

IV IMMUNOGLOBULIN IN NEPHROLOGY

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INTRODUCTION

- First commercial immunoglobulin product for IVIG was approved in 1980.
- Uses in nephrology :-Desensitization , ABMR, ABOi kidney transplantation, Post transplant infections [BKV].
- Components IV IG :- Immunoglobulin G (IgG) constitutes 95-98% of the preparation. Mainly IgG1 IgA and IgM - present in small amounts, cytokines and soluble receptors.

Anti-inflammatory effects



- Modulation of the inflammatory cytokines
- Neutralization of proinflammatory cytokines, chemokines, integrins, anaphylatoxins
- Augmentation of anti-inflammatory cytokines
- Neutralization of bacterial toxins
- Inhibition of neutrophil rolling and adhesion and recruitment into inflammatory tissues
- Suppression of activation and production of NO in polymorphonuclear cells
- Neutralization of activated complement compounds
- Complement compound scavenging
- Anti-inflammatory IgG glycovariants



Effects on dendritic cells and NK cells

- Inhibition of dendritic cell differentiation and maturation
- Modulation of inflammatory cytokine production
- Modulation and regulation of NK cells



Effects on apoptosis

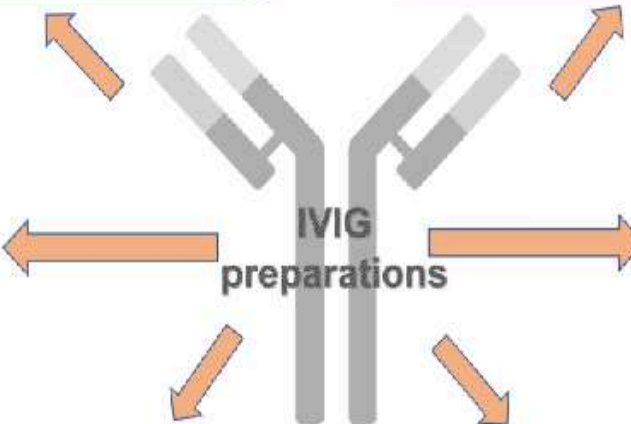
- Regulation of apoptosis via anti-Fas antibodies
- Regulation of cell proliferation



Fc receptor-mediated effects

- Blocking Fcγ receptors
- Modulate the affinity of the Fcγ receptors
- Saturation of protective FcRn receptors to enhance the catabolism of autoantibodies
- Saturation of activating Fcγ receptors
- Upregulating of inhibitory FcγRIIIB
- Blocking the uptake of C3b and C4b on target cells
- Prevents the generation of C5b-C9 membrane attack complex
- Neutralization of C3a and C5a anaphylatoxins

IVIG preparations



Effects on T cells

- Shifting the effector Th cell balance (Th1 and Th17)
 - Expansion of Tregs
- Inhibition of T cell activation
 - Neutralization of T cell superantigens
- Modulation of T cell-derived cytokine production



