Immunoglobulin Replacement Therapy in Patients with Immunodeficiencies – Impact of Administration Method on Patient-Reported Outcomes

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Introduction

- Primary and secondary immunodeficiencies (PID and SID, respectively) are disorders of the immune system that predispose individuals to an increased rate and severity of infections, allergies, malignancies, and autoimmune diseases[1]
- Immunoglobulin (Ig) replacement therapy (IgRT) is an effective and well-tolerated treatment for patients with immunodeficiencies and is available to administer subcutaneously (SCIg) or intravenously (IVIg)[2,3]
  - SCIg is an important alternative to IVIg for many patients with PID due to an improved safety profile, flexible dosing, and the possibility of home treatment[4]
- Previous studies of patients with immunodeficiencies receiving IgRT have suggested that treatment satisfaction, health status, and quality of life are associated with IgRT infusion characteristics[4–6]
- A better understanding of the impact of different IgRT administration methods on treatment experience can potentially facilitate optimization of patient outcomes, including continued compliance with treatment
- To help raise awareness and promote early diagnosis, the Association of Immunodeficient Patients of Québec (APIQ) conducts regular surveys to provide evidence on health and wellbeing in patients with immunodeficiencies

Objective

To analyze 2020–2021 APIQ survey data in order to compare patient-reported outcomes (PROs) between different modes of IgRT administration, such as SCIg and IVIg

Methods

- Using the Canadian Immunodeficiencies Patient Organization-APIQ database, 1,164 patients with immunodeficiencies in Canada were contacted via email regarding an incentivized online survey between October 2020 and March 2021
- The survey contained questions on demographic characteristics, underlying conditions, IgRT history, IgRT infusion duration characteristics, and PROs
- PROs included:
  - The Treatment Satisfaction Questionnaire for Medication (TSQM), 9-item version which measured the following three domains: *effectiveness*, *convenience*, and *global satisfaction*
  - A Patient Acceptable Symptom State (PASS) question to measure satisfaction with overall symptom state
  - The PROs Measurement Information System (PROMIS) general health 4-item tool incorporating physical and mental health
  - A General Health Perception (GHP) question to rate overall observation of health from very poor to excellent
- Adult respondents (≥18 years old) were stratified by their current IgRT administration mode into a SCIg or IVIg cohort
- The SCIg cohort was further stratified by patients who were naïve to Ig ('SCIg naïve') or patients with previous IVIg experience ('previous IVIg')
- Categorical variables were compared between the two cohorts using the Chi-squared test; continuous variables were analyzed using an unpaired t-test if found to be normally distributed, or the Mann-Whitney test otherwise
- Multivariable regression analyses adjusted the IgRT administration cohorts (SCIg and IVIg) for age, sex, weight, IgRT history, PASS, PROMIS physical and mental health, and GHP using linear regression

Results

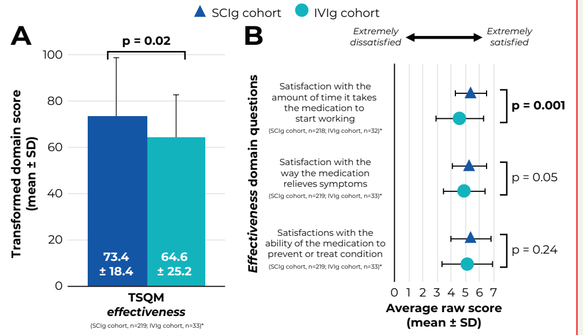
- Of the responses, 296 adult patients with PID/SID were eligible for analysis; 81.8% (n=242) were receiving SCIg and 18.2% (n=54) IVIg (**Table 1**)
- Overall, the SCIg cohort had significantly fewer years of IgRT history than the IVIg cohort (p=0.02; **Table 1**)

Table 1: Summary of APIQ survey respondent demographic characteristics, IgRT history, and infusion duration characteristics in the SCIg and IVIg cohorts

