High irrigation nasal steroids versus intranasal steroids in chronic sinusitis with polypi under treatment of dupilumab

Osama Elsayad 1, Said Abdou 2, Ahmed Hussain 3

1. Department of otolaryngology, Benha University, Egypt.  
2. Department of laboratory, Tanta University, Egypt.  
3. Department of otolaryngology Cairo university, Egypt

Correspondence to: Osama Elsayad Department of otolaryngology, Benha University, Egypt  
E Mail: drsayado@yahoo.com

Abstract

Background: Patients with chronic rhinosinusitis with nasal polyps (CRSwNP) have severe health problems require systemic steroids and multiple sinus surgery. Dupilumab is a new biological treatment of type 2 inflammation by its effect on interleukin 4 and interleukin 13 which used in atopic dermatitis and bronchial asthma. Aim of the work is to investigate the effect of High irrigation nasal steroids versus intranasal steroids in chronic sinusitis with polypi under treatment of dupilumab. Patients and Methods: This study included 70 patients under treatment of dupilumab 300 mg in the form of injection every 2 weeks for 24 weeks, the patients divided into GI n=35 who receive high irrigation nasal steroid and GII n=35 who receives nasal steroids for 24 weeks, this study assess the management Plan for chronic sinusitis with nasal polypi as regards nasal congestion, smell score, nasal endoscopy score, CT score (Lund Mackay).  
Results: This study found that both techniques improve nasal congestion score which is significant p<0.0001, difference in Lund-Mackay CT scores was significant in both groups p<0.0001, the nasal endoscopy polyp size score were improved in both groups more at 24 weeks, the difference was significant, smell score were significantly improved in both groups p<0.0001, but more at 24 weeks of treatment, difference between both groups was insignificant but GI was superior to GII overall assessment parameters.  
Conclusion: Patients with chronic sinusitis with polypi under treatment of dupilumab had marked reduction in nasal polyp size, sinus opacification, improvement in smell score and nasal congestion score

Keywords

Biologics, nasal steroids, rhino sinusitis, nasal polyps, asthma

Introduction:

Chronic rhino sinusitis (CRS) affects 6%-12 % of all general population, worldwide according to epidemiological studies (1) prevalence of clinically based CSR is between 3% and6.4%, CRS is classically divided into a phenotype with and without nasal polyps (CRSwNP and CRSsNP, respectively). Asthma is associated with 30%-70% of the CRSwNP patients which is more severe in nasal polypi as both share in type 2 inflammation process (2). Type 2 inflammation showed the presence of eosinophilic airway inflammation and
related cytokines IL4 and IL13 also high IgE level, guideline management of CRS includes anti-inflammatory treatment, corticosteroid and nasal local steroids (3).

Now biological treatment is an era in management of CRSwNP as it is anti-IgE and its monoclonal antibodies targeting type 2 inflammation, anti-IL4R, Anti-IL13 (4).

Most patients with CRSwNP needed systemic corticosteroids and repeated sinus surgery, 16 local nasal steroids have small effects on polyp size, smell when medical treatment is unsuccessful, so surgery is mandatory for reduction of nasal polyp size and relieve nasal obstruction without effect on underlying inflammatory process (5).

Management of CRS includes anti-inflammatory treatment, corticosteroid, and nasal local steroids, now biological treatment is an era in management of CRSwNP as it is anti-IgE, and now the biological treatment is an era in management of CRSwNP as it is anti-IgE and its monoclonal antibodies targeting type 2 inflammation, anti-IL4R, Anti-IL13 (6).

Most patients with CRSwNP needed systemic corticosteroids and repeated sinus surgery, 16 local nasal steroids have small effects on polyp size, smell. When medical treatment is unsuccessful, so surgery is mandatory for reduction of nasal polyp size and relieve nasal obstruction without effect on underlying inflammatory process (7).

Type 2 inflammation of CRSwNP is not affected by repeated sinus surgery and oral steroids so biological treatment is new tool to be used as in asthma and atopic dermatitis management. Dupilumab is a monoclonal antibody that inhibits signaling by IL-4 and IL13, approved by the US Food and Drug Administration over 12 years in USA in atopic dermatitis and asthma (8).

Patients and methods
This study is a prospective randomized case series clinical study. The study was conducted on Otorhinolaryngology clinics of Saudi German Hospital Jeddah and Saudi Airline Medical Services and during the period from February 2020 till March 2021. This study included 70 patients divided into two groups with the following criteria:

Inclusion criteria:
- Adult with bilateral nasal polypi, with history of previous nasal polypi surgery
- Type 2 inflammation in the form of high IgG and eosinophilia
- Smell affection
- Diagnosis of co-morbid Asthma
- Disturbed quality of life
- Need for systemic steroids in the past 2 years.

Exclusion criteria:
- Unilateral nasal polypi
- Allergic fungal sinusitis
- Malignant nasal mass
- Complicated sinusitis

The study was approved by the local ethics committee of Saudi German Hospital in Jeddah according to Saudi health regulations, all patients in this study have oral and written consent.

The patients divided into two groups G1: n=35 under treatment of dupilumab in the form dupixent 300 mg ampule intra-muscular every 2 weeks for 24 weeks and nasal high irrigation steroids 50 ml from the mixture in each side twice daily for 24 weeks (the mixture:1 liter saline mixed with 2 ampules of Pulmicort).

GII: n=35 treatment of dupilumab in the form dupixent 300 mg ampule intra-
muscular every 2 weeks for 24 week and Mometasone Furoate spray 50 ug two puffs twice daily for 24 weeks.

**Patient evaluation:**
both groups evaluated for:
- Nasal congestion score (scale 0-3) done at before treatment and 12&16&24 week after treatment
- Nasal Endoscopy score. (Scale 0-8) done at before treatment and 12&16&24 week after treatment
- CT paranasal sinus (Lund Mackay Scale 0-24) done before treatment and 24 weeks after treatment
- IgE level IU/mL, done before treatment and 12& 24 weeks after treatment.
- Co-morbid asthma and previous surgery

**Statistical analysis:** all patients who were randomly assigned, data were analyzed according to intervention using the computer program SPSS (Statistical package for social science) version 25 to obtain descriptive data. It was used t test while categorial data were compared using Chi square test, p value less (p<0.0001) was considered statistically significant.

**Results:**

The present study included 70 patients, under treatment of dupilumab, 41(58.6%) male and 29 (41.4%) female with age range from 22-55 years, they included two groups: GI=35 was subjected nasal high irrigation steroids 50 ml from the mixture in each side twice daily for 24 weeks (the mixture:1 liter saline mixed with 2 ampules of Pulmicort) and GII=35 was subjected to Mometasone Furoate spray 50 ug two puffs twice daily for 24 weeks.

Baseline demographics and characteristics were balanced between both groups regarding age, sex, nasal congestion score, bilateral nasal polypi duration, total IgE, and smell impairment (Table 1).

As regards nasal congestion score: in GI, there was significant difference between baseline and at 12&24 weeks p<0.0001) but it was higher at 24 weeks, this occur same in GII, but score improved more in group I than Group II (table 2).

As regards nasal endoscopy score in GI, there was significant difference between baseline and at 12 weeks (T. Test 2.06. )24 week (T. Test 1.93,), p<0.0001 but it was higher at 24 weeks, this occurs same in GII, but score improved more in GI than GII (table 2).

Lund-Mackay CT scores improved significantly in both groups (t. Test -7.44-4.53) GI while it was (t.test -5.13.—3.97) in GII, both (p<0.0001) but the score was Higher in GI than GII. (Table 2)

Patients treated in both groups had improvement of smell which assessed by
Smell score (vas score) in GI (2.63 - 1.98) while it was in GII (2.44- 1.84), there was significant difference in both groups p<0.0001. (Table 2).

We also observed improvement in total IgE level in both groups the difference was statically significant p<0.0001 (table 2).

As regards asthma history 28 in GI while it was 27 in GII, also the nasal polyp duration was 10.71 years in GI, while 11.1 years in GII, the percentage of previous surgery one or more in GI :26 cases 74.2% and GII: 25 cases 71.4%, while it was in previous surgery in more than 3 times in GI: 9 cases 25.7% and 11 cases 31.4% (Fig:1).

Patients under treatment of dupilumab with nasal irrigation had higher rate of improvement than patients treated with dupilumab and Mometasone Furoate spray for 24 weeks, but difference was insignificant (Fig 2).

As observed analysis the improvement of in smell score was higher in GI than GII especially at 24 weeks but the difference was insignificant (Fig 3).
Discussion

Patients with chronic rhinosinusitis with nasal polypi generally have a high symptom burden, including nasal obstruction, smell affection, asthma comorbidity, high post-operative recurrence rates, headache and many other symptoms affecting quality of life. The prevalence of eosinophilic chronic rhinosinusitis (ECRS) is increasing all over the world. Deregulation of the coagulation cascade and fibrinolysis may induce abnormal fibrin deposition in nasal mucosa, type 2 inflammation plays major role in the imbalance of coagulation and fibrinolysis in nasal mucosa (9).

There was significant effect reflected on nasal polyp size in all patients under treatment of dupilumab which agree with other studies who concluded same results when compare it with placebo, but our results showed better results in GII more than GI, but it was not significant difference. (10).

The goals of our treatment are to achieve control of symptoms in the form of loss of smell, nasal obstruction and decrease the risk effects of systemic steroids and recurrent sinus surgery. Our results were effective in both groups while it was better in GII than GI especially in smell recur which agree with studies concluded same results (11).

