

# Quality of life after tonsillectomy versus azithromycin

DIAA EL DIN MOHAMED EL HENNAWI, MOHAMED RIFAAT AHMED\*

Otolaryngology Unit, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

\*Corresponding author: Mohamed Rifaat Ahmed, MD, Assistant Professor of Otolaryngology; Faculty of Medicine, Suez Canal University, Ismailia 41511, Egypt; Phone: +20 1285043825; Fax: +20 663415603; E-mail: m\_rifaat@hotmail.com

(Received: July 28, 2016; Revised manuscript received: August 29, 2016; Accepted: October 3, 2016)

**Abstract:** *Background:* Recurrent tonsillitis is a common disease with marked evidence of affecting children quality of life (QOL) such as their progression in school and increased burden to extended families. The aim of this study was to compare the QOL outcomes after conventional dissection tonsillectomy versus azithromycin treatment in controlling recurrent tonsillitis. *Methods:* A double-blind, randomized clinical trial was carried out in 184 children with recurrent tonsillitis randomly divided into two groups: Group A was subjected to conventional dissection tonsillectomy, whereas Group B received single 250 mg (children  $\leq 25$  kg) and 500 mg (children  $\geq 25$  kg) of oral azithromycin once weekly. *Results:* There were no significant differences between the groups with regard to ear, nose, and throat infections during the 5-year follow-up. Better QOL was observed in both groups when compared with the pretreatment, but similar QOL in both groups QOL after treatment. *Conclusion:* Azithromycin is an effective method as a prophylaxis against recurrent tonsillitis with a great benefit for better QOL outcomes.

**Keywords:** quality of life, tonsillectomy, azithromycin, children, recurrent tonsillitis

## Introduction

Tonsil plays an important role in immune defense mechanism especially in the production of IgA and regulation of secretory immunoglobulin production against many exogenous microorganisms [1].

It also protects from the invading pathogens as a part of Waldeyer's ring, which is responsible for B- and T-cell activities in response to a variety of antigens. Thus, it is involved in humoral and cellular immunities [2].

Recurrent tonsillitis is defined as five or more episodes of true tonsillitis a year, symptoms for at least a year, and episodes that are disabling and prevent normal functioning [3].

Although the lifetime prevalence of common recurrent tonsillitis is 7%–11% and has significant burden on families, most of the previous studies on tonsillitis evaluated only the role of upper respiratory tract infections and not enough attention has been given to improve children's quality of life (QOL) [4].

Because of the incomplete development of the immune organs in childhood, the immune activity of tonsil is considered to be more important in children than in adults [5].

Main indications for tonsillectomy are obstructive sleep apnea because of the enlarged tonsils, suspicion of malignant disease, and recurrent infections [6].

An ideal tonsillectomy operation usually results in little morbidity and mortality, and improves patients QOL [6].

Conventional dissection method is still the most common standard procedure for tonsillectomy with the advantage of being a safe procedure without any tonsillar remnants [7].

In general, tonsillectomy also affects the patient's immune system, especially significant levels of interleukin is diminished postoperatively [8].

Bhattacharyya and Kepnes [9] showed that tonsillectomy resulted in significant improvement in the QOL of patients by decreasing the burden of recurrent tonsillitis.

The levels of IgG, IgA, and IgM in the tonsillectomy patient group significantly decreased compared with those in the age-matched healthy control group [10].

Drugs such as penicillin and azithromycin are widely used for controlling recurrent tonsillitis. Sirimanna et al. [11] reported the usefulness of long-acting penicillin in preventing recurrent tonsillitis. But in long-term use, it was found that treatment with penicillin resulted in

This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium for non-commercial purposes, provided the original author and source are credited.

hypersensitivity reactions, anaphylaxis, irritative responses, gluteal abscesses, severe local pain, and dysfunction [12].

Azithromycin is an azalide, a subclass of macrolide antibiotics. It is rapidly absorbed and widely distributed throughout the body, achieving higher concentrations in tissues with the therapeutic levels present in tonsil tissue during weekly medication with minimal side effects [13].

Gopal et al. [14] mentioned the use of 500 mg once weekly oral azithromycin was effective in the prevention of streptococcal throat infection compared with oral penicillin therapy.

Pediatric QOL is an important endpoint in health outcomes researches, as the life-threatening illness usually affects the progression of the child in school and increases the burden to the extended families, affects satisfaction and safety experienced by both family and patients, and results in child being usually upset, expressing anger, and appearing flustered [15].

The aim of this study was to compare the QOL outcomes after conventional dissection tonsillectomy versus azithromycin treatment controlling recurrent tonsillitis.

## Materials and Methods

### *Design, setting, and participants*

A double-blind, randomized clinical trial was carried out in the Otolaryngology Department, Suez Canal University Hospital, Ismailia, Egypt from March 2005 to May 2012. The study protocol was approved by the local ethics committee and written informed consent was obtained from all the patients.

### *Patient eligibility and enrolment*

A total of 184 pediatric patients were eligible and enrolled in this study. Children attending the ENT outpatient department with recurrent tonsillitis (five or more episodes of true tonsillitis a year and with symptoms for at least a year) [3] of both sexes (age range 5–12 years) were included. The main inclusion criteria for this study were recurrent tonsillitis and tonsillar hypertrophy (grades 1–2 according to Brodsky [16]) with seronegative for anti-streptolysin O (ASLO) titer, while the exclusion criteria included rheumatic heart, patients receiving long-acting penicillin, previous tonsillectomy, diabetes mellitus, grades 3–4 tonsillar hypertrophy according to Brodsky [16], history of obstructive sleep apnea, or seropositive for ASLO titer.

### *Study plan*

Complete medical history, including recurrent tonsillitis symptoms, of all the children was recorded and visual

analog scale (VAS) was used for the assessment of symptom severity.

The assessment of QOL relevant to all children was rated on a 4-point scale consisting of 23 questions in four subscales: physical (8 items), emotional (5 items), social (5 items), and school functioning (5 items) [17].

Age-adjusted questions and rating scales were used for parents reporting for children or self-reporting child, and the scores of all subscales are then transformed to scale from 0 (worse score) to 100 (best score).

All children underwent complete ENT and oral examinations, nasal and paranasal sinus examination, and X-ray nasopharynx. Complete investigations including complete blood count, ASLO titer, erythrocyte sedimentation rate, and C-reactive protein were also carried out.

All children were required to complete a relevant questionnaire assessing their recurrent tonsillitis symptoms using a VAS to assess subjective symptoms (0 = no symptoms and 10 = severe and/or constant symptoms).

### *Randomization*

Blocked randomization scheme using computer-generated random numbers was performed to divide children into two groups: Group A and Group B. Group A ( $n=92$ ) was subjected to conventional dissection tonsillectomy, whereas Group B ( $n=92$ ) received single 250 mg (children  $\leq 25$  kg) and 500 mg (children  $\geq 25$  kg) of oral azithromycin once weekly [14].

### *Surgical technique*

A signed consent was obtained from the parents of all the children.

In the conventional blunt dissection series, Boyle–Davis mouth gag was applied, tonsil was retracted medially, incision was made using Waugh's dissection forceps and tonsillectomy was performed by blunt dissection, and tonsil was removed with control of bleeding if present using ligatures and/or electrocautery [18].

Intraoperative antibiotic treatment was administered (50 mg/kg of ceftriaxone). Antibiotic therapy was continued for 10 days postoperatively (90 mg/kg of amoxicillin and clavulanate).

All patients received a combined analgesics non-steroidal anti-inflammatory drugs (1 mg/kg of diclofenac) with paracetamol (15 mg/kg) given every 8 h for the pain control.

### *Objective and outcome measurement assessment*

The objective was to clinically evaluate the recurrent throat infection and QOL in both the groups.

In this study, 5-year follow-up after the tonsil surgery and azithromycin treatment assessments were performed in the same manner as before and 1 year after surgery, using VAS for recurrent throat infection and pediatric QOL assessment scale questionnaires.

Parent proxy version of the PedsQL 4.0 consisting of 23 questions that cover four domains (physical, emotional, social, and school functioning) was used to assess the pediatric QOL. A domain-specific score is calculated from the corresponding questions, ranging from 0 (worst QOL) to 100 (best QOL), which can be combined for a total functioning score – poor ( $\leq 0.2$ ), fair (0.2–0.49), average (0.5–0.79), and good ( $\geq 0.8$ ).

#### Data collection, allocation concealment, and blinding

Parents of all children underwent a brief interview with the physician to complete a questionnaire and provided demographic and disease-related information.

Outcomes after tonsillectomy and azithromycin treatment were assessed again each year by interviews for five consecutive years.

#### Statistical analysis

Statistical analysis of the data was processed using software package for statistical analysis (SPSS) version 15 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as means  $\pm$  SD, whereas qualitative data were expressed as numbers and percentages. The Student's *t*-test was used to compare the significance of difference for quantitative variables that followed a normal distribution.

## Results

A total of 184 children with recurrent tonsillitis (112 males and 72 females) aged between 5 and 12 years (mean age 7.4 years) were randomly divided into two groups: Group A ( $n = 92$ ) subjected to conventional dissection tonsillectomy, whereas Group B ( $n = 92$ ) received single 250 mg (children  $\leq 25$  kg) and 500 mg (children  $\geq 25$  kg) of oral azithromycin once weekly.

Children in Group A were hospitalized for 1–2 days for conventional dissection technique with the operating time ranging from 20 to 45 min (average 30 min).

Five children in Group A had complication of reactionary hemorrhage after conventional dissection, and tonsillectomy required homeostasis in operative room under general anesthesia.

The reported postoperative minor complaints like halitosis and blood-stained saliva were treated conservatively with mouthwashes containing hydrogen

peroxide. The return to a regular solid diet was achieved in  $9.5 \pm 2.5$  days.

In Group A, 86 children (93.4%) reported no illnesses or recurrent throat inflammation, whereas in Group B, five children (5.4%) reported recurrent pharyngotonsillitis in 5-year follow-up duration without any significant difference between the two groups.

The mean intensity of recurrent tonsillitis symptoms severity according to VAS before treatment among the Groups A and B were summarized in *Table I* without any statistically significant difference between both groups.

Five-year follow-up from starting the treatment (tonsillectomy vs. azithromycin), the mean intensity of pharyngitis or tonsillitis symptoms according to VAS among Groups A and B were compared. There were marked improvement from the pretreatment regimen, but there was no statistically significant difference between the two groups (*Table II*).

QOL scale was calculated and assessment at 5-year follow-up after the treatment was done in both groups. There was a better QOL in both groups compared with the pretreatment (*Tables III and IV*), but similar in both groups QOL after treatment (*Fig. 1*) without statistically significant difference (*Table V*).

There were no significant differences between the groups with regard to ENT infections. But during the final year of the study period, four children in Group A (4.3%) and five children in Group B (5.4%) complained of ENT infections.

**Table I** Mean degree of different recurrent tonsillitis symptoms in both groups before treatment

	Group A ( $n = 92$ )		Group B ( $n = 92$ )		<i>t</i> -test	<i>p</i> value
	Mean	SD	Mean	SD		
Dysphagia	8.1	1.5	8.7	1.1	0.14	0.864
Fever	9.3	1.1	8.9	2.3	0.9	0.719
Arthralgia	7.2	0.9	7.9	1.4	0.66	0.782
Body ache	8.7	1.4	8.1	0.8	0.48	0.965

Insignificant  $p > 0.05$

**Table II** Mean degree of different recurrent tonsillitis symptoms in both groups after treatment

	Group A ( $n = 92$ )		Group B ( $n = 92$ )		<i>t</i> -test	<i>p</i> value
	Mean	SD	Mean	SD		
Dysphagia	5.3	1.8	4.9	1.4	0.9	0.568
Fever	4.3	0.9	4.1	1.2	0.7	0.759
Arthralgia	3.9	1.8	3.6	0.9	1.5	0.657
Body ache	3.7	1.1	3.2	1.7	0.8	0.801

Insignificant  $p > 0.05$

**Table III** Quality of life scale assessment in Group A pre- and post-tonsillectomy

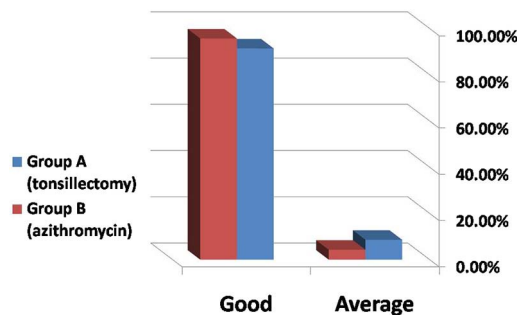
	Preoperative (n = 92)		Postoperative (n = 92)		t-test	p value
	n	%	n	%		
Poor	44	47.7	0	0	$X^2 = 3.27$	0.0001*
Fair	36	39.1	0	0		
Average	9	9.9	8	8.6		
Good	3	3.3	84	91.4		

\*Highly significant at  $p < 0.01$

**Table IV** Quality of life scale assessment in Group B pre- and post-tonsillectomy

	Pre-treatment (n = 92)		Post-treatment (n = 92)		t-test	p value
	n	%	n	%		
Poor	48	47.7	0	0	$X^2 = 3.67$	0.0001*
Fair	32	39.1	0	0		
Average	7	9.9	4	4.3		
Good	5	3.3	88	95.7		

\*Highly significant at  $p < 0.01$



**Fig. 1.** Quality of life scale assessment in both groups after treatment

**Table V** Quality of life scale assessment in both groups after treatment

	Group A (n = 92)		Group B (n = 92)		t-test	p value
	n	%	n	%		
Poor	0	0	0	0	$X^2 = 4.73$	0.548
Fair	0	0	0	0		
Average	8	8.6	4	4.3		
Good	84	91.4	88	95.7		

Insignificant  $p > 0.05$

## Discussion

Recurrent tonsillitis is considered as one of the common primary care visits to physicians, and tonsillectomy represents the most common pediatric operations; however, its effectiveness, safety, and the net benefit of tonsillectomy is unclear. Hence, research for long-term outcomes is needed [19].

Although the absolute indications for tonsillectomy is grade 4 tonsillar hypertrophy (kissing tonsil), which usually leads to obstructive sleep apnea, still more than 75% of tonsillectomies operated due to recurrent tonsillitis in the great proportion neglected the number of pharyngitis episodes and upper respiratory tract infections after tonsillectomy. No consensus has yet been reached concerning the number of annual episodes [20, 21].

Tonsillectomy morbidity had marked impact on the QOL of patients such as socioeconomic factors and increased burden to parents from the suffering of the child [22].

Some studies did not find any significant difference between patients with mild symptoms of recurrent tonsillitis and patients who have undergone tonsillectomy [23].

On one hand, tonsillectomy should not be considered as the only solution as there is a possibility of immunological deficit that must be carefully considered when selecting the actual need for operative intervention as the function of tonsils in the immune system is not completely clear as an important constituent of the upper respiratory tract defense system [24].

On the other hand, some studies have shown that patients who undergone tonsillectomy are at high risk of developing bronchial asthma, ulcerative colitis, goiter, and arterial hypertension at a later stage because of the loss of the immunologic barrier proving its immunological basis [25].

Azithromycin is an azalide antibiotic, which penetrates to the cell membranes and concentrates within the lysosomal compartment. Consequently, it is widely distributed throughout the whole body, achieving higher concentrations in tissues, and thus, serum delivery to infected tissue is further enhanced by inflammatory processes [26].

There were no significant differences between the groups with regard to ENT infections in 5-year follow-up duration.

Casey and Pichichero [27] showed that azithromycin treatment for Group A streptococcal tonsillopharyngitis in children and adults is more effective than other treatment regimens in eradicating and providing clinical cure of tonsillopharyngitis.

O'Doherty [28] also showed that azithromycin treatment is safe, well tolerated, and effective, given the longer duration of action, better side effect profile and lack of P450 interaction, greater stability in the presence of acid,

better absorption, and without gastroparesis action as more than or penicillin.

Snider et al. [29] demonstrated the azithromycin efficacy as a prophylaxis in decreasing streptococcal infections and rheumatic activity.