Variable	Category	IVIg cohort (n=54)		SCIg cohort (n=242)		p value
		Summary	Collected responses	Summary	Collected responses	
Demographic characteristics						
Age (years)		60 [37, 67]	54	59 [48, 67]	242	0.43
Sex, n (%)	Female	24 (44.4%)	54	151 (63.0%)	240	**0.01**
	Male	30 (55.6%)		89 (37.1%)		
Underlying condition, n (%)	CVID	21 (51.2%)	49	85 (45.0%)	191	0.35
	IgG Sub	9 (22.0%)		48 (25.4%)		
	DGS	2 (4.9%)		8 (4.2%)		
	SID	1 (2.4%)		22 (11.6%)		
	Other	8 (19.5%)		26 (13.8%)		
Weight (kg), mean ± SD		74.2 ± 15.1	47	75.8 ± 17.4	216	0.56
IgRT history (years), mean ± SD		9.1 ± 6.7	47	6.8 ± 6.2	238	**0.02**
IgRT infusion duration characteristics						
Pre-infusion time (mins)		30 [15, 30]	27	15 [10, 20]	207	**<0.001**
Infusion time (mins)		165 [126, 255]	28	60 [40, 90]	207	**0.001**
Post-infusion time (mins)		15 [6, 20]	27	5 [5, 10]	201	**0.005**

Results are median [IQR] unless otherwise stated. Categorical variables were compared between the two cohorts using the Chi-squared test and continuous variables were analyzed using an unpaired t-test if found to be normally distributed, or the Mann-Whitney test otherwise. Significant p values are in bold. CVID, common variable immune deficiency; DGS, DiGeorge syndrome; IgG Sub, immunoglobulin subclass deficiency; IgRT, immunoglobulin replacement therapy; IQR, interquartile range; IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin; SD, standard deviation; SID, secondary immunodeficiency.

Figure 1: Perceived treatment effectiveness in the SCIg and IVIg cohorts. (A) Transformed TSQM *effectiveness* domain scores and (B) raw scores from the corresponding TSQM questions



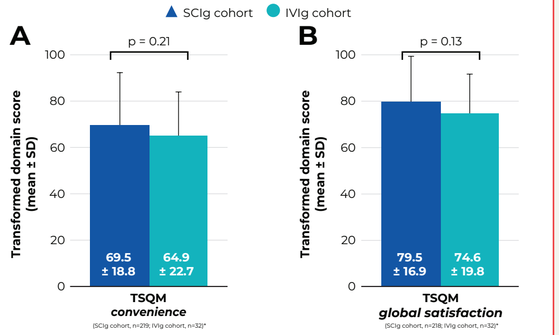
*n numbers vary due to missing respondent data for various survey questions. Transformed domain scores are on a 0–100 scale from worst to best and the raw scores are on a 1–7 scale from extremely dissatisfied to extremely satisfied. Continuous variables were compared using an unpaired t-test and the significant p values are in bold. IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.

- The average duration of infusions was significantly shorter in the SCIg cohort compared with the IVIg cohort (p=0.001; **Table 1**)
  - On average, the SCIg cohort also had significantly quicker pre- and post-infusion times compared with the IVIg cohort (p<0.001 and p=0.005, respectively; **Table 1**)

PROs

- Respondents in the SCIg cohort scored significantly higher in the TSQM *effectiveness* domain compared with those in the IVIg cohort after univariable analysis (p=0.02; **Figure 1A**)
  - However, this result did not remain significant after multivariable analysis (p=0.40; **Table 2**)
  - Respondents with a positive PASS and with a 'very good' or 'excellent' GHP were more likely to have a higher TSQM *effectiveness* domain (p=0.03 and p=0.009, respectively; **Table 2**)
  - Examining individual questions on TSQM *effectiveness*, the SCIg cohort reported greater satisfaction with the amount of time it takes the medication to start working compared with the IVIg cohort (p<0.001; **Figure 1B**)
- The SCIg cohort scored higher in *convenience* and *global satisfaction* compared with the IVIg cohort, but after univariable and multivariable analysis the differences were not significant (**Figure 2** and **Table 2**)
  - Examining individual questions in *convenience* and *global satisfaction*, no significant differences were found (results not shown for brevity)
- Overall, a higher proportion of the SCIg cohort perceived their current symptom state to be acceptable compared with the IVIg cohort (90.8% [n=187] vs. 75.0% [n=24], respectively; p=0.009)
- There was no significant difference between the GHP scores of the SCIg and IVIg cohorts (p=0.61)

Figure 2: Perceived treatment convenience and satisfaction in the SCIg and IVIg cohorts. Transformed TSQM (A) *convenience* and (B) *global satisfaction* domain scores



*n numbers vary due to missing respondent data for various survey questions. Transformed domain scores are on a 0–100 scale from worst to best. Continuous variables were compared using an unpaired t-test. IVIg, intravenous immunoglobulin; SCIg, subcutaneous immunoglobulin; SD, standard deviation; TSQM, Treatment Satisfaction Questionnaire for Medication.

