

POST-ADENOTONSILLECTOMY MONOCYTE MODULATION IN CHILDREN WITH OBSTRUCTIVE CHRONIC ADENOTONSILLITIS

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ABSTRACT

Obstructive chronic adenotonsillitis (OCAT) is an inflammation of adenoid and tonsil that may result in obstruction and followed by hypoxia. As a stressor, hypoxia may modulate immunity. Adenotonsillectomy (ATE) is an indication for surgery for children with OCAT. ATE is a surgical procedure that most commonly undertaken to children. However, the necessity of such operation remains controversial, since adenoid and tonsil are parts of the immune system. The objective of this study was to identify the role of monocyte as a component of post-operative natural immunity. This study used prospective pre-post design. A number of 15 children with obstructive chronic adenotonsillitis (OCAT) underwent operation. Two weeks after operation, a significant reduction of monocyte ($p < 0.05$) was found. The post-ATE reduction of monocyte count resulted from successful surgical eradication of hypoxia and the source of infection from adenoid and tonsil.

Keywords: obstructive chronic adenotonsillitis, hypoxia, stressor, adenotonsillectomy

INTRODUCTION

Until recently, a proportion of 60% of patients with chronic adenotonsillitis still experience recurrent infection. Additionally, these patients also showed obstructive upper respiratory symptoms (Paradise et al, 2003) that often occur during bedtime (Onal et al, 1986; Spabis, 1994; Lamberg, 2001). Chronic adenotonsillitis accompanied with obstruction at night is termed as obstructive sleep apnea syndrome (OSAS) (Suen et al, 1995; Adams, 1997; Cowan and Hibbert, 1997; Ischizuka et al, 1997). Obstructive chronic inflamed adenoid and tonsil is called as obstructive chronic adenotonsillitis (OCAT) (Jensen et al, 1991; Salah et al, 2001). Obstruction accompanied with a chronic inflammation presents as a vicious circle. Infection-resulted inflammatory process may produce tonsillar enlargement, while the enlargement of tonsil and adenoid may result in the obstruction of upper respiratory tract. Increased morbidity rate among the patients may further disturb growth and development, particularly during childhood (Paradise et al, 2002; 2003). The obstruction of respiratory tract, particularly the one that occurs during bedtime, may result in hypoxia, a condition that may reduce the immunological defense of the body (Lamberg et al, 2001; Paradise et al, 2003). Adenoid enlargement can be measured by means of lateral cephalic x-ray photo using soft-tissue technique. A comparison of adenoid size and that of nasopharyngeal cave is available today (Ranidewi, 1995; Kemalloglu et al, 1999). If the ratio of adenoid and nasopharynx (A - N) is between 0 and 0.52, this

indicate the absence of hypertrophy, while 0.52 - 0.72 indicated the presence moderate non-obstructive hypertrophy, and 0.72 indicated obstructive hypertrophy (Ranidewi, 1995). According to MacKency (Priyanto, 1997), the size of tonsil is determined by T1, T2, and T3. Adenotonsillectomy (ATE) is a procedure to overcome OCAT-resulted obstruction, although this procedure remains controversial, which is due to the fact that adenoid and tonsil are parts of the immune system, while, on the other hand, their enlargement leads to hypoxic condition (Paradise et al, 2002; 2003). In addition, tonsil and adenoid are organs where B and T cells reside (Yamanaka et al, 1988; Boyoka et al, 2000). Prusek et al (1991) and Friday et al (1992) reported post-ATE immunity reduction. Paulussen et al (2000) found a post-ATE increase of cellular and humoral response. However, the mechanism of post-ATE immunity modulation still requires further elaboration.

