Poster S15

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Reductions in Infections and Associated Complications in Nine Common Variable Immunodeficiency Patients Treated with Immune globulin intravenous, human-slra

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Introduction

Common variable immunodeficiency (CVID) is a primary immune deficiency disease characterized by defects in humoral immunity. Individuals with CVID often experience frequent bacterial and viral infections of the upper airway, sinuses, and lungs despite standard immunoglobulin replacement therapy (IgRT). IgRT's are subject to requirements established in 21 CFR 640 that define minimum concentrations for antibodies against only measles, diphtheria, and polio[1]. There is no standardization of IgG titers against common, problematic respiratory pathogens.

Immune globulin intravenous (IVIG), human-slra 10% (ASCENIV™) is a unique IgRT that meets all CFR 640 criteria and is manufactured from blending normal source plasma with plasma from donors that possess high antibody titers against RSV[2] and other common circulating respiratory viruses including influenza A and B, parainfluenza serotypes 1, 2, and 3, human metapneumovirus, and seasonal coronaviruses 229E and OC43[3].

Purpose

To evaluate the clinical efficacy of this unique IgRT in the management of nine CVID patients.

Methods

Demographic data, past medical and respiratory history, IgRT history, clinical reason(s) for initiation of IVIG human-slra and clinical course for each patient was collected and evaluated pre-and post-initiation of IVIG human-slra.

Results

Most patients were female (88.9%), with a mean age of 64.5 years (range- 57-73). All patients had a diagnosis of CVID and suffered from recurrent infections and associated complications. Patients received IgRT an average of 9.7 years. IgRT dosing ranged from 600 – 1000 mg/kg to maintain individualized IgG trough levels between 900-1400 mg/dL as per clinical response and at the discretion of the prescriber.

Eight patients switched from other IgRT preparations and one patient with high-risk features (bronchiectasis, severe asthma, chronic and recurrent infections) was initiated on IVIG human-slra. All patients responded to therapy with decreased antimicrobial utilization and incidence of respiratory infections with over one-third of patients reporting no infections after initiating IVIG human-slra. Patients also reported reduced exacerbations of underlying asthma and decreased rescue medication utilization, better control of chronic respiratory disease, and improvement in associated complications (summarized in Table 1). All patients tolerated therapy well with no serious adverse events reported.

Summary of Patient Demographics, Medical History, and Clinical Course

Table 1

			Treatment Course			
Demographics	**PMH**	**Respiratory History**	**IgRT initiation**	**IVIG human-slra start date**	**Clinical reason(s) for initiation**	**Clinical course post IVIG human-slra**
Caucasian Male, 65 yo	• CVID • CAP • Chronic bronchitis • Sinusitis • Extrinsic asthma	• Two to three hospitalizations/year for pneumonia • Multiple courses of anti-infectives in winter months for bronchitis and pneumonia	Q3W since 2015	08/2020	Increased frequency of bronchitis, sinusitis, and pneumonia	• Prophylactic antibiotics discontinued 04/2021; resumed post-hospitalization • Single hospitalization for pneumonia 05/2021 • Increased productive cough with increased work of breathing 03/2022 (placed on antibiotic)
Caucasian Female, 60 yo	• CVID • Reactive airway disease • Seasonal allergic rhinitis • Asthma	• Increased use of rescue inhalers and anti-infectives (winter months) • At least 4 upper respiratory infections/year	Q3-4W since 2014	• 10/2020-07/2021 • Restarted 11/2021	Increased frequency of infections, asthma exacerbations, cough, and congestion	• Decrease in rescue inhaler usage • No evidence of sinusitis or pulmonary infections and improvement of seasonal rhinitis from 10/2020-07/2021; switched back to standard IVIG 07/2021 and developed increased asthma flairs with increased use of rescue inhalers • 12/2021 placed on antibiotic for sinusitis; 06/2022 placed on antibiotic for URI/increased wheezing • Patient reported reduction in side effects post infusion
African American Female, 64 yo	• CVID • Bronchiectasis • Chronic sinusitis • Severe persistent asthmallergic rhinitis	• Recurrent bimonthly sinopulmonary infections (bronchitis and sinusitis) • Severe asthma • Chronic fatigue • CT of chest showed moderate to severe bronchiectasis	Q4W since 01/2021	01/2021	PMH and high-risk features (bronchiectasis, severe asthma, chronic and recurrent infections)	• Patient reported asthma notably improved • One case each of otitis media (06/2021), bronchitis (04/2022) and sinusitis (10/2022); placed on antibiotics
Caucasian Female, 66 yo	• Recurrent infections • Hospitalizations for pneumonia • Poorly controlled asthma	• Recurrent infections, including pseudomonas pneumonia • Poorly controlled asthma • Bronchioscopies • Hospitalizations, on average 3 times a year	Q3-4W since 2006; (interrupted intermittently due to patient's perceived lack of benefit and insurance challenges)	10/2020	Extensive and recurrent respiratory illness	• Contracted COVID 19 in 01/2022 (unvaccinated, not hospitalized, no related respiratory issues) • Patient reports that IVIG human-slra helps keep her out of hospital for respiratory illnesses; continues with chronic respiratory infections (5 in 2022) • Patient noncompliant with IVIG therapy; typically received treatments Q6 weeks
Caucasian Female, 71 yo	• PID • COPD • Asthma	• Increased usage of albuterol inhaler and steroids for asthma exacerbations • Multiple courses of antibiotics (minimum 3-4 times/year) • Nebulizer therapies and steroids frequently required • Sinus infections	Q4W since 2018	11/2021	Frequent infections requiring multiple courses of antimicrobials	• Asthma better controlled with fewer exacerbations and steroid utilization • Sinusitis 03/2022 and 11/2022; treated with antibiotics and steroid taper • Decreased use of rescue inhaler from Q4-6 hours daily to 1x per day
Caucasian Female, 73 yo	• Asthma • Bronchiectasis • Sinus respiratory syndrome • Selective Ig deficiency	• Frequent asthma exacerbations requiring steroids and rescue inhalers • Upper respiratory infections (at least 4 infections per year requiring multiple courses of rotating antibiotics)	Q4W since 2011	01/2022	Recurrent infections	• From December 2020 to October 2021, the patient had a total of 5 months of antibiotics due to frequent asthma exacerbations and upper respiratory infections • No reported infections since starting IVIG human-slra • Rotating antibiotics stopped • Rescue inhaler utilization decreased to "once in a blue moon"
Caucasian Male, 57 yo	• PID • Bronchiectasis • CVID • ALL	• Continual rotation of prophylactic antibiotics • Multiple inhalers • HFCWO therapy vest	Q3W since 2005	03/2022	Recurrent infections	• Patient reports decreased bronchiectasis flares since starting, only one flare this year 06/2022 • Patient continues monthly antibiotic use due to his disease processes and 20% lung capacity/ O_2 requirements
Caucasian Female, 58 yo	• Asthma • Progressive bronchiectasis • CID • Pneumonias • Bronchitis • Sinusitis	• Recurrent pseudomonas and nocardia infections requiring chronic prophylactic antibiotics • Multiple courses of antibiotics (as frequent as every 2 months) for sinusitis/ bronchitis • Steroids for asthma exacerbations • Typically gets the flu every year • Hospitalized 2-to-3 times a year for respiratory issues (pneumonia/asthma exacerbations) despite IgRT	Q4W since 2014	10/2021	Increases frequency of infections and hospitalizations	• Continues prophylactic antibiotic therapy • Decreased antibiotic usage and a marked decrease in frequency and severity of infections • One sinus infection reported 02/2022 and pneumonia reported 06/2022 (no hospitalization required; however placed on home O_2) • Did not contract the flu this past year
Caucasian Female, 67 yo	• PID • Bronchiectasis • Recurrent Infections • Pneumonia • Bronchitis • Rhinorrhea • Dyspnea increased each spring and fall	• Frequent antibiotics (4 different antibiotics and steroid treatments July to September 2021) • 2L O_2 via NC at baseline • Increased albuterol inhaler use and systemic steroids • Multiple hospitalizations, averaging 3 times/ year • Admitted to hospital approximately twice a year for pneumonia despite IgRT	Q3W since 2019	11/2021	Requiring frequent antibiotics and steroids; hospitalizations	• Continues concomitant prophylactic antibiotics • One hospitalization for pneumonia 06/2022 • Stopped using O_2 (10/2022)

Abbreviations: ALL=acute lymphocytic leukemia, CAP=community-acquired pneumonia; CID=combined immunodeficiency pneumonia; COPD=chronic obstructive pulmonary disease; CT=computerized tomography; CVID=common variable immunodeficiency; HFCWO=high frequency chest wall oscillation; Ig=immunoglobulin; IgG=immunoglobulin G; IgRT=immunoglobulin replacement therapy; IVIG=intravenous immunoglobulin; Kg=kilogram; mg=milligram; NC=nasal cannula; O_2=oxygen; PID=primary immune deficiency; PMH=past medical history; PsA=psoriatic arthritis; Q3W=every 3 weeks; Q4W=every 4 weeks; yo=years old

Discussion

While all patients responded positively to IVIG human-slra, treatment could have occurred during the COVID 19 pandemic. The impact of public health initiatives may have limited exposure to certain pathogens. One patient started prophylactic antibiotics concomitantly with IVIG human-slra, possibly providing additional infection prevention. Despite these potential limitations and the case-based nature of this report, IVIG human-slra has proven to be clinically beneficial in CVID patients by providing them enhanced protection against common, problematic respiratory pathogens that cause infection and sequelae in this vulnerable patient population.

Conclusion

This case report series has demonstrated the beneficial effects of IVIG human-slra in CVID patients as evidenced by decreased respiratory infections and associated complications, less antimicrobial and ancillary medication utilization, and fewer health care provider visits and hospitalizations.

References

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