QOL is defined as physical, social, and emotional aspects of a patient's well-being that are relevant and important to the individual. This is based primarily on the multidimensional concept of health used as assessments of the outcome of medical care, the impact of disease, and treatments [30].

Many studies have mentioned marked improvement in QOL after tonsillectomy from reducing infections with increase in the body weight of children [31].

Better QOL was observed in both groups when compared with the pretreatment, but similar outcomes in both groups after 5-year follow-up without statistically significant difference.

Our data showed the benefit from the use of azithromycin (500 mg oral once weekly) in preventing recurrent tonsillopharyngitis similarly to tonsillectomy outcomes.

Finally, it should be noted that QOL is also affected by family situation and other physical activity outcomes. In conclusion, tonsillectomy is not the only solution to prevent recurrent throat infection as patients could be properly treated well with better QOL outcomes if prophylactic azithromycin was used.

## Conclusion

Azithromycin is an effective method as a prophylaxis against recurrent tonsillitis with a great benefit for better QOL.

\* \* \*

**Funding sources:** None.

**Authors' contribution:** Both authors made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, participated in drafting the article and gave final approval of the version to be submitted and any revised version to be published.

**Conflict of interest:** None.

## References

- Sharma K, Kumar D: Ligation versus bipolar diathermy for hemostasis in tonsillectomy: A comparative study. *Indian J Otolaryngol Head Neck Surg* 63, 15–19 (2011)
- Zielnik-Jurkiewicz B, Jurkiewicz D: Implication of immunological abnormalities after adenotonsillotomy. *Int J Pediatr Otorhinolaryngol* 64, 127–132 (2002)
- Georgalas CC, Tolley NS, Narula PA: Tonsillitis. *BMJ Clin Evid* 2014, 0503 (2014)
- Kvestad E, Kvaerner K, Roysamb E, Tambs K, Harris J, Magnus P: Heritability of recurrent tonsillitis. *Arch Otolaryngol Head Neck Surg* 131, 383–387 (2005)
- Hallissey CM, Heyderman RS, Williams NA: Human tonsil-derived dendritic cells are poor inducers of T cell immunity to mucosally encountered pathogens. *J Infect Dis* 209, 1847–1856 (2014)
- Oomen KP, Modi VK, Stewart MG: Evidence-based practice: Pediatric tonsillectomy. *Otolaryngol Clin North Am* 45, 1071–1081 (2012)
- Sharma K, Kumar D: Ligation versus bipolar diathermy for hemostasis in tonsillectomy: A comparative study. *Indian J Otolaryngol Head Neck Surg* 63, 15–19 (2011)
- Unal M, Ozturk C, Gorur K: Effect of tonsillectomy on serum concentrations of interleukins and TNF-alpha in patients with chronic tonsillitis. *ORL J Otorhinolaryngol Relat Spec* 64, 254–256 (2002)
- Bhattacharya N, Kepnes LJ: Economic benefit of tonsillectomy in adults with chronic tonsillitis. *Ann Otol Rhinol Laryngol* 111, 983–988 (2002)
- Kaygusuz I, Alpay HC, Godekmerdan A, Karlidag T, Keles E, Yalcin S, Demir N: Evaluation of long-term impacts of tonsillectomy on immune functions of children: A follow-up study. *Int J Pediatr Otorhinolaryngol* 73, 445–449 (2009)
- Sirimanna KS, Madden GJ, Miles SM: The use of long-acting penicillin in the prophylaxis of recurrent tonsillitis. *J Otolaryngol* 19, 343–344 (1990)
- Petri WA Jr (2008): Penicillin, cephalosporin and other beta lactam inhibitor antibiotics. In: Goodman and Gilman's Pharmacological Basis of Therapeutics, eds Brunton LL, Chabner BA, Knollman BC, McGraw-Hill, New York, pp. 730–752.
- Lister PJ, Balechandran T, Ridgway GL, Robinson AJ: Comparison of azithromycin and doxycycline in the treatment of non-gonococcal urethritis in men. *J Antimicrob Chemother* 31, 185–192 (1993)
- Gopal R, Harikrishnan S, Sivasankaran S, Ajithkumar VK, Titus T, Tharakan JM: Once weekly azithromycin in secondary prevention of rheumatic fever. *Indian Heart J* 64, 12–15 (2012)
- Schor EL; American Academy of Pediatrics Task Force on the Family: Family pediatrics: Report of the Task Force on the Family. *Pediatrics* 111, 1541–1571 (2003)
- Brodsky L: Modern assessment of tonsils and adenoids. *Pediatr Clin North Am* 36, 1551–1569 (1989)
- Lindman JP, Lewis LS, Accortt N, Wiatrak BJ: Use of the Pediatric Quality of Life Inventory to assess the health-related quality of life in children with recurrent respiratory papillomatosis. *Ann Otol Rhinol Laryngol* 114, 499–503 (2005)
- Sargi Z, Younis RT: Tonsillectomy and adenoidectomy techniques: Past, present and future. *ORL J Otorhinolaryngol Relat Spec* 69, 331–335 (2007)
- Little P: Recurrent pharyngo-tonsillitis. *BMJ* 334, 909 (2007)
- Van Staaij BK, van den Akker EH, Rovers MM, Hordijk GJ, Hoes AW, Schilder AG: Effectiveness of adenotonsillectomy in children with mild symptoms of throat infections or adenotonsillar hypertrophy: Open, randomised controlled trial. *Clin Otolaryngol* 30, 60–63 (2005)
- Bond J, Wilson J, Eccles M, Vanoli A, Steen N, Clarke R, Zarod A, Lock C, Brittain K, Speed C, Rousseau N: Protocol for north England and Scotland study of tonsillectomy and adenotonsillectomy in children (NESSTAC). A pragmatic randomised controlled trial comparing surgical intervention with conventional medical treatment in children with recurrent sore throats. *BMC Ear Nose Throat Disord* 6, 13–22 (2006)
- Sorin A, Bent JP, April MM, Ward RF: Complications of microdebrider-assisted powered intracapsular tonsillectomy and adenoidectomy. *Laryngoscope* 114, 297–300 (2004)
- Paradise JL, Bluestone CD, Colborn DK, Bernard BS, Rockette EH, Kurs-Lasky M: Tonsillectomy and adenotonsillectomy for recurrent throat infection in moderately affected children. *Pediatrics* 110, 7–15 (2002)