The otolaryngologists in Indonesia have frequently undertaken ATE. During the year 2002 in Dr Moewardi Hospital, Surakarta, a number of 220 ATE and Tonsillectomy (TE) procedures had been carried out among other 501 otolaryngological procedures or operations. More than 65% of patients undergoing ATE or TE aged between 2 and 15 years (Dr Moewardi Hospital, 2002). In Turkey, ATE comprised 75% of otolaryngological operations in children (Erisen et al, 1999). Enlarged adenoid and tonsil may result in obstruction, and physiologically it may also impede respiratory function and swallowing process. Due to these considerations, patients with OCAT should undergo ATE. Otherwise, the pediatric patients' quality of life may reduce (Gatehouse et al, 1996). OCAT may lead to a hypoxic condition, and the latter may modulate immunocompetent cells (Eike and Jorgensen, 1994; Albert, 1997; Battistini et al,

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1998; Paradise et al, 2003). Obstructive symptoms would be eradicated after ATE procedure is carried out (Franz and Mennicken, 1977; Harrington, 1978; Skevas et al, 1978). Since the benefit of the ATE remains less totally clear, an elaborate study is worth to be done.

Hypoxic stressor may serve as a triggering factor for the reduction of immunity (Putra, 1999). One component of natural immunology is the monocyte. In hypoxic condition, monocyte and macrophage may release more abundant IL-1 β (Hempel et al, 1996; Carta et al, 2001). Furthermore, IL-1 β stimulates Th1 to release IFN- γ . As a MAF (macrophage activating

factor), IFN- γ may raise macrophage capacity to process and destroy immunogen. Monocyte and macrophage are components of natural immunity that are able to modulate adaptive immune system, either cellular or humoral. Both are immune cells that often receive external reactions. Therefore, stressor that presents as hypoxia may also induce stress in monocyte. In addition to activate monocyte in producing cytokine, stress may also increase or reduce monocyte count. This study was aimed to identify post-ATE change of monocyte count in patients with OCAT.

PATIENTS AND METHOD

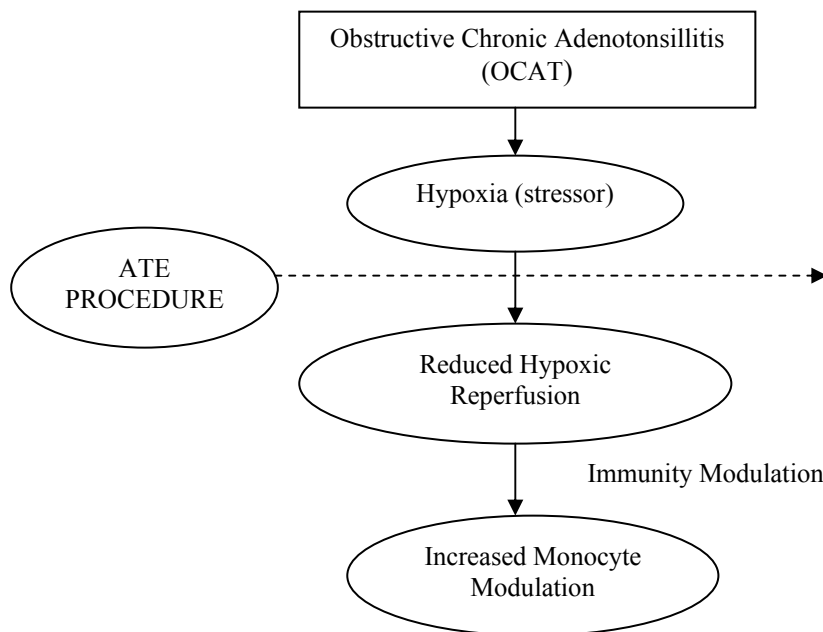


Figure 1. Conceptual framework

This study used prospective pre- and posttest design. No control used in this study since it was ethically not allowable to perform ATE in normal subjects. Samples were populaton that met the treatment criteria (accessible sampling), i.e., pediatric patients with OCAT visited the Outpatient Clinic of the Department of Otolaryngology, Sebelas Maret University, Dr Moewardi Hospital, Surakarta. The inclusion criteria were adenoid enlargement (A - N ratio 0.72); tonsillary enlargement (T2, T3, bruised, enlarged crypt orifice with positive detritus); male; aged 5 - 15 years; normal bodyweight (height - 110) $\pm$ 10% kg; normal health status as proved by laboratory test to erythrocyte, hemoglobin, Hct, leucocyte count, blood clotting and bleeding time, hepatic function (SGOT/SGPT), renal function (creatinine), and total protein; and informed consent by the parents or

family. The exclusion criteria were as follows: presence of other abnormalities that result in nasal blockade, such as polyp, deviated septum, and tumor; other causes of immunity modulation, such as allergic rhinitis, asthma, atopic dermatitis, and diabetes mellitus; and ATE contraindication, for example, blood clotting abnormalities. Sample size was based on the estimation of Hulley et al (1988) using a (one tailed) of 0.05 and b 0.20, with expectation of 0.90. Estimation revealed that the number of minimal sample was 15.

