e-ISSN 2248 – 9142 print-ISSN 2248 – 9134



# PRELIMINARY RESULTS OF A POTENTIAL NEW USE OF CLARITHROMYCIN IN THE MANAGEMENT OF CHRONIC RHINOSINUSITIS

#### Dr. Anupam Bahe

Assistant Professor, Department of Paediatrics, Sri lakshminarayana Institute of medical sciences, Puducherry, India.

## ABSTRACT

After endoscopic sinus surgery, patients with chronic rhinosinusitis with polyps (CRSwP) should get long-term treatment with low-dose clarithromycin to test its effectiveness and safety (ESS). We found 10 people who had CRSwP and had them undergo bilateral electroshock therapy (ESS). After surgery, patients were given nasal saline solution and steroid sprays to cleanse out their nasal passages (beclomethasone). During follow-up, when nasal obstruction, odour loss, headache, and the onset of viscous secretions appeared in some patients, their symptoms worsened. As a result, all patients continued treatment with saline nasal irrigation, topical steroid therapy, and macrolide (clarithromycin 500 mg/pill: 1 pill per day for 3 days per week). It was determined that the effectiveness of therapy was determined by conducting a SNOT-22 questionnaire and an endoscopic appearance score (EAS). Sneezing, As well as, hyposmia, thick mucus secretions on the SNOT-22, and reduced secretions and enlargement of the nasal mucosa on the EAS all exhibited statistically significant improvements (p<0.05) in both tests, according to the researchers' findings. This study's early findings suggest an antibacterial and immunomodulatory effect of low-dose clarithromycin for a duration of one month on CRSwP patient complaints.

Key words: Chronic Rhinosinusitis with Polyps Clarithromycin Eosinophil.

#### **INTRODUCTION**

Chronic rhinosinusitis (CRS) is related 7-13 percent of individuals have bronchial asthma (BA), and 36-96 percent have aspirin-exacerbated respiratory disease (AERD) and NP [1]. The eosinophil, which may be detected in both tissue and mucus in the airways, is the most common inflammatory cell type in CRSwNP [2]. Although there is a link between CRSwNP and neutrophilic inflammation, it does not seem to be a fundamental cause of the disease [3]. CRSwNP does not seem to be caused primarily by allergy, but rather as a comorbid disease [4]. Both medicinal and surgical interventions are currently ineffective at providing lasting cures [5]. Topical glucocorticoid nasal sprays, either alone or in combination with other methods are currently the only proven therapy for CRSwNP (GCS) [6]. However, recurrences of CRSwNP are not always averted even when systemic GCS is used. We chose to investigate "long-term" therapy utilising low dosage macrolide antibiotics since disease management may be problematic even with systemic GCS [7].

Rather than its antibacterial capabilities, the sensible application of this medication is its ability to reduce inflammation by inhibiting neutrophils and eosinophils [8]. The macrolides have the ability to alter the immune system.

Response, limiting the formation of polyps, eliminating biofilms, and improving the protective qualities of the respiratory tract mucosa [9,10]. It has been shown that macrolides are helpful in patients with CRS without NP, but they haven't yet been thoroughly tested in CRSwNP patients [11,12]. Patients with CRSwNP who had endoscopic sinus surgery.

Corresponding Author: Dr. Bahe Anupam Bapan

To see whether clarithromycin at a low dosage for a longtime medication would be effective and safe [13,14].

## MATERIALS AND METHODS

A total of 10 patients with CRSwNP was included. The presence of asthma or sensitivity to aspirin or atopy and/or peripheral blood eosinophilia; nasal blockage; a reduction in or loss of smell; headaches; bilateral nasal polyps; viscous nasal secretions; and eosinophilia highlighted by "histological study". The following were among the exclusions: pregnancy, lactation, pregnancy with unilateral CRSwNP, resistance to macrolides, systemic steroid usage, and life-threatening physical ailments. The ages of a few patients were known. They have age of below 15. Each patient was given a copy of the informed consent form. Four Twelve of the patients were female, with the other twelve being male. Patients of all ages and genders were able to participate CT computerised tomography scan with fiberoptic and craniofacial parts (CT). The same surgeon performed bilateral ESS on all 10 patients.

