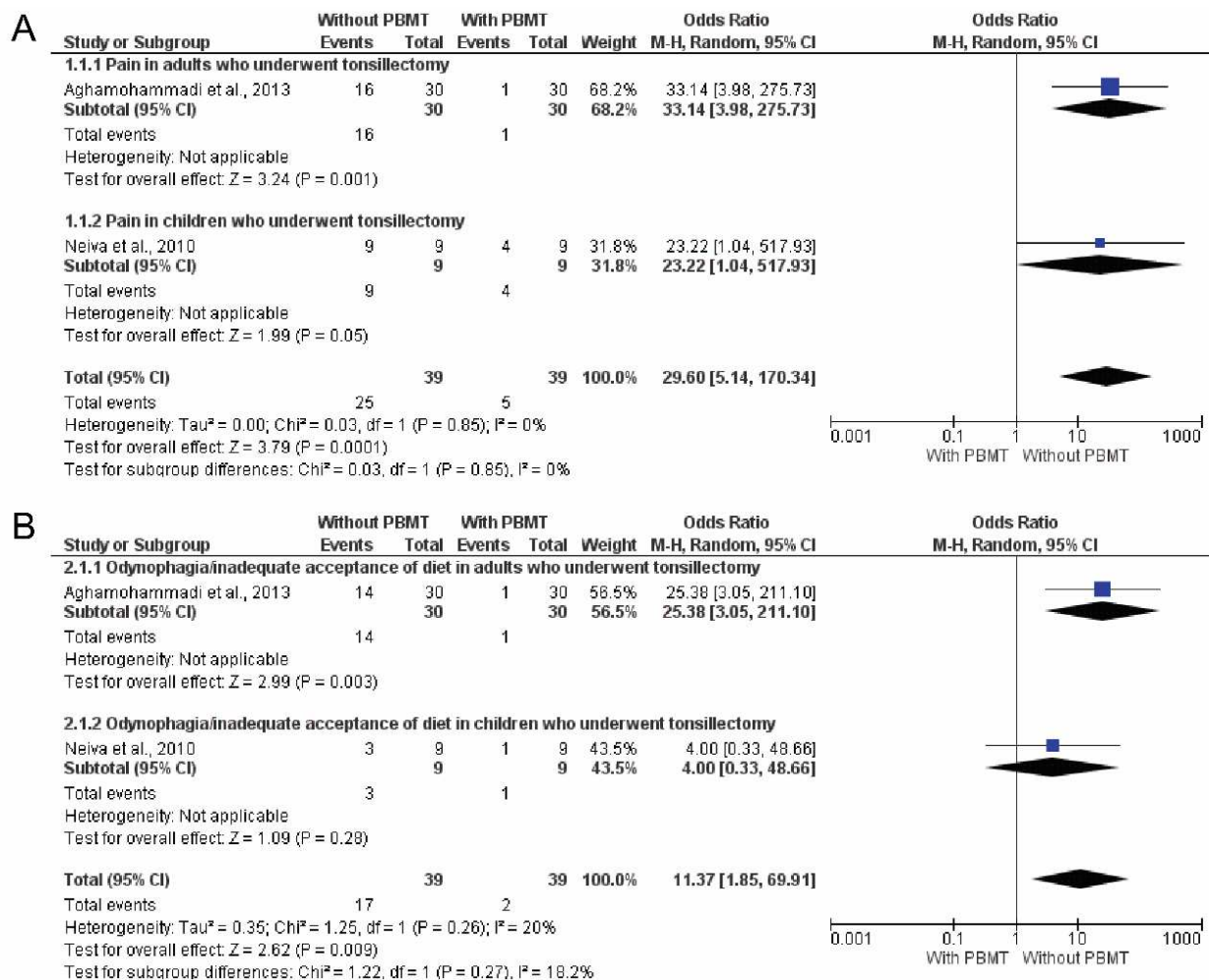
For the postoperative pain outcome, adults who had not undergone PBMT after tonsillectomy were more likely to report pain within the first 24 hours after surgery than adults who had undergone PBMT after tonsillectomy. Children and adolescents who had not undergone PBMT after tonsillectomy were also more likely to report pain within the first 24 hours after surgery than children and adolescents who had undergone PBMT after tonsillectomy. In the aggregate, individuals who had not undergone PBMT after tonsillectomy were more likely to report pain within the first 24 hours after surgery than individuals who had undergone PBMT after tonsillectomy (Figure 2A).