The dependent variable in this study was monocyte count, as measured by means of peripheral blood examination with an instrument Cell dyn 3500. This study was undertaken at the Department of Otolaryngology, Sebelas Maret University, Dr

Moewardi Hospital, Surakarta, from February to September 2002. Data analysis was performed using statistical test with significance level of 0.05. Homogeneity test was done to the data of moderator variable in order to find the homogeneity of samples, thereby it would be possible to conclude that monocyte modulation was an effect of ATE.

RESULTS

Results of this study can be seen in the following table:

Table 1. Monocyte

	Total Cases	Mean	Standard Deviation
Pre	15	519.65204	142.34015
Post	15	203.41219	52.52080
Total	30	437.26684	35.01299

Note:

Results of Anova test revealed significant difference pre- and post-operation (Wilk's Lambda, estimated F value 6.607, $p = 0.016$).

DISCUSSION

OCAT is a condition of chronic infectious process that is accompanied with obstructive and inflammatory symptoms. Obstruction due to OCAT may result in hypoxia. Hypoxic condition may stimulate monocytes to act more actively, and the activity of bone marrow will increase as well to produce more monocytes. Post-operatively, the hypoxic symptoms may disappear, while monocyte and macrophage counts may also reduce. In addition, the inflammatory process, either due to infection or traumatic process from ATE itself, may stimulate the bone marrow to produce more monocytes. Relieve from hypoxia to non-hypoxic condition may lead to a better oxygenation. This condition may in turn relieve inflammation, that also reduces monocyte and macrophage count. The reduction of monocyte count was proved to demonstrate significant difference ($p < 0.05$).

CONCLUSION AND RECOMMENDATION

OCAT in children who undergo adenotonsillectomy results in significant reduction of monocyte count in 2 weeks post-operatively. ATE procedure to these children is allowed since it improves natural immunity. Serial post-operative study for more than 2 weeks should be carried out to find the course of natural immunity modulation. Other studies involving immunity components that disclose the immunity modulation of Th1 and Th2 should also be carried out

in order to have a more comprehensive understanding on the mechanism of adaptive immunity modulation.

ACKNOWLEDGMENT

The author thanks to Prof. Dr. H. Soedijono Tirtowidjaja, dr, Sp. THT (K), Prof. Dr. J.B. Suparyatmo, dr, Sp. PK, Prof. Dr. Suhartono Taat Putra, dr, MS, dan Dr. Sunarko Setyawan, dr, MS for their suggestion and correction to the materials for this article, and to Yuliati, drg, MKes who had assisted the process in making this article.

REFERENCES

- Adams GL, 1997. Boeis : Buku Ajar Penyakit THT (Boeis Fundamental of Otolaryngology). Translated by Caroline Wijaya. Editor: Harjanto Efendi. Ed-6, Jakarta: EGC, hal: 320-55.
- Albert D, 1997. Nasal Obstruction and Rhinorrhoea in Infants and Children. Paediatric Otolaryngology in Scott-Brown's Otolaryngology : Kerr, AG (Edit) 6 th edition. Butterworth Heinemann. Oxford, Boston, Johannesburg, Melbourne, New Delhi, Singapore, pp. 171-86.
- Baratawidjaja KG, 1996. Immunologi Dasar. Edisi 3. Fakultas Kedokteran Universitas Indonesia Jakarta, hal : 3, 20-3, 65-7, 249.
- Battistini A, Siepe F, Marvasi R, 1998. The tonsils and adenoids as a site of infection and the cause of obstruction. *Pediatr Med Chir Jul-Aug* 20(4). pp 237-47.

