

The Use Of Adjuvant Therapies For Tonsillectomy

Hussein M. Hassan * C.A.B.M.S/ENT

Summary

Background: The aim was to ascertain the current practice of adjuvant therapy for tonsillectomy and to determine whether it is evidence based.

Methods: A questionnaire answers were obtained from sixty otolaryngologists in Baghdad.

Results: There was no any enthusiasm for routine intra-operative local anaesthesia.

Paracetamol (Acetaminophen) is prescribed by nearly all surgeons for postoperative analgesia, and the current literature supports its efficacy and safety.

Further, some practitioners combine paracetamol with NSAIDs, and/or Tramadol-Opioids. Evidence to support the additional use of these agents is, however non existent or limited.

For the use of antibiotics, we found some of the otolaryngologists do use a course of few days of pre-operative antibiotics and almost all of them do give postoperative antibiotics for seven-ten days.

Some aspects of tonsillectomy care are uniform and evidence based. Others are heterogenous and suffer from lack of adequate data in the literature.

Key words: Adjuvants; Questionnaires; Tonsillectomy.

Introduction:

Tonsillectomy continues to be one of the commonest surgical procedures performed in the world, and attracts a significant proportion of the total healthcare expenditure on surgical and postoperative care.¹ Tonsillectomy is associated with significant postoperative pain, and is indeed one of the most painful surgical procedures otolaryngologists perform. Adequate analgesia is imperative to minimize pain-associated morbidity, encourage an earlier return to fluid intake and feeding, and to prevent potential complications associated with ineffective pain relief, such as infection. There is a wide spectrum of analgesic drugs currently available, with significant differences in mode of delivery, efficacy, safety and side effects.

Numerous studies on adjuvant therapy for tonsillectomy have been published, and various drug regimens have been proposed. However, their impact on what Otolaryngologists actually prescribe has not so far been studied.

We undertook a questionnaire survey of sixty otolaryngologists in Baghdad to ascertain their current practice of adjuvant therapy for tonsillectomy. We measured the results of this survey against current best evidence in the literature, to uncover potential areas of concern and controversy.

* Dept. of Surgery College of Medicine/Baghdad University

Methods

The final questionnaire was created as a one page computer generated sheet. A total of 75 questionnaire lists were obtained. Incomplete, irrelevant and blank responses were excluded to give a total of 60 valid responses which were obtained as the following:-

Aljerahat Hospital for Surgical Specialty10 specialists

Al yarmouk teaching Hospital.....5 specialists

The University Hospital5 specialists

Different other public and private Hospitals.....40 specialists

The following questions (with choices illustrated in parentheses) were included:-

***Tonsillectomy dissection technique** (Cold steel, Bipolar Diathermy, Co-ablation, Laser or other).

***Intra-operative local anaesthesia used** (None, Pre- or Post-incisional, Infiltration or topical, Lignocaine or bupivacaine and/or epinephrine).

***Details of routine postoperative analgesia and antibiotics including:**

The choice of drug(s) {Paracetamol (Acetaminophen), Non-steroidal anti-inflammatory drug (NSAID), and Tramadol/Opioid}.

Duration of prescription (in days), and whether prescribed regularly or rescue only. The responders were also given the option of writing a free text answer.

Similar but separate sets of questions for children and adults were produced.

The levels of evidence used, in descending order of priority, are given in (Table 1).

TABLE 1
LEVELS OF EVIDENCE (IN DESCENDING ORDER OF PRIORITY)

1. Cochrane Review
2. Meta-analysis, systematic review
3. Randomized controlled study
4. Non-randomized prospective controlled study
5. Retrospective controlled study
6. Case series
7. Case report
8. Expert opinion

Results:

Dissection method:

Choice of postoperative adjuvant(s):

Cold steel is the dissection method used by almost all of the surveyed surgeons (only two of them used on occasions Bipolar diathermy dissection as an additional method) with no significant differences in technique between children and adults.

Intraoperative analgesic technique:

Non of the responders routinely employ intraoperative local anaesthesia. Although it is claimed to provide a pre-emptive analgesic effect^{2,3}, a recent Cochrane review has concluded that the studies so far have been too small and have failed to show a significant benefit.⁴ Furthermore, the agents used in this technique are associated with serious side effects.⁵

Figures (1) and (2) illustrate the drugs and combinations used in postoperative analgesia.

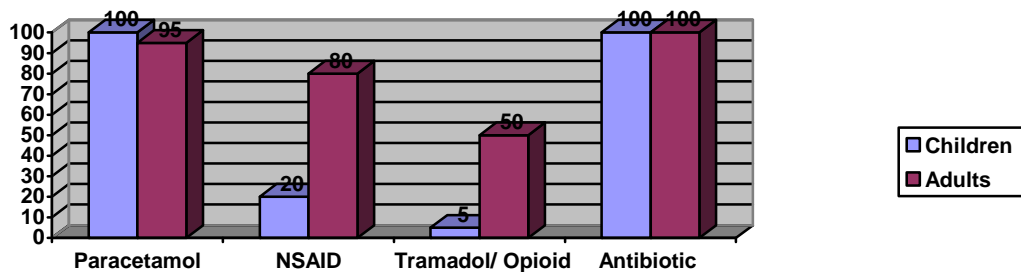


FIGURE (1): POST OPERATIVE ORAL ANALGESICS PRESCRIBED.

Paracetamol (Acetaminophin):

Nearly all responders prefer acetaminophen for postoperative analgesia, consistent with several randomized controlled trials emphasizing the relative efficacy and safety of this drug⁶⁻¹⁰. Only

one randomized controlled trial found acetaminophen to be inferior to tramadol for pain relief¹¹. In this trial, however, the dose of acetaminophen used was lower than the recommended dosage.

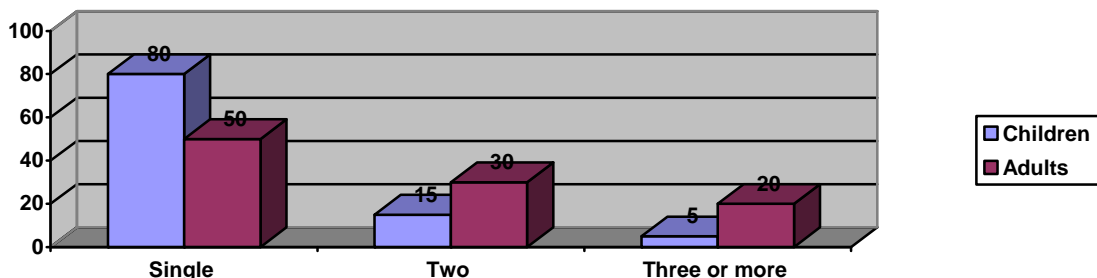


FIGURE (2): NUMBER OF ORAL ANALGESICS PRESCRIBED AS PART OF THE POSTOPERATIVE REGIMEN.

Additional adjuvants:

In addition to acetaminophen, few of our responders prefer NSAIDs (Ibuprofen or

diclofenac) and/or opioids for postoperative analgesia, mainly for the cases of adult

tonsillectomy. However, evidence to support their additional use is non-existent or limited.

Opioids:

There is a paucity of studies comparing the opioid-acetaminophen combination versus acetaminophen following tonsillectomy.

Only Moir *et al.*, have addressed this issue in a randomized controlled trial, and they found the regimen to be equianalgesia⁷. Further, opioids are

associated with sedation and gastrointestinal side effects.

NSAIDs:

There is no study comparing NSAIDs-paracetamol with paracetamol alone. Although NSAIDs have been established to be superior to placebo, they have been found to be no more efficacious than paracetamol and/or opioids (Table 2).

TABLE 2: EFFICACY OF NSAIDS VERSUS PARACETAMOL AND/OR OPIOIDS* (ALL STUDIES RANDOMIZED CONTROLLED).

Study	n	NSAID	Comparing group	Conclusion
1. Courtney&Cabraal ¹²	64	Diclofenac	Tramadol	NSAID equivalent
2. Harley <i>et al</i> ¹³	27	Ibuprofen	Paracetamol+codeine	NSAID inferior
3. St Charles <i>et al</i> ¹⁴	110	Ibuprofen	Paracetamol+codeine	NSAID equivalent
4. Pasquale <i>et al</i> ¹⁵	35	Nimuselide	Paracetamol	NSAID equivalent
5. Parker <i>et al</i> ¹⁶	77	Ibuprofen	Placebo	NSAID superior
6. Dommerby ¹⁷	97	Diclofenac	Placebo	NSAID superior

* Studies on enteral analgesia only included.

n = total number of patients.

The risk of postoperative haemorrhage with NSAIDs, which are potent inhibitors of platelet aggregation, has been analyzed in three separate meta-analyses. Table 3 is culled from these meta-analyses and illustrates all randomized controlled trials comparing postoperative enteral NSAIDs with

an enteral control drug. All documented postoperative haemorrhages are presented in the data. The pooled odds ratio of 0.98 for NSAIDs does not suggest a higher bleeding risk with these agents.

TABLE 3: RISK OF HAEMORRHAGE * WITH ENTERAL NSAIDS (ALL STUDIES RANDOMIZED CONTROLLED).

Study	NSAID	Comparison group	Incidence of haemorrhage		OR (95% CI)
			NSAID	Control	
1. Courtney <i>et al</i> ¹²	Diclofenac	Tramadol	6/25	7/24	0.77 (0.22-2.71)
2. Harley <i>et al</i> ¹³	Ibuprofen	Paracetamol+codeine	2/16	0/11	5.78 (0.33-103)
3. St Charles <i>et al</i> ¹⁴	Ibuprofen	Paracetamol + codeine	4/55	5/55	0.79 (0.20-3.06)
4. Dommerby ¹⁷	Diclofenac	Placebo	5/47	4/50	1.36 ((0.35-5.34)
5. Pasquale <i>et al</i> ¹⁵	Nimuselide	Paracetamol	0/16	0/19	n/a
6. Parker <i>et al</i> ¹⁶	Ibuprofen	Placebo	0/44	0/33	n/a
Pooled odds ratio			17/203	16/192	0.98

* Any documented postoperative haemorrhage.

OR = Odds ratio; CI = Confidence interval.

Antibiotics:

Like in the United States, where antibiotics are routinely used in the postoperative period⁵, all of the surveyed surgeons prescribe them and about (50%) prescribe them for 5-7 days preoperatively. This is unlike that in the UK where only a small

proportion of clinicians prescribe them postoperatively⁵.

Only five randomized controlled trials so far have investigated the role of oral antibiotics and the results are mixed. (Table 4)

TABLE 3: BENEFIT OF ANTIBIOTIC * (ALL STUDIES RANDOMIZED CONTROLLED).

Study	n	Antibiotic	Effect of antibiotic
-------	---	------------	----------------------

1. O'Reilly <i>et al</i> ²¹	95	Amoxicillin	No benefit
2. Mann <i>et al</i> ²²	18	Amoxicillin	No benefit
3. Colreavy <i>et al</i> ²³	78	Amoxicillin+ clavulanate	Less analgesic, less time to resume normal diet and pain scores
4. Grandis <i>et al</i> ²⁴	101	Amoxicillin+ clavulanate	Less mouth odour, earlier return to normal diet and activities
5. Telian <i>et al</i> ²⁵	85	Amoxicillin	Less mouth odour, fever, number of days in pain and earlier return to normal diet and activities

* Control group – no antibiotic
 n = total number of patients

Regular versus rescue analgesia:

Most responders prescribe postoperative analgesia on a regular basis, whereas 10% prefer rescue only pain relief (figure 3). Only two trials so far have compared regular versus rescue analgesia following tonsillectomy, and the results are conflicting. The earlier trial (non- randomized

controlled) found regular analgesia to be more efficacious (better pain control and earlier return to solid feeds)²⁶, whereas a more recent (randomized controlled) trial found no significant benefit with a regular regimen²⁷.

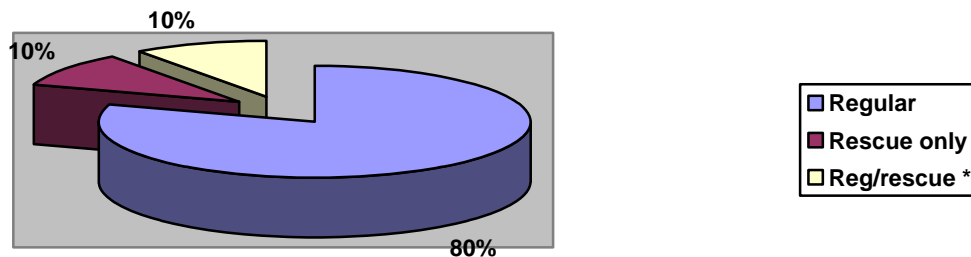


FIGURE (3): REGULAR OR RESCUE ANALGESIA.