For the odynophagia outcome, adults who had not undergone PBMT after tonsillectomy were more likely to report odynophagia within the first 24 hours after surgery than adults who had undergone PBMT after tonsillectomy. Children and adolescents who had not undergone PBMT after tonsillectomy were equally affected by odynophagia within the first 24 hours after surgery than children and adolescents who had undergone PBMT after tonsillectomy. In the aggregate, individuals who had not undergone PBMT after tonsillectomy were more likely to report odynophagia within the first 24 hours after surgery than individuals who had undergone PBMT after tonsillectomy (Figure 2B).

The Kaplan-Meier method and the log-rank test confirmed that adults who had undergone PBMT after tonsillectomy were more likely not to report pain (Figure 3A) or odynophagia (Figure 3B) within the first 24 hours after surgery than adults who had not undergone PBMT after tonsillectomy ( $P<0.001$ ). The Kaplan-Meier method and the log-rank test also demonstrated that children and adolescents who had undergone PBMT after tonsillectomy were equally affected by pain (Figure 3C) and odynophagia (Figure 3D) during the first seven days after surgery than children who had undergone PBMT after tonsillectomy ( $P>0.05$ ).

### **Risk of Bias**

The overall bias of the studies for each category of bias is portrayed in Figure 4. In the studies, the risk of bias was high for “blinding of personnel” since providers were aware of whether or not the individuals had received PBMT. The risk of bias was unclear for “allocation concealment” because researchers did not provide details



**Figure 2.** Effects of Photobiomodulation Therapy (PBMT) During the Post-tonsillectomy Period. The meta-analysis indicates that PBMT reduces (A) pain and (B) odynophagia in the first 24 hours' post-tonsillectomy.

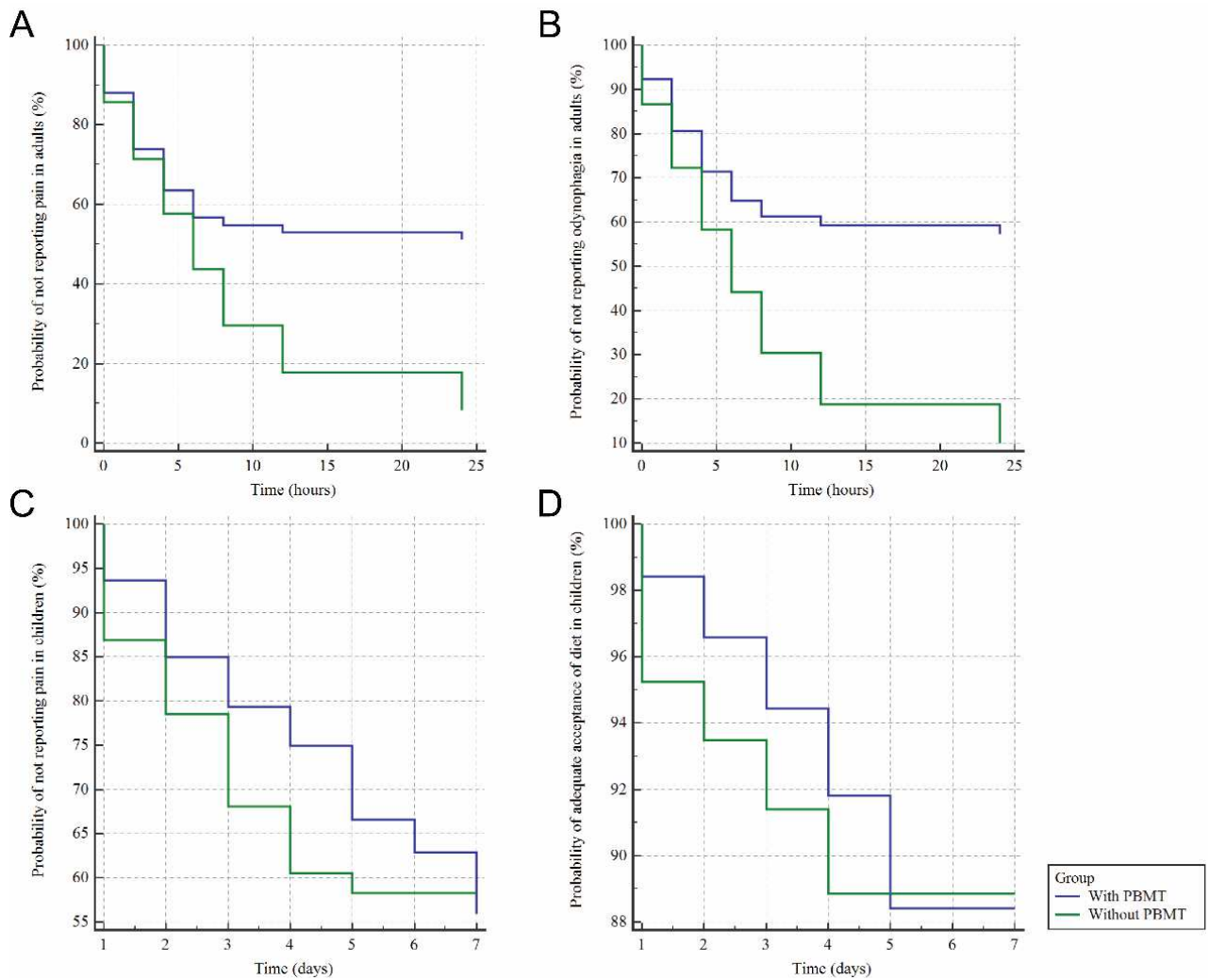
about the random distribution of participants in the groups, which should ideally have been accomplished using computer software. The risk of bias was low for “blinding of participants” (adults, parents/guardians and children were unaware of whether they had undergone PBMT or otherwise), “incompleteness of the data of the outcome”, “selective outcome reporting”, and “other biases” since the articles provided general information about the main and secondary results. In addition to that, there was no loss of results. Moreover, in both articles included, information regarding the sources of financial or nonfinancial support was not reported.

## Discussion

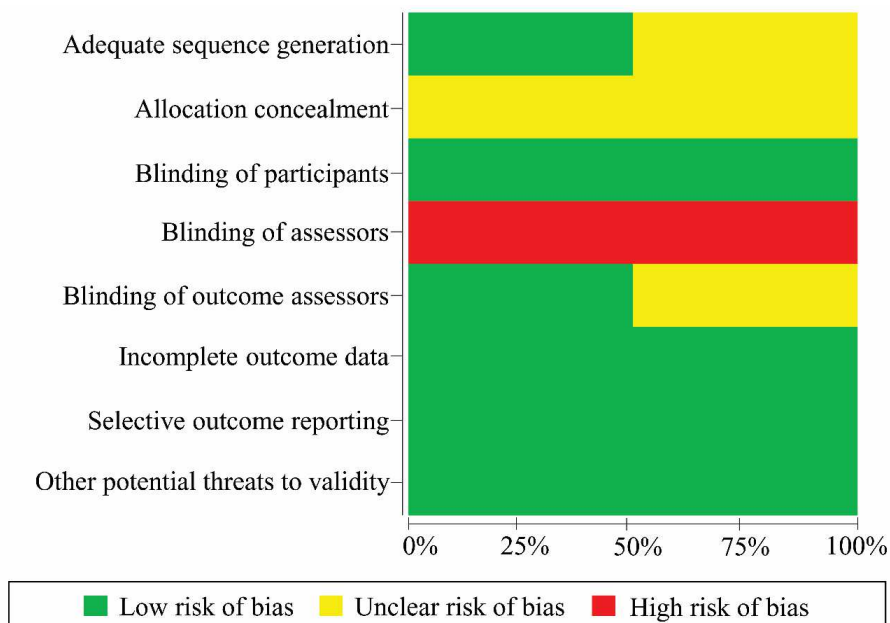
Attention has been closely paid to specific risks during the tonsillectomy recovery period since undesirable outcomes such as pain and bleeding have been frequently reported, regardless of the optimal technique or instrumentation employed.<sup>23-25</sup> Whilst the debate about which technique yields the best outcome still continues,<sup>26,27</sup> the clinical effectiveness in terms of the balance among the invasiveness of analgesic supply, the level of postoperative

pain, and the occurrence of side effects have also been questioned.<sup>8</sup> In the meantime, adjunctive therapies combined with classical analgesia for managing pain/discomfort subsequent to tonsillectomy have shown promising results.<sup>9,28</sup> Based on this background, the present study attempted to synthesize the influence of PBMT used during the postoperative period of tonsillectomy. The hypothesis that PBMT reduces pain and analgesic consumption after tonsillectomy in children, adolescents, and adults when compared to the control group has been accepted. Nonetheless, the two randomized clinical trials included herein reported heterogeneous data with respect to the irradiation parameters and treatment protocols.<sup>21,22</sup> The results of both selected RCTs were also assorted with respect to clinicodemographic characteristics, PBMT protocols, as well as methods of outcome assessment. Thus, the limited data available force us to be cautious when interpreting the results of the action of PBMT on the postoperative management of tonsillectomy.