Table 2: Results of the multivariable regression analyses of the TSQM domains

Variable	Category	TSQM *effectiveness*		TSQM *convenience*		TSQM *global satisfaction*	
		Coefficient (95% CI)	p value	Coefficient (95% CI)	p value	Coefficient (95% CI)	p value
Administration method	IVIg	0	0.40	0	0.72	0	0.30
	SCIg	3.3 (-4.5, 11.1)		4.0 (-3.9, 11.9)		3.7 (-3.3, 10.7)	
PASS	No	0	**0.03**	0	0.97	0	0.23
	Yes	10.1 (0.3, 19.4)		0.2 (-9.3, 9.6)		5.2 (-3.2, 13.5)	
PROMIS *mental health*	T-score <50	0	0.97	0	**0.001**	0	0.30
	T-score ≥50	0.1 (-5.9, 6.1)		10.1 (4.0, 16.2)		2.7 (-2.7, 8.1)	
GHP	Very poor, poor, fair, & good	0	**0.009**	0	0.15	0	**<0.001**
	Very good or excellent	8.2 (2.1, 14.4)		4.6 (-17.0, 10.8)		10.6 (5.0, 16.1)	

Significant p values are in bold. Multivariable regression analyses adjusted the IgRT administration cohorts (SCIg and IVIg) for age, sex, weight, IgRT history, PASS, PROMIS physical and mental health, and GHP using linear regression. Only statistically significant and non-IgRT modes of administration covariates are shown for brevity. CI, confidence interval; GHP, general health perception; IgRT, immunoglobulin replacement therapy; PASS, patient acceptable symptom state; PROMIS, patient reported outcome measurement information system.

IgRT history

- Of the current SCIg users, 65 were 'SCIg naïve' and 151 were in the 'previous IVIg' subgroup
- Compared with current IVIg users, the SCIg naïve subgroup had a statistically significant greater satisfaction in both *effectiveness* and *convenience* (p=0.02 and p=0.03, respectively), but not *global satisfaction* (p=0.12) of treatment (univariable analysis)
- There was a statistically significant greater satisfaction with treatment for *effectiveness* (p=0.03), but not *convenience* and *global satisfaction* (p>0.09) when the previous IVIg subgroup was compared with the current IVIg users (univariable analysis)
- Examining individual questions on the TSQM, the SCIg naïve and previous IVIg subgroups reported greater satisfaction with the time for the medication to work (p=0.001 and p=0.004, respectively), and confidence that taking their medication was good for them (p=0.04 for both) compared with current IVIg users
  - In addition, the SCIg naïve subgroup reported greater satisfaction in the ease of planning treatment compared with the IVIg cohort (p=0.02)

Discussion

- Respondents with PID/SID receiving SCIg reported their infusions to be significantly quicker and perceived their treatment to be more effective compared with IVIg after univariable analysis
  - However, after multivariable analysis there was no significant differences between cohorts for all three TSQM domains
- A significantly higher proportion of current SCIg patients reported their overall symptom state to be satisfactory compared with patients receiving IVIg
- Among current SCIg patients, those that were naïve to Ig reported better treatment effectiveness and convenience than current IVIg patients
- These findings may be partially attributed to the self-infusing SCIg cohort, (especially those that were SCIG naïve) feeling more empowered due to playing a more active role in their treatment and a more stable serum Ig profile due to greater frequency of SCIg infusions compared with those receiving IVIg

Conclusions

It is hoped our findings on variations on patient reported treatment satisfaction across IgRT administration methods will enable more evidence-based decision making and ultimately improved patient outcomes

References

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Conflicts of interest

OL has no conflicts to declare. GS works for the APIQ, a patient advocacy group that facilitated the planning and execution of the survey, which was sponsored by CSLB. RM and PP work for CSLB and own stock in the company. Editorial and statistical assistance was provided by Meridian HealthComms Ltd, funded by CSLB.

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