The pharmacology of human polyvalent immunoglobulins in patients with primary immunodeficiency diseases

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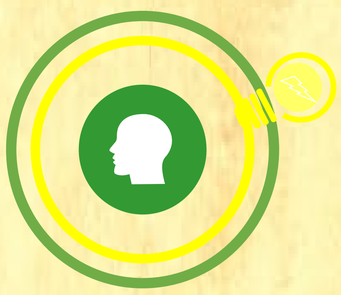
Introduction:

Primary immune deficiencies **(PIDs)** comprise 406 distinct disorders including **430** different genetic defects listed in the International Union of Classifications of Immunological Societies **(IUIS) (1)**, awareness of these values is fundamental to establishing a rapid diagnosis approriate treatment. Intravenous **(IVIG)** or subcutaneos **(SCIG)** immunoglobulins are therapeutic preparations of human Ig obtained from a pool of plasma from thousands of donors, thus providing a wide range of immunoglobulins, which have been shown to be effective in many primary and secondary immune deficiencies and systemic autoimmune and inflammatory diseases.

Purpose:

Our objective is to answer the following research question :



Is the therapeutic dose of 0.5 g/kg/month that all patients receive sufficient to provide a protective residual dose?

Methods:

We collected **25** Moroccan children with **DIP** who are under **IVIG** treatment, after a dose of **IVIG** of **0.5 g/kg** is administered, then after **3** to **4** weeks (the next appointment) an immunoglobulin G assay was performed before the infusion of the treatment (Residual Doses). Residual IgG determination was performed by the automated turbidimetric assay at the Immunology Laboratory of the University Hospital.

Results:

Table I: Distribution of patients by diagnosis correlated with age and gender

Primary immune deficiency	Number of patients	Number of patients (%)	Middle age	Gender	
Antibody deficiency	11	44	9	M:8	F:3
Combined immunodeficiency	14	56	6	M:7	F:7

Table II: Residual doses for patients with antibody deficiencies

Number	Age	Antibody deficiency	Type of IgG	Residual dose	Normal values	The middle value	Standard deviation
1	3	Agammaglobulinemia	IVIG	3.63	(4.80-9.00)	5,03109	2,2593
2	13	Bruton		5.95	(6.20-12.20)		
3	11	Hyper IgM sydrome		6.02	(6.20-12.20)		
4	14	Hyper IgM sydrome		6.16	(6.20-12.20)		
5	9	IgA deficiency		3.69	(5.80-10.80)		
6	13	Bruton		2.82	(6.20-12.20)		
7	11	Bruton		2.73	(6.20-11.50)		
8	6	Agammaglobulinemia		8.76	(4.80-10.20)		
9	8	Agammaglobulinemia		5.98	(8.20-11.50)		
10	3	Hyper IgM sydrome		1.72	(3.40-9.00)		
11	6	Agammaglobulinemia		7.89	(4.80-10.20)		

Table III: Residual doses in patients with combined immunodeficiencies

Number	Age	Antibody deficiency	Type of IgG	Residual dose	Normal values	The middle value	Standard deviation
12	8	HLA II deficiency	IVIG	6.4	(4.54-13.60)	8,575	6,3012
13	13	HLA II deficiency		12	(6.20-12.20)		
14	1	SCID		7.08	(2.40-4.40)		
15	12	Ataxia-telangiectasia		3.25	(6.20-12.20)		
16	1	SCID		10.86	(2.40-4.40)		
17	3	Wiskott-Aldrich Sd		11.04	(3.40-9.00)		
18	3	SCID		2.9	(3.40-9.00)		
19	9	SCID		5.74	(5.80-10.80)		
20	4	SCID		3.26	(4.80-9.00)		
21	3	Wiskott-Aldrich Sd		10.28	(3.40-9.00)		
22	11	SCID		5.8	(5.80-10.80)		
23	3	SCID		5.03	(3.40-9.00)		
24	9	CID		27.71	(5.80-10.80)		
25	4	Wiskott-Aldrich Sd		8.7	(4.80-9.00)		

Table IV: Comparison of middle residual doses (DIC, Antibody deficiency)

Primary immune deficiency	Middle residual dose (± standard deviation
Antibody deficiency	5.03±2.26
Combined immunodeficiency	8.58± 6.30

Discussion:

A set of clinical studies used a mean dose of IVIG ranges from **387** to **560** mg/kg every **3** to **4** weeks in patients with CID and agammaglobulinemia, and the residual IgG level obtained ranges from **660** to **1000 mg/dl**, the random-effect meta-regression slope shows that the residual IgG level increases significantly by **73 mg/dl** with each **100 mg/kg** dose increase of **IVIG (2).**

Conclusion:

Comparison of our results with literature data, allowed us to answer the research question posed: The therapeutic dose of **0.5 g/Kg** that patients receive every **3** to **4** weeks is sufficient to give a protective residual dose **≥ 5 g/l**, and that the residual IgG level increases significantly with each increase in the infused dose.

References :

- **(1)- Bousfiha AA, Leila J, Capucine P, Waleed A, Fatima A, et al (2020).** Human inborn errors of immunity: 2019 updates of the IUIS phenotypical classification. Journal of Clinical Immunology. 40 : 66-81.
- **(2)- Jian LL, et al (2020).** A Systematic Review and Meta-regression Analysis on the Impact of Increasing IgG Trough Level on Infection Rates in Primary Immunodeficiency Patients on Intravenous IgG Therapy. Journal of Clinical Immunology. 40 : 682-698.

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