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Outcomes of aspirin exacerbated respiratory disease patients treated with aspirin desensitization and biologics

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INTRODUCTION

Aspirin exacerbated respiratory disease (AERD) is characterized by a triad of chronic rhinosinusitis with nasal polyposis (CRSwNP), asthma and reactivity to aspirin and other non-steroidal anti-inflammatory drugs.

Its complex pathophysiology poses challenges to optimizing and instituting standard comprehensive therapy. Functional endoscopic sinus surgery (FESS), steroids, aspirin desensitization (AD) and biologics help in disease control in both the upper and lower respiratory tract.¹ As more biologics previously used for asthma are being approved in managing CRSwNP, studies are needed to look at overall clinical outcomes, and the comparison to existing treatments such as AD.

There are three FDA-approved monoclonal antibodies for the treatment of CRSwNP which target immunoglobulin E (IgE) (omalizumab), IL4/IL-13 (dupilumab) and IL-5 (mepolizumab). All reduce polyp size and improve CRSwNP related symptoms. Benralizumab and reslizumab are anti-IL5 monoclonal antibodies approved for eosinophilic asthma. Substantial data shows that they improve lung function and reduce exacerbations in severe eosinophilic asthma patients, many of whom have AERD; however, there is limited data suggesting they have a positive effect on the treatment of nasal polyps.^{2,3}

MATERIALS AND METHODS

This is an IRB approved single-institution retrospective chart review from 2011 to 2021. Inclusion criteria included a diagnosis of AERD following automated electronic medical record search of ICD codes for AERD criteria: asthma (J45.909), sensitivity to aspirin and NSAID's (Z.88.6) and sinonasal polyposis (J33.9). Patients who received a single biologic agent or only AD were included in the study (Figure 1).

TABLE 1. Sinonasal outcomes and days between functional endoscopic sinus surgery (FESS) and initiation of single treatment modality

Sino-nasal outcomes	AD	Aspirin desensitization (AD)	B	Biologics	<i>p</i> value
Meltzer Polyp Scores (mean)	N		N		
Pre-treatment	18	1.61 (SD-2.3, 0-6)	17	4.53 (SD-2.6, 0-8)	0.001
6 months post	16	0.88 (SD- 1.33, 0-4)	17	1.47 (SD- 2.2, 0-7)	0.34
1 year post	15	1 (SD- 1.8, 0-6)	17	0.82 (SD-1.2, 0-3)	0.74
SNOT 22 scores					
Pre-treatment	12	25 (SD-28.4, 5-101)	9	58 (SD-24, 23-95)	0.011
6 months post	13	16 (SD-8, 4-30)	8	21 (SD-19, 5-62)	0.42
1 year post	8	12 (SD-10.7, 0-31)	8	33 (SD-29, 0-93)	0.08
Mean days between FESS and starting AD or biologic	20	101.5	14	561.5	

TABLE 2. Asthma outcomes

Asthma	N	Aspirin desensitization (AD)	N	Biologic (B)	<i>p</i> value
Mean asthma control test scores (ACT)					
Pre-treatment	6	20.40 (SD-4.03, 14-25)	5	15.2 (SD-6.1, 9-25)	0.08
6 months post-treatment (mean)	6	24.0 (SD-1.1, 22-25)	4	20.42(SD- 5.2, 14-25)	0.12

Asthma	N	Aspirin desensitization (AD)	N	Biologic (B)	<i>p</i> value
Median fractional exhaled nitric oxide (FENO)					
Pre-treatment	6	43.8 (IQR: 22)	5	46 (IQR: 13)	0.91
6 months post-treatment (mean)	6	45 (IQR:32)	4	26.6(IQR: 9)	0.38

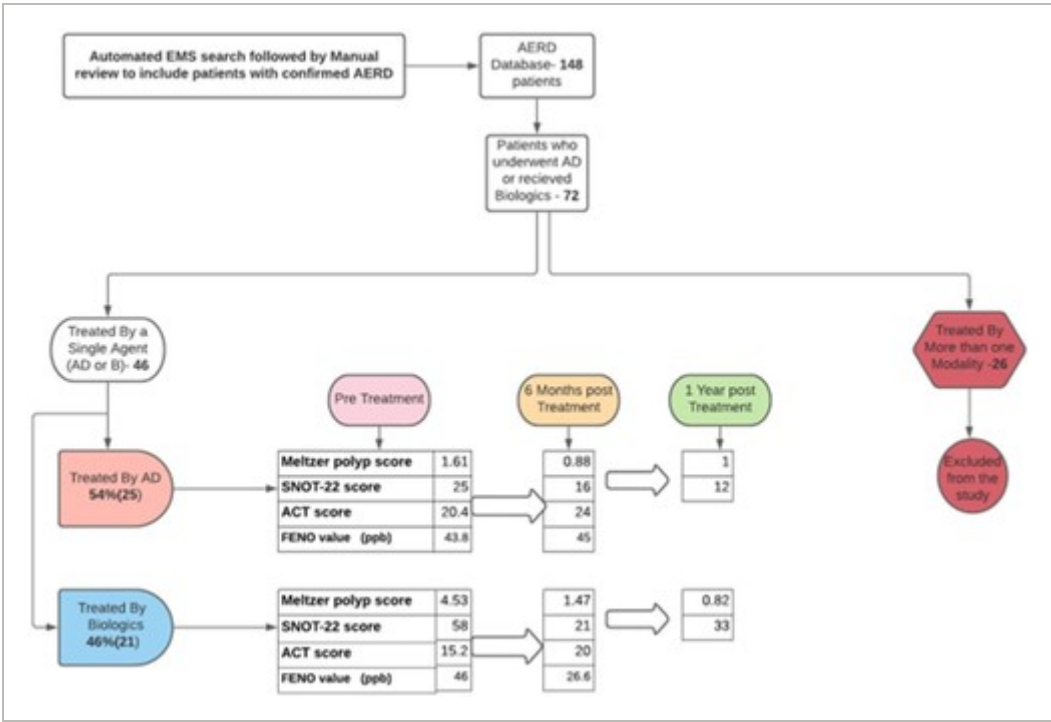


FIGURE 1

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This figure describes the patient population included in the study along with the results. Colors are used to delineate each patient subgroup and the period in which the outcomes were measured. The tables show the change in outcomes at 6 months and 1 year