Dupilumab was safe and tolerable for most of the patients only 17.1% in Group I and 8.5% in GII had erythema at site of injection also Epistaxis was 5.7% in Group I, and 8.5% in Group II. The reductions in IgE levels were concluded in both groups which prove the effect of Dupilumab on type 2 biomarkers in our patients which agree with another study who conclude the results on studies on asthma and atopic dermatitis, in addition, our study noted that high irrigation nasal steroids are better than nasal steroids spay in chronic rhinosinusitis with polypi under treatment of dupilumab which agree with recent study concluded similar results (12).

In prespecified analyses of patients with comorbid asthma in GI was 80% while it was 74% in GII which prove the unified airway diseases which another author concluded that clinical characteristics between nasal polypi and asthma, as regards duration of nasal polypi it ranges from 10-11 years in both groups, also the previous surgery in both groups was insignificant difference (13).

Conclusion:

High irrigation nasal steroids are superior to intranasal steroids in chronic sinusitis with polypi under treatment of dupilumab in reduction of polyp size, smell correction, nasal congestion, and CT score Lund Mackay after treatment.

Conflicts of interest:
No conflicts of interest

Sources of funding:
This research did not receive any specific grant from funding agencies in the public.

References:


3- Tomassen P, Vandeplas G, Van Zele T, Inflammatory endotypes of chronic rhinosinusitis based on cluster analysis of


13- Stevens WW, Peters AT, Hirsch AG, Clinical characteristics of patients with chronic rhinosinusitis with nasal polyps, asthma, and aspirin-exacerbated respiratory disease. of patients with chronic rhinosinusitis with nasal polyps, J Allergy Clin Immunol Practice 2017; 5: 1061–70.
Table 1: Patient baseline demographics and clinical characteristics, mean ( ) is standard deviation.

<table>
<thead>
<tr>
<th>Age</th>
<th>GI n=35</th>
<th>GI n=35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>22-50</td>
<td>21-55</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre.</td>
<td>At 12 W</td>
</tr>
<tr>
<td>Nasal congestion score (0-3)</td>
<td>2.45 (0.55)</td>
<td>2.26 (0.47)</td>
</tr>
<tr>
<td>Nasal endoscopy score (0-8)</td>
<td>5.86 (1.31)</td>
<td>4.64 (1.04)</td>
</tr>
<tr>
<td>CT Score Lund Mackay (0-24)</td>
<td>21.26 (4.26)</td>
<td>16.82 (3.01)</td>
</tr>
<tr>
<td>Total IgE (IU/mL)</td>
<td>122.25 (56.21)</td>
<td>126.21 (25.97)</td>
</tr>
<tr>
<td>Smell Score (Vas 0-10)</td>
<td>9.12 (3.61)</td>
<td>6.48 (2.98)</td>
</tr>
</tbody>
</table>

Table 2: Summary of primary and secondary efficacy endpoints for each intention-to-treat patients at 12 and 24 weeks (p<0.0001) is significant.

<table>
<thead>
<tr>
<th>Nasal congestion score (0-3) at 12 weeks</th>
<th>GI n=35</th>
<th>T.test</th>
<th>p.value</th>
<th>GII n=35</th>
<th>T.test</th>
<th>p. Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.92.</td>
<td></td>
<td>-0.87</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal congestion score (0-3) at 24 weeks</td>
<td>-0.78.</td>
<td>p&lt;0.0001</td>
<td>-0.72.</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal endoscopy score (0-8) at 12 weeks</td>
<td>2.06.</td>
<td>p&lt;0.0001</td>
<td>-1.8</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal endoscopy score (0-8) at 24 weeks</td>
<td>1.93.</td>
<td>p&lt;0.0001</td>
<td>-1.41</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT score Lund Mackay (0-24). At 12 weeks</td>
<td>-7.44.</td>
<td>p&lt;0.0001</td>
<td>-5.13.</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT score Lund Mackay (0-24). At 24 weeks</td>
<td>-4.53.</td>
<td>p&lt;0.0001</td>
<td>-3.97</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smell score (vas 0-10) at 12 weeks</td>
<td>2.63</td>
<td>p&lt;0.0001</td>
<td>2.44</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smell score (vas 0-10) at 24 weeks</td>
<td>1.98.</td>
<td>p&lt;0.0001</td>
<td>1.84</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fig 1: comparison between both groups as regards no. of patients have asthma (1), nasal polyp duration per year (2), no. of patients had one or more surgery (3), no. of patients had 3 or more surgery (4), there was no significant difference in all parameters between both groups.

Fig 2: Comparison between both groups regarding nasal endoscopy score, there was significant difference in both groups.
Fig 3: comparison between both group regarding smell score (Vas score), there was significant difference in both groups.