Evidence indicates that PBMT used after a wide range of oral and maxillofacial procedures not only relieves pain but also reduces swelling, trismus, infections and



**Figure 3.** Survival Curves of Photobiomodulation Therapy (PBMT) During the Post-tonsillectomy Period According to (A) Pain in Adults, (B) Odynophagia in Adults, (C) Pain in Children and Adolescents, and (D) Odynophagia in Children and Adolescents. Curves were compared by the log-rank test.



**Figure 4.** Quality Assessment of the Included Studies.



accelerates wound healing.<sup>29</sup> Due to its anti-inflammatory properties, PBMT has been shown to be effective in the management of several painful events in the oral cavity and oropharynx.<sup>29-31</sup> Among the possible mechanisms of action of PBMT, it has been suggested that the analgesic effects of the procedure are probably related to an increased secretion of endorphin since PBMT may assist in the release of neurotransmitters (e.g., serotonin), sharply improving endorphin performance.<sup>15,32</sup> The reduction of the level of pain-related molecules such as prostaglandin E2 and cyclooxygenase-2 has also been documented.<sup>33</sup> As we well know, the postoperative pain of individuals submitted to tonsillectomy lasts about 14 days, delaying the return to daily activities and to a normal diet, with the risk of dehydration.<sup>27</sup> In severe cases, postoperative pain may result in delayed discharge, emergency department visits, or readmission to the hospital for pain control and hydration.<sup>27</sup> Importantly, PBMT applied during surgery and within the first five postoperative days was powerful in drastically mitigating pain/discomfort subsequent to surgery for removing individuals' palatine tonsils.<sup>21,22</sup> In addition, individuals who did not undergo PBMT after tonsillectomy were more likely to report pain and odynophagia within the first 24 hours after surgery than those who underwent PBMT. This is in line with an earlier series of authors from Russia, who showed significant anti-inflammatory and analgesic outcomes and a shorter recovery period after applying a low-energy helium-neon laser to tonsillectomized individuals.<sup>34</sup>

Although pain measurement tools, such as VAS, often provide subjective data, previous studies that have evaluated different conditions in the oral cavity have documented the effects of PBMT in a satisfactory and safe way for the control of the whole pain process.<sup>29</sup> Both studies covered herein used the VAS for pain assessment.<sup>21,22</sup> However, as the age of the participants was distinct, that is, one study included patients aged 8 to 15 years<sup>21</sup> and the other patients aged 20 to 40 years,<sup>22</sup> an overestimation of the sensation of pain, particularly in the paediatric age group, cannot be ruled out. Notably, studies have demonstrated that older patients used painkillers for a longer mean number of days.<sup>35</sup> This finding that adults experience more post-tonsillectomy pain than children has been well documented.<sup>35</sup>

Another relevant aspect was that children and adolescents who had received PBMT required sparse use of analgesics and their mean pain scores during the first four days were lower than those of the group that received dipyrone.<sup>21</sup> According to Aghamohammadi et al,<sup>22</sup> of the 30 individuals allocated to the PBMT group, only two (6.6%) received 50 mg of tramadol. Certainly, these results can also be linked to pharmacological management during the pre- and intraoperative periods. Indeed, intraoperative pain management for tonsillectomy involves careful titration of opioids.<sup>36</sup> Although oral

opioids, such as codeine, are often used to control pain after hospital discharge, there are many cases of deaths after tonsillectomy due to respiratory depression caused by the use of opioids with liver microenzyme variations or the use of relatively excessive doses of opioids with unsatisfactory monitoring.<sup>36</sup> Of note, some studies have pointed out that parents were reluctant to administer painkillers to their children during the tonsillectomy recovery period or did not administer them regularly.<sup>24,37</sup>

In addition, other outcomes should also be considered. First, the overall risk of unsatisfactory outcomes may be related to the surgical technique. Although there is still no consensus of opinion, in a study that compared the effects of coblation, cold dissection and diode laser on adolescents (10-15 years) who had undergone a tonsillectomy,<sup>38</sup> the authors demonstrated that, during the first 24 hours, patients enrolled in the diode laser group had the same score of pain as patients in other groups. Nevertheless, the level of pain of individuals who had undergone therapy with the diode laser was significantly higher on the seventh postoperative day. The authors argued that this could be related to the thermal tissue injury caused by the diode laser, leading to an intensified inflammatory response that would cause severe pain.<sup>38</sup> On the other hand, more recently, a systematic review disclosed that among the hot techniques available, the use of laser after tonsillectomy has emerged as a procedure that leads to surgery with reduced bleeding. In individuals among whom bleeding occurred, the amount was significantly lower than techniques of dissection.<sup>39</sup> Moreover, the panel of recommendations is supportive in indicating a cautionary application of hot techniques. Moreover, practitioners should undertake continuing education before the adoption of a novel approach (e.g., laser; coblation).<sup>39</sup>