The patient was released the next day after the nasal pack was removed. It was suggested that patients undergo seven days of antibiotic treatment with. A mixture of amoxicillin and clavulanate, nasal irrigation with salt, and gomenolato oil spray application.

Every week for the next week, patients were rigorously observed and tested for medication. Immediately after exposure, patients were given a topical steroid (beclomethasone) and saline nasal irrigation (M = 18.1; SD =+ 3.06). Clearance of scabs and scars was seen in the patients at that time. Drastically reduced/lost scent; headache; and high viscosity secretions were all reported by patients who continued to use saline nasal irrigation and topical steroids for three days a week for a month after surgery (M = 35.04, SD = 4.33).

Clarithromycin treatment results were evaluated using a 22-item SinoNasal Outcome Test (SNOT-22) and an endoscope appearance score (EAS) before and after treatment.

Rhinosinusitis patients' quality of life may be assessed using the 20-item SinoNasal Outcome Test (SNOT-20).

In order to do an endoscopy, using cotton soaked in adrenaline and mepivacaine to clear the nasal passages, the endoscope was introduced into the patient's oesophageal cavity. For both nasal cavities, EAS was given to the following findings: There were three levels of severity for the polyps: zero, one, and two. The first level was the smallest, with no polyps; the second was the largest, with polyps totally blocking the nose; the third level was the second largest, with polyps fully obstructing the nose. As a result, discharge was graded as follows: 3 is a thick and mucosal secretion; 0 means no discharge. Thirdly, the mucosal edoema was measured as follows: There are three levels of severity: zero, one, and two for postoperative scarring, the following scale was used: 0, 1, and 2 represent severity.

## **Statistical Analysis**

The data was analysed using SPSS version 17.0 for Windows which was then input into a computerised database. Before and after clarithromycin usage, T student signed rank tests were conducted to see whether there was any significant change. Means and standard deviations were used to show the data. When p values were less than 0.05, Statistical significance was found in the findings.

# RESULTS

Ninety percent of the patients (9/10) had BA, while forty percent (4/10) had AERD. According to skin prick testing, 70 percent of those tested had atopic dermatitis. Clarithromycin-related side effects were not observed. For several metrics, there were statistically significant improvements in the SNOT-22 and EAS scores before and after clarithromycin medication (p<0.05). Sneezing, sneezing, hyposmia, and copious mucous discharge were all improved by the use of SNOT-22, which demonstrated a 2.52 (0.87 vs. 0.67 vs. 1.3) 0.67 improvement in blowing the nose. Two EAS indicators, secretions (1.6 (0.69) vs. 0.3 (0.48)) and oedema (1.3 (0.48) vs. 0.2 (0.42)), improved significantly following clarithromycin medication.

In the six months after treatment with clarithromycin, there were no significant changes in SNOT-22 or EAS scores compared to those at the conclusion of treatment.

# DISCUSSION

For individuals with persistent CRS connected to BA and/or AERD and/or atopy, extended treatment with low dose clarithromycin seems to be helpful when combined with ESS and nasal irrigation.

A major role seems to be played by the paranasal sinus mucosal dysfunction [15], even if its processes are not well understood. Inflammatory cells such as neutrophils are seen in the squamous epithelium, as well as an increase in submucosal glands. According to Fujita et al, the nasal concentration of IL-8 was higher in patients with CRSwP than healthy persons [16]. It is believed that the mucosal epithelium produces pro-inflammatory cytokines such as IL-8 in chronic rhinosinusitis when bacteria are present in the sinus pus and thick [17], viscous mucus [18]. By producing a neutrophilic and eosinophilic infiltration, these cytokines damage the ciliated epithelium while also increasing the number of submucosal glands [19]. One cannot break the vicious circle of chronic inflammation. According to et al., 3 months of Fujita macrolide therapy significantly reduces nasal discharge neutrophil, eosinophil, and IL-8 concentrations [20].