*** REGULAR INITIALLY FOLLOWED BY RESCUE.**

Duration of postoperative analgesia:

Approximately 80% of responders prescribe postoperative analgesia for seven days or less (figure 5). Although the duration of post-tonsillectomy pain can show considerable individual variation²⁸⁻³¹, several studies document significant pain lasting beyond the first week. Others estimate such pain to last for an average of 8-11 days³². Salonen and Kokki³² also estimate the average duration of analgesic consumption to be 12 days.

Given the data, the current practice of analgesic prescription for seven days or less among our responders is probably inadequate.

There was no difference in the duration of postoperative analgesics prescribed for adults versus children. However, in the literatures, postoperative pain in children is reported to resolve faster than in adults³³.

Discussion

Adjuvant care after tonsillectomy is almost uniform among our responders.

There is consensus on some aspects of care, and still diversity on others. The latter is chiefly attributable to the lack of robust data in the literature. Well-designed studies on adjuvant therapy for tonsillectomy are few, use varying methodologies and end-points, focus on peri-operative care to the relative exclusion of longer term postoperative pain relief, and often arrive at conflicting results.

There is no enthusiasm for intraoperative local anaesthesia; in contrast there is an increasing enthusiasm for the use of postoperative antibiotics. This is consistent with the lack of robust evidence to support practices. Further, any putative benefit of antibiotics has to be carefully weighed against the possible emergence of resistant bacteria, fungal infection, and the risk of adverse events.

Paracetamol is justifiably the most popular operative analgesic. In addition, few prefer opioids and/or NSAIDs. This theoretically enhances efficacy, by combining two drugs with different mechanisms of action, and also allows for a reduction of their individual doses, thereby minimizing side effects. An enhanced efficacy effect has been reported for such combination

therapy following non-otolaryngological procedures such as laparotomy³⁴.

However, evidence to support such combined therapy following tonsillectomy is non-existent or limited. It is also unknown whether spacing the additional adjuvant in between paracetamol doses improves analgesia. Enteral NSAIDs have been shown not to incur a higher risk of postoperative bleeding. Nevertheless, current data are few and more trials are needed to establish conclusively the safety of this drug.

It is logical to assume that regular, as opposed to rescue-only, postoperative analgesia is better for pain control, because it sustains drug concentration largely within the therapeutic range, whereas rescue-only doses may result in deep troughs in serum levels and significant 'breakthrough' pain³⁵. Evidence to support a regular regimen following tonsillectomy is, however, scant and further trials are needed. As significant postoperative pain can potentially last for more than seven days, patients need to be appropriately warned and told about the need for adequate analgesia until the resolution of pain and resumption of normal diet.

Several limitations are acknowledged in the present report. Preference for a particular adjuvant

therapy however has negligible influence on the response rate of an anonymized survey, and it is reasonable to assume that the adjuvant regimen of non-responders will not be significantly different from that of the responders.

Secondly, this report focuses on adjuvant therapy as practiced by surgeons, and largely ignores other aspects of perioperative care, such as parenteral analgesics/adjuvants, which fall under the purview of anesthetists. The effect of such perioperative adjuvant is, however, restricted to the immediate postoperative period, with little impact on surgeon-controlled, longer term postoperative care.

Aforementioned limitation notwithstanding, this report is significant for two reasons: areas of consensus and diversity in contemporary practice have been uncovered; and areas with a robust as well as those with a poor evidence base have been illustrated. The former will serve as a reference point for comparison with peer practice, and the latter will serve as a guide for evidence based medicine. Both will be important to the practicing otolaryngologists when making informed decisions regarding the care of the tonsillectomy patient.