24. Brandtzaeg P: Immunology of tonsils and adenoids: Everything the ENT surgeon needs to know. *Int J Pediatr Otorhinolaryngol* 67, S69–S76 (2003)
25. Johansson E, Hultcrantz E: Tonsillectomy – Clinical consequences twenty years after surgery? *Int J Pediatr Otorhinolaryngol* 67, 981–988 (2003)
26. Lakoš AK, Pangerčić A, Gašparić M, Kukuruzović MM, Kovačić D, Baršić B: Safety and effectiveness of azithromycin in the treatment of respiratory infections in children. *Curr Med Res Opin* 28, 155–162 (2012)
27. Casey JR, Pichichero ME: Higher dosages of azithromycin are more effective in treatment of group A streptococcal tonsillopharyngitis. *Clin Infect Dis* 40, 1748–1755 (2005)
28. O'Doherty B: Azithromycin versus penicillin V in the treatment of paediatric patients with acute streptococcal pharyngitis/tonsillitis. Paediatric Azithromycin Study Group. *Eur J Clin Microbiol Infect Dis* 15, 718–724 (1996)
29. Snider LA, Lougee L, Slattery M, Grant P, Swedo SE: Antibiotic prophylaxis with azithromycin or penicillin for childhood-onset neuropsychiatric disorders. *Biol Psychiatry* 57, 788–792 (2005)
30. Climent JM, Reig A, Sanchez J, Roda C: Construction and validation of a specific quality of life instrument for adolescents with spine deformities. *Spine* 20, 2006–2011 (1995)
31. Koskenkorva T, Koivunen P, Penna T, Teppo H, Alho OP: Factors affecting quality of life impact of adult tonsillectomy. *J Laryngol Otol* 123, 1010–1014 (2009)