Before and after treatment, the saccharine test time in CRSwP was reduced from 11.5 to 8.2 minutes by

Wall work *et al*, demonstrating that mucociliary clearance had been restored. Medical therapy and endoscopic sinus surgery are commonly recommended to cure damaged mucosa and to remove viscous mucus, respectively, from the sinuses notwithstanding the positive effects of macrolides therapy. Using saccharin as a measure of mucociliary function, Inanli *et al*. Examined the effects of surgery on mucociliary function before and after the procedure (at 12:15 minutes and 9:08 minutes, respectively, before and after surgery). However, only a partial restoration of the ciliated epithelium was achieved, and the diseased mucosa remained 3 months following surgery.

After therapy, Wallwork *et al* found that the CRSwP saccharine test time decreased from 11.5 to 8.2 minutes, indicating that mucociliary clearance had been restored. It's typical for doctors to offer medical treatment and endoscopic sinus surgery to treat and remove mucus from the sinus cavities.

To six weeks following surgery, ECP levels in the control group rose by three times the average level, but ECP levels in the macrolide-treated group gradually decreased.

As a result, macrolide may help to minimise postoperative inflammation, promote the earliest possible normalisation of diseased mucosa, and alleviate symptoms after surgery.

The right period of therapy with erythromycin 400–600 mg was shown to be helpful in individuals with symptomatic chronic sinusitis after long-term low-dose treatment. One hundred percent of their research participants reported a reduction of their symptoms, including runny nose (60%) and postnasal drip (50%) as well as nasal blockage (60%).

The average treatment time was 7.9 months; however, the exact length of therapy hasn't been determined. Following

this, while 70.6 percent of patients improved after 12 weeks of therapy with macrolide 400 mg, the researchers concluded that there was still ambiguity regarding the drug's safety, and that treatment should be discontinued after symptoms had subsided. Even while our 6-month follow-up does not enable us to determine how long the favourable benefits of macrolide are sustained, the bulk of following research used a 3-month treatment period, which had similar outcomes to our 1-month methodology.

However, we have developed a clarithromycin strategy that is easier to follow and may be administered again if symptoms reappear. To prevent the adverse effects of systemic corticosteroids (GS), a month of treatment with the macrolide is adequate, as long as symptoms such nasal respiratory obstruction and headache are alleviated.

Both Mycoplasma and Chlamydia are well-served by macrolide antibiotics, as is Helicobacter pylori (the bacteria that has been implicated in chronic gastritis), and both can be eradicated with them. Although it has been proven in the literature that there is no growth in Samples from the middle meatus had bacteria that were resistant to macrolides in culture a continuous treatment with antibiotics may lead to antimicrobial resistance.

## CONCLUSION

Patients with persistent eosinophilic rhinosinusitis may benefit with a month of low-dose clarithromycin not only because of its antibacterial capabilities but also because of the immunomodulatory effects.

Long-term macrolide usage in the prevention of recurrence of nasal polyposis after ESS has to be evaluated in a case–control double-blind study with a large number of patients and a treatment regimen universally verified for broad use in order to determine its efficacy.