***The current practice of adjuvant therapies for tonsillectomy and whether they are evidence based have not previously ascertained.**

***Among most otolaryngologists there is no enthusiasm for intraoperative local anesthesia, in contrast to an increasing enthusiasm for the use of post-operative antibiotics. However, there's a lack of robust evidence to support any of these practices**

***Paracetamol is the most preferred postoperative analgesic, with current evidence supporting its efficacy and safety.**

***Evidence to support the additional use of opioids or non-steroidal anti-inflammatory drugs (NSAIDs) is non-existent or limited.**

Conclusion

Some aspects of tonsillectomy care are uniform and evidence based. Others are varied, and suffer from lack of adequate data in the literature. In the latter instance, practice appears to be influenced by conventional wisdom, anecdotal evidence and individual/institutional experience, preferences and guidelines. Although paracetamol is justifiably the most popular postoperative analgesic, it is sometimes combined with opioids and/or NSAIDs, for a theoretically better analgesia. However, any such added beneficial effect remains to be proven. Side effects and adverse events also need to be

carefully considered before additional adjuvants are prescribed. Further well-designed trials are called for to address aspects of tonsillectomy care with a limited evidence base.

References:

1. McKerrow WS. *Tonsillectomy and adenoidectomy. In: Statements of Clinical Effectiveness. London: British Association of Otolaryngologist & Head and Neck surgeons, 1998.*
2. Wong AK, Bissonnette B, Braude BM, Macdonald RM, St-Louis PJ, Fear DW. *Post-tonsillectomy infiltration with bupivacaine reduces immediate postoperative pain in children. Can J Anaesth 1995; 42: 770-4.*