- Boyoka PN, Wright PF, Marinaro M, Kiyono H, Johnson JE, Gonzales RA, Kizler MR et al, 2000. Human nasopharyngeal-associated lymphoreticular tissue. Functional analysis of subepithelial and intraepithelial B and T cells from adenoids and tonsils. *Am J Pathol.* 157(6), pp 2023-35.
- Carta L, Pastorino S, Melillo , Bosco MC, Massazza S, Varesio L, 2001. Engineering of Macrophages to Produce IFN in Response to Hypoxia. *The Journal of Immunology* (166): 5374-80 (abstract).
- Cowan DL, Hibbert J, 1997. Tonsil and adenoid. *Paediatric Otolaryngology*. Adams DA, Cinnamon MJ, (Edit). *Scott-Brown's Otolaryngology*, 6 th edition. Butterworth Heinemann. pp 6/18/1-6/18/15.
- Eike AM, Jorgensen BG, 1994. Hypertrophic tonsil as a cause of hypoxia and growth stagnation. *Ugeske-Laeger* 156 (22), pp 3328-9.
- Ellstrom M, Bengtsson A, Tylman M, Haeger M, Olsson JH, Hahlin M, 1996. Evaluation of tissue trauma after laparoscopic and abdominal hysterectomy measurements of neutrophil activation and release of interleukin-6, cortisol, and C-creative protein. *Journal of American College of Surgeons*. Vol:182, pp 423-30.
- Erisen L, Basut O, Coskun H, Tezel I, HizalanI, Onart S, 1999. Evaluation of the Adenotonsillectomy Cases and the Indications. IV International Symposium on Tonsils and Adenoids. Ghent, Belgium, 2-5 November 1999. Final Programme and Abstracts, p 26.
- Franz C, Mennicken U. 1977. Chronic tonsillar hypertrophy as a cause of cor pulmonale, pulmonale oedema and hypersomnia in children. *Dtsch Med Wochenschr* 102 (31), pp 1120-3.
- Friday GA, Paradise JL, Rabin BS, Colborn DK, Taylor FH, 1992. Serum immunoglobulin changes in relation to tonsil and adenoid surgery. *Ann allergy* 69(3), pp 225-30.
- Gatehouse S, Robinson K, Browning G, 1996. Measuring patient benefit from otorhinolaryngological surgery and therapy. *Anna Otol Rhinol Laryngol* 105, pp 415 - 22.
- Harrington R, 1978. Tonsillar hypertrophy and chronic hypoxia. *Med J Aust* 2 (5), pp 175-7.
- Hempel SI, Monick MM, Hunninghake GW, 1996. Effect of hypoxia on release of IL-1 and TNF by human alveolar macrophages. *American Journal of Respiratory Cell & Molecular Biology*. 14, pp 170-6.
- Hulley SB, Feigal D, Martin M, Cumming SR, 1988. Designing New Study : IV. Experiments in Designing Clinical Research An Epidemiologic Approach by Hulley SB, Cumming SR. Williams & Wilkins, pp 110-127.
- Ishizuka Y, Terashima K, Imamura Y, 1997. Effect of tonsillectomy in children with obstructive sleep apnea syndrome. XVI World Congress of Otorhinolaryngology Head and Neck surgery. Sydney Australia. 2-7 March.
- Jensen PF, Kristensen S, Juul A, Johannessen NW, 1991. Episodic Nocturnal Hypoxia and Nasal Packs. *Clin. Otolaryngol*, 16(5): 433-5 (abstract).
- Kemaloglu YK, Goksu N, Inai E, Akyildiz N, 1999. Radiographic evaluation of children with nasopharyngeal obstruction due to the adenoid. *Annals of Otolaryngology, Rhinology and Laryngology*. Vol:108. Iss:1, pp 67-72.
- Lamberg L, 2001. Role of Sleep Disorders In ADHD Explored. *Psychiatric News*. Vol: 36, pp 21-2.
- Onal E, Burrows L, Hart RH, Lopata M, 1986. Induction of periodic breathing during sleep causes upper airway obstruction in humans. *J Appl Physiol* 61: 1438-43 (abstract).
- Paradise JL, Bernard, Colborn DK, Janosky JE, 1998. Assessment of adenoidal obstruction in children: clinical sign versus roentgenographic findings. *Pediatrics*. 101, pp 979-86.
- Paradise J, Bluestone CD, Colborn KD, Bernard BS, Rockette HE, Lasky MK, 2002. Tonsillectomy and adenotonsillectomy for recurrent throat infection in moderately affected children. *Pediatrics*. 110 (1) pp 7-15 (abstract).
- Paradise J, Bluestone CD, Colborn KD, Bernard BS, Rockette HE, Lasky MK, 2003. Tonsillectomy and adenotonsillectomy showed modest benefits in children moderately affected with recurrent throat infection. *Evidence-Based Medicine* 8:25.
- Paulussen C, Claes J, Claes G, Jerissen M, 2000. Adenoids and tonsils, indications for surgery and immunological consequences of surgery. *Acta Otorhinolaryngol Belg*. 54 (3), pp 403-8.
- Prijanto S, 1997. Perubahan isi kripta yang mencerminkan pola imunopatobiologik tonsillitis kronik non spesifik sebagai dasar indikasi tonsilektomi. Disertasi. Program Pascasarjana Universitas Airlangga Surabaya.
- Prusek W, Mohgoub MK, Podwysocka M, Wiczorek E, 1991. Circulating immune complexes in Waldeyer's ring hypertrophy. *Arch Immunol Ther Exp (Warsz)* 39(1-2), pp 61-6.
- Putra ST, 1999. Perkembangan Paradigma dan Konsep Psikoneuroimunologi. Workshop Psikoneuroimunologi 25 - 26 September 1999. Gramik, Fakultas Kedokteran Universitas Airlangga.
- Ranidewi AAAM, 1995. Rasio Adenoid-Nasofaring sebagai sarana penunjang diagnosis adenoiditis kronis obstruktif. Karya akhir untuk ijazah keahlian. Lab/UPF THT Fak. Kedokteran Unair/RSUD Dr. Sutomo Surabaya.
- RSUD dr Moewardi-Surakarta, 2002. Data Primer Penderita yang dilakukan tindakan ATE di RSUD dr Moewardi-Surakarta selama tahun 2002.