#### REFERENCES

- 1. Hedman J, Kaprio J, Poussa T, Nieminen MM, *et al.* Prevalence of asthma, aspirin intolerance, nasal polyposis and chronic obstructive pulmonary disease in a population-based study. *Int J Epidemiol* 28, 1999, 717–722
- 2. Settipane G. Epidemiology of nasal polyps. In: Settipane G, Lund VJ, Bernstein JM, Tos M (eds) Nasal polyps: epidemiology, pathogenesis and treatment. Oceanside Publications, Providence, 1997, 17–24
- 3. Ogino S, Harada T, Okawachi I, Irifune M, Matsunaga T, Nagano T, *et al.* Aspirin-induced asthma and nasal polyps. Acta Otolaryngol Suppl 430, 1986, 21–27
- 4. Fokkens W, Lund V, Mullol J, *et al.* European position paper on rhinosinusitis and nasal polyps group. European position paper on rhinosinusitis and nasal polyps 2007. *Rhinol Suppl* 20, 2007, 1–136
- Martines F, Salvago P, Ferrara S, Messina G, Mucia M, Plescia F, *et al.* Factors influencing the development of otitis media among Sicilian children affected by upper respiratory tract infections. *Braz J Otorhinolaryngol* 82(2), 2016, 215– 222
- 6. Martines F, Salvago P, Ferrara S, Mucia M, Gambino A, Sireci F, *et al.* Parietal subdural empyema as complication of acute odontogenic sinusitis: a case report. *J Med Case Rep* 21(8), 2014, 282
- 7. Desrosiers MY & Kilty SJ. Treatment alternatives for chronic rhinosinusitis persisting after ESS: what to do when antibiotics, steroids and surgery fail. Rhinology 46, 2008, 3–14
- 8. Kudoh S, Uetake T, Hagiwara K, Hirayama M, Hus LH, Kimura H, *et al.* Clinical effect of low-dose, long-term erythromycin chemotherapy on diffuse panbronchiolitis (English Abstract). *Jpn J Thorac Dis* 25, 1984, 632–642

- 9. Kudoh S, Asuma A, Yamamoto M, Izumi T, Ando M, *et al.* Improvement of survival in patients with diffuse panbronchiolitis treated with low-dose erythromycin. *Am J Respir Crit Care Med* 157, 1998, 1829–1832
- 10. Cervin A & Wallwork B. Macrolide therapy of chronic rhinosinusitis. Rhinology 45, 2007, 259–267
- 11. Cervin A, Wallwork B, Mackay-Sim A, Coman WB, Greiff L, *et al.* Effects of long-term clarithromycin treatment on lavagefluid markers of inflammation in chronic rhinosinusitis. *Clin Physiol Funct Imaging* 29, 2009, 136–142
- Canevari FR, Giourgos G, Pistochini A, *et al.* The endoscopic transnasal paraseptal approach to a sphenoid sinus osteoma: case report and literature review. *Ear Nose Throat J.* 92(12), 2013, E7–E10. Review. Erratum in: *Ear Nose Throat J* 93(4– 5), 2014, 148
- 13. Vitali M, Canevari FR, Cattalani A, Grasso V, Somma T, Barbanera A, *et al.* Direct fascia lata reconstruction to reduce donor site morbidity in endoscopic endonasal extended surgery: a pilot study. *Clin Neurol Neurosurg* 144, 2016, 59–63
- 14. Piccirillo J, Merritt M, Richards M, *et al.* Psychometric and clinimetric validity of the 20-item Sino-Nasal Outcome Test (SNOT-20). *Otolaryngol Head Neck Surg* 126, 2001, 41–47
- 15. Lund VJ, Mackay IS. Staging in rhinosinusitus. Rhinology 31, 1993, 183-184
- 16. Inanli S, Tutkun A, Batman C, Okar I, Uneri C, Sehitoglu MA, *et al*. The effect of endoscopic sinus surgery on mucociliary activity and healing of maxillary sinus mucosa. *Rhinology* 38, 2000, 120–123
- 17. Fujita K, Shimizu T, Majima Y, Sakakura Y, *et al.* Effects of macrolides on interleukin- 8 secretion from human nasal epithelial cells. *Eur Arch Otorhinolaryngol* 257, 2000, 199–204
- Wallwork B, Coman W, Mackay-Sim A, Greiff L, Cervin A, et al. A double-blind, randomized, placebo-controlled trial of macrolide in the treatment of chronic rhinosinusitis. Laryngoscope 116, 2006, 189–193
- 19. Fang SY. Normalization of maxillary sinus mucosa after FESS. A prospective study of chronic sinusitis with nasal polyps. Rhinology 32, 1994, 137–140
- 20. Varvyanskaya A, Lopatin A. Efficacy of long-term lowdose macrolide therapy in preventing early recurrence of nasal polyps after endoscopic sinus surgery. *Int Forum Allergy Rhinol* 4(7), 2014, 533–54.