Patient demographics, Meltzer polyp scores, sinonasal outcomes test-22 (SNOT-22) scores, asthma control test (ACT) scores and fractional exhaled nitric oxide levels (FENO), collected pre and 1-year post-initiation of treatment were analyzed.

Chi-square test, independent samples *t*-test and Wilcoxon sum rank test were performed using SPSS 26. Statistical significance was defined as *p* < 0.05.

RESULTS

Of the 46 patients included, 54.3% were on AD (25) and 45.7% (16) were treated by a single biologic. Patients in the biologics' cohort were on omalizumab- 57% (12), dupilumab-28.5%

(6), mepolizumab-9.5% (2) and benralizumab-5% (1).

Mean age was 44 years (SD -15, range- 19 to 73 years), mean BMI was 29.7 (SD- 7, range 19-40), 70% (n = 32) were female and 70% (n = 32) were Caucasian.

SINONASAL OUTCOMES (Table I)

The AD cohort had significantly lower Meltzer polyp scores at treatment initiation (mean = 1.61, SD-2.3, range 0-6) compared to biologics cohort (mean = 4.53, SD-2.6, range 0-8) ($p = 0.001$). The mean polyp scores reduced by 82% in biologics cohort (Mean = 0.82, SD-1.2, range 0-3) compared to 38% reduction in AD cohort (Mean = 1, SD-1.8, range 0-6) at 1 year.

SNOT-22 scores were significantly lower in AD cohort at treatment initiation (mean = 25, SD-28.4, range 5-101) compared with Biologics (mean = 58, SD-24, range 23-95) ($p = 0.011$). At 1 year the Biologics cohort had a 43% reduction (Mean = 33, SD- 29, range 0-93) while AD cohort had 25% reduction (Mean = 12, SD-10.7, range 0-31) in mean SNOT-22 scores.

All patients had a history of undergoing FESS. The mean number of surgeries pre-treatment in the AD cohort was 3.4 (SD- 2.7, range 1-9), compared to 2.9 (SD-1.57, range 1-6) ($p = 0.24$) in the Biologics cohort. Revision surgery rates were comparable between the groups (AD-0.25, SD-0.6, range 0-2), (B-0.17, SD-0.1, range 0-1) ($p = 0.59$) at median days of follow-up of 627 days (IQR: 417.25) for AD and 705 days (IQR 1411.75) for Biologics cohorts. The AD cohort had a shorter interval between surgery and initiation of treatment -101.5 days (SD- 514.7, range 9-2170 days) compared to the Biologics cohort- 561.5 days (SD-1078.9, range 7-3053 days).

ASTHMA OUTCOMES

Mean pre-treatment ACT scores were 20.40 (SD-4.02, range 14-25) in the AD cohort and 15.2 (SD-6.1, 9-25) in the biologics' cohort. ACT scores improved in both groups 6 months post-treatment (AD- 24.0 [SD-1.1, 22-25] vs. Biologics - 20.42 [SD- 5.2, 14-25]).

FENO values pretreatment were similar in both cohorts (AD -43.8 (IQR: 22) vs. Biologics- 46 [IQR: 13]), but after 6 months, the Biologics cohort had a 42% reduction (26.6, IQR: 9) while the AD cohort had a 2.7% increase in FENO (45, IQR: 32).

The AD cohort had a significantly higher rate of developing gastritis compared to Biologics (13 [52%] vs. 6 [29%], $p = 0.03$).

DISCUSSION

Symptomatic control of AERD is typically achieved through steroids and FESS. FESS by itself has demonstrated short-term efficacy in improving sinonasal symptoms. However, in the long term, without adjunct medical management, symptoms and polyps recur and revision

surgery is often required.⁴

Indications for AD include intractable nasal symptoms and/or asthma despite medical therapy, as well as AERD cases requiring revision FESS or COX-1 inhibitors. Similar to Larivee et al.,⁵ we report improved sinonasal outcomes and ACT scores in the AD patient cohort. However, the safety profile, associated gastrointestinal adverse events and need for repeat desensitization with missed doses should be considered prior to starting AD.

Biologics have shown promising results in the management of AERD. This study found that polyp size reduced 3-fold while SNOT 22 scores almost halved within one year of treatment in the biologic cohort with a concomitant improvement in ACT scores. The reduction in FENO only in the biologics group suggests biologics target lower airway inflammation more than AD.

Limitations to this study include its retrospective nature, inability to include patients who changed from AD to biologics or switched biologics due to the confounding effect that this would create, and the varied time frame for implementing these therapies. This may have excluded the patients who were refractory to treatment while further reducing our sample size.

CONCLUSION

Aspirin desensitization and biologics are effective in managing AERD symptoms in selected patients. This study showed more significant improvement in sinonasal and asthma outcomes with biologics. Further studies are needed to determine which subgroups most benefit from these treatment options.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST

None.

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