It is reasonable to assume that, when the practitioner uses PBMT to handle the swelling and other oral complications, odynophagia is reduced, and consequently, the individual will be able to eat properly.<sup>40</sup> Nevertheless, one of the studies included here demonstrated that paediatric patients who had undergone PBMT after tonsillectomy did not show good acceptance of the diet.<sup>21</sup> While children and adolescents needed low doses of analgesics for pain management, the effect of just two laser applications did not prevent odynophagia, in turn impairing diet acceptance.<sup>21</sup> This scenario was different for adults. The mean odynophagia severity of individuals who had received PBMT within 24 hours was markedly lower than those of the control group.<sup>22</sup> Nonetheless, the time of exposure to PBMT as well as the evaluation time used during the postoperative period probably influenced the outcome since different evaluation times were employed in the two included studies.<sup>21,22</sup> In addition, there was a striking spike in oral complications, that is, swelling and odynophagia about 72 hours after

surgery.<sup>41</sup> Thus, evaluation of only the first 24 hours after tonsillectomy is too limited to draw any conclusions.<sup>22</sup> On certain occasions, shortly after surgery, there is no time for laser biomodulation.<sup>41</sup> For instance, in the case of procedures used to correct dentofacial deformities, such as orthognathic surgery, in which pain and swelling need monitoring, a study reported that swelling was reduced considerably over the irradiated area of individuals in postoperative evaluations during the 3<sup>rd</sup>, 7<sup>th</sup>, 15<sup>th</sup>, and 30<sup>th</sup> days.<sup>41</sup>

A variety of parameters in terms of laser properties and dosage influence the effects of PBMT.<sup>11,12,14-16</sup> Herein, apart from the energy density, which was 4 J cm<sup>-2</sup> in both studies, different wavelengths, 685 nm and 980 nm, were used.<sup>21,22</sup> The two studies on the effects of PBMT during the postoperative period of tonsillectomy available in the literature failed to consider the selection of the ideal parameters, or they did not provide information about the precise instrumentation, thus limiting our considerations about the effect of PBMT for this procedure.<sup>21,22</sup>

In one included study, a laser was used to irradiate the surgical wounds,<sup>21</sup> while in the other it was used to irradiate the region from the mandibular angle to the bed of the tonsils.<sup>22</sup> For other oral and maxillofacial conditions, studies are performed with intraoral devices through which a laser is applied directly to the oral mucosa.<sup>13,31,32,42</sup> However, some other forms of photobiomodulation, such as the extraoral light emitter diode laser or the intraoral defocused high-power diode laser, have also produced satisfactory results.<sup>43,44</sup> Accordingly, a recent study showed that the extraoral diode laser using 6 J/cm<sup>2</sup> reduced the inflammatory process and promoted faster reepithelialisation of oral mucositis in an animal model when compared to intraoral irradiation.<sup>45</sup> Likewise, the 800 nm laser applied over the extraoral region favoured decreases in postoperative facial swelling and trismus after the removal of impacted lower third molars.<sup>46</sup> Although some potential benefits have been described in the studies reviewed here using intraoral or extraoral protocols,<sup>21,22</sup> there were no details regarding the operating mode, irradiance, power output, or mode of application.

Finally, we encourage new studies for the investigation of the effects of PBMT on post-tonsillectomy bleeding since primary haemorrhage (i.e., within 24 hours) takes place in 0.2% to 10% of the patients, whereas secondary haemorrhage (i.e., after 24 hours, often in 7 to 10 days) occurs in 0.1% to 5% of the patients.<sup>27</sup> Studies with a large sample size, longer follow-up, and PBMT application with different doses/protocols are also recommended, including complete descriptions of the device and parameters employed. However, the results of the present study have limitations that should be recognized. Although we have carried out an extensive systematic review and meta-analysis without any restrictions concerning the date or language of publication, there is still a scarcity of studies

using PBMT in post-tonsillectomy.

## Conclusion

In summary, PBMT represents an appealing new frontier in the management of individuals undergoing tonsillectomy, particularly regarding the optimization of the management of pain and reduction in the intake of analgesics. However, further well-designed studies are mandatory in order to offer evidence-based recommendations.

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## Availability of Data

Data available upon request from the authors.

## Conflict of Interests

The authors have no conflicts of interest to declare.

## Ethical Considerations

Not applicable.

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