- Salah EB, Taylor A, Ford R, Siddiqi S, Badr S, 2001. Long-term facilitation in obstructive sleep apnea patients during NREM sleep. *J Appl Physiol* 91: 2751-7.
- Schilder AGM, Akker EH, Hordijk GJ, Hoes AW, 1999. Tonsillectomy and adenoidectomy in children: surgical rates over the world. IV International Symposium on Tonsils and Adenoids. Ghent, Belgium, 2-5 November 1999. Final Programme and Abstracts, p 74.
- Skevas A, Karamberis S, Barlamis G, Sklavounou-Tsoyrouktsoglou S, 1978. Cor pulmonale due to upper airway obstruction by hypertrophied tonsil and adenoids. *Laryngol Rhinol Otol* 57 (9), pp 804-7.
- Sonnex, 1998. Influence of ovarian hormones on urogenital infection. *Sexually Transmitted Infection* 74, pp 11-9.
- Spabis J, 1994. Sleepless nights: Obstructive sleep apnea in the pediatric patient. *Pediatr Nurs* 20(5): 469-72 (abstract).
- Stallone DD, 1994. The influence of obesity and its treatment on the immune system. *Nutr. Rev.* 52: 37-50 (abstract).
- Stenfors LE, 1999. Acute streptococcal tonsillitis : interaction between epithelium and bacteria. IV International Symposium on Tonsils and Adenoids. Ghent, Belgium, 2-5 November 1999. Final Programme and Abstracts, p 81.
- Suen JS, Arnold JE, Brooks LJ, 1995. Adenotonsillectomy for treatment of obstructive sleep apnea in children. *Arch Otolaryngol Head and Neck Surg.* 121. May, pp 525-30.