3. Giannoni C, White S, Enneking FK, Morey T. Ropivacaine with or without clonidine improves pediatric tonsillectomy pain. *Arch Otolaryngol Head Neck Surg* 2001; 127: 1265-70.
4. Hollis LJ, Burton MJ, Millar JM. Peri-operative local anaesthesia for reducing pain following tonsillectomy. *Cochrane Database Syst Rev* 2000; (2): CD001874.
5. Thomsen J, Gower V. Adjuvant therapies in children undergoing adenotonsillectomy. *Laryngoscope* 2002; 112: 32-4.
6. Anderson BJ, Woollard GA, Holford NH. Acetaminophen analgesia in children: placebo effect and pain resolution after tonsillectomy. *Eur J Clin Pharmacol* 2001; 7: 559-69.
7. Moir MS, Bair E, Shinnick P, Messner A. Acetaminophen versus acetaminophen with codeine after pediatric tonsillectomy. *Laryngoscope* 2000; 110: 1824-7.
8. Romsing J, Ostergaard D, Drozdiewicz D, Schultz P, Ravn G. Diclofenac or acetaminophen for analgesia in paediatric tonsillectomy outpatients. *Acta Anaesthesiol Scand* 2000; 44: 291-5.
9. Rusy LM, Houck CS, Sullivan LJ et al. A double blind evaluation of ketorolac tromethamine versus acetaminophen in pediatric tonsillectomy: analgesia and bleeding. *Anesth Analg* 1995; 80: 226-9.
10. Stage J, Jensen JH, Bonding P. Post-tonsillectomy haemorrhage and analgesics. A comparative study of acetylsalicylic acid and paracetamol. *Clin Otolaryngol* 1988; 13: 201-4.
11. Pendeville PE, Von Montigny S, Dort JP, Veyckemans F. Double blind randomized study of tramadol vs. paracetamol in analgesia after day-case tonsillectomy in children. *Eur J Anaesthesiol* 2000; 17: 576-82.
12. Courtney MJ, Cabraal D. tramadol vs. diclofenac for posttonsillectomy analgesia. *Arch Otolaryngol Head Neck Surg* 2001; 127: 385-8.
13. Harley EH, Dattolo RA. Ibuprofen for tonsillectomy pain in children: efficacy and complications. *Otolaryngol Head Neck Surg* 1998; 119: 492-6.
14. St Charles CS, Matt BH, Hamilton MM, Katz BP. A comparison of ibuprofen versus acetaminophen with codeine in the young tonsillectomy patient. *Otolaryngol Head Neck Surg* 1997; 117: 76-82.
15. Pasquale G, Scaricabarozzi I, D'Agostino R, Taborelli G, Vallarino R. An assessment of the efficacy and tolerability of nimesulide vs. paracetamol in children after adenotonsillectomy. *Drugs* 1993; 46 (suppl 1): 234-7.
16. Parker DA, Gibbin KP, Noyelle RM. Syrup formulations for posttonsillectomy analgesia: a double blind study comparing ibuprofen, aspirin and placebo. *J Laryngol Otol* 1986; 100: 1055-60.
17. Dommerby H, Rasmussen OR. Diclofenac (Voltaren). Pain relieving effect after tonsillectomy. *Acta Otolaryngol* 1984; 98: 185-92.
18. Marret E, Flahault A, Samama CM, Bonnet F. Effects of postoperative, non steroidal, anti-inflammatory drugs on bleeding risk after tonsillectomy: meta-analysis of randomized controlled trials. *Anesthesiology* 2003; 98: 1497-502.
19. Moiniche S, Romsing J, Dahl JB, Tramer MR. Nonsteroidal anti-inflammatory drugs and the risk of operative site bleeding after tonsillectomy: a quantitative systematic review. *Anesth Analg* 2003; 96: 68-77.
20. Krishna S, Hughes LF, Lin SY. Postoperative haemorrhage with non steroidal anti-inflammatory drug use after tonsillectomy: a meta-analysis. *Arch Otolaryngol Head Neck Surg* 2003; 129: 1086-9.
21. O'Reilly BJ, Black S, Fernandes J, Panesar J. Is the routine use of antibiotics justified in adult tonsillectomy? *J Laryngol Otol* 2003; 117: 382-5.
22. Mann EA, Blair EA, Levy AJ, Chang A. Effect of topical antibiotic therapy on recovery after tonsillectomy in adults. *Otolaryngol Head Neck Surg* 1999; 121: 277-82.
23. Colreavy MP, Nanan D, Benamer M, et al. Antibiotic prophylaxis post-tonsillectomy: is it of benefit? *Int J Pediatr Otorhinolaryngol* 1999; 50: 15-22.
24. Grandis JR, Johnson JT, Vickers RM et al. The efficacy of peri-operative antibiotic therapy on recovery following tonsillectomy in adult: a randomized double blind placebo-controlled trial. *Otolaryngol Head Neck Surg* 1992; 106: 137-42.
25. Telian SA, Handler SD, Fleisher GR, Baranak CC, Wetmore RF, Potsic WP. The effect of antibiotic therapy on recovery after tonsillectomy in children. A controlled study. *Arch Otolaryngol Head Neck Surg* 1986; 112: 610-15.
26. Thorneman G, Akervall J. Pain treatment after tonsillectomy: advantages of analgesics regularly given compared with analgesics on demand. *Acta Otolaryngol* 2000; 120: 986-9.
27. Sutters KA, Miaskowski C, Holdridge-Zeuner D, et al. A randomized clinical trial of the effectiveness of a scheduled oral analgesic dosing regimen for the management of postoperative pain in children following tonsillectomy. *Pain* 2004; 110: 49-55.
28. Warnock FF, Lander J. Pain progression, intensity and outcomes following tonsillectomy. *Pain* 1998; 75: 37-45.
29. Kotiniemi LH, Ryhanen PT, Valanne J, Jokela R, Mustonen A, Poukkula E. Postoperative symptoms at home following day-case surgery in children: a multicenter survey of 551 children. *Anaesthesia* 1997; 52: 963-9.
30. Murthy P, Laing MR. Dissection tonsillectomy: pattern of postoperative pain, medication and resumption of normal activity. *J Laryngol Otol* 1998; 112: 41-4.
31. Rungby JA, Romeling F, Borum P. Tonsillectomy: assessment of quality by consultation rate after discharge. *J Laryngol Otol* 1999; 113: 135-9.
32. Salonen A, Kokki H, Nuutinen J. Recovery after tonsillectomy in adults: a three week follow up study. *Laryngoscope* 2002; 112: 94-8.
33. Lavy JA. Post-tonsillectomy pain: the difference between younger and older patients. *Int J Pediatr Otorhinolaryngol* 1997; 42: 11-15.
34. Sunshine A, Olson NZ, O'Neill E, Ramos I, Doyle R. Analgesic efficacy of a hydrocodone with ibuprofen combination compared with ibuprofen alone for the treatment of acute post-operative pain. *J Clin Pharmacol* 1997; 37: 908-15.
35. Rang HP, Dale MM, Ritter JM. Drug elimination and pharmacokinetics. In: Rang HP, Dale MM, Ritter JM, and eds. *Pharmacology*. Edinburgh: Churchill Livingstone, 1999; 78-92.