Effects on B cells and antibodies

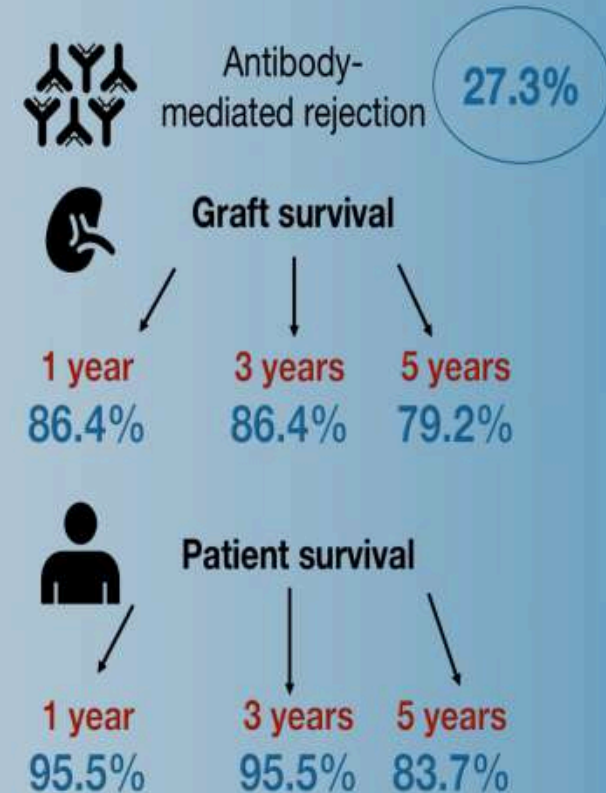
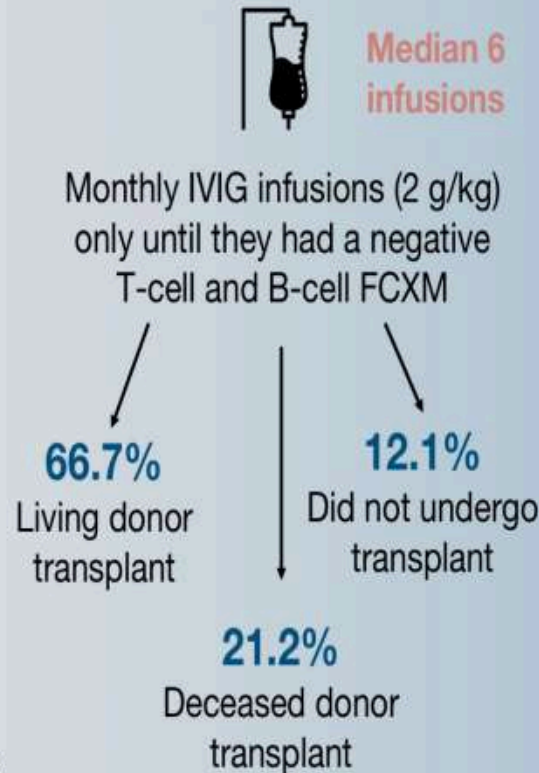
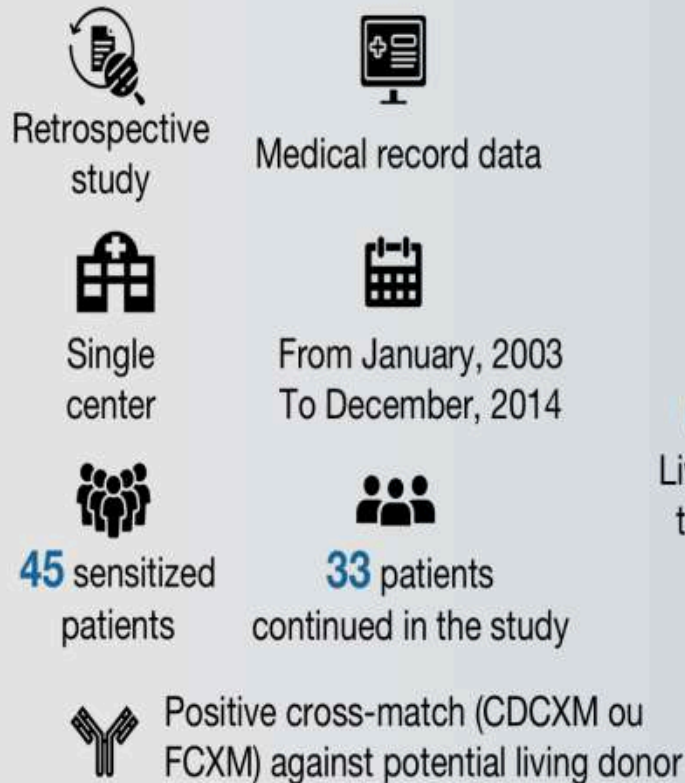
- Modulation of B cell activation and repertoire
 - Neutralization of autoantibodies via anti-idiotypic antibodies
- Enhanced clearance of autoantibodies
- Solubilization of immune complexes



ACTIONS AND EFFECTS

Desensitization using IVIG alone for living-donor kidney transplant: impact on donor-specific antibodies

METHODS AND RESULTS



Conclusions: Desensitization using IVIG alone is an effective strategy, allowing successful transplantation in these highly sensitized patients.

Referência: Ulisses LRS, et al. Braz J Nephrol. 2022. DOI: <https://doi.org/10.1590/2175-8239-JBN-2021-0200>.

Visual abstract by Jenyffer Ribeiro Bandeira

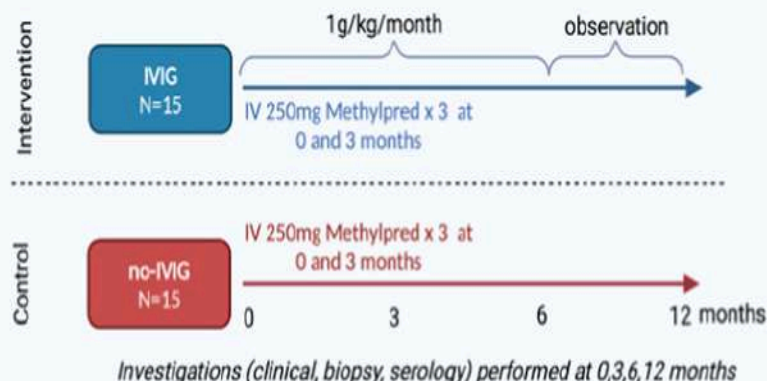
A randomized controlled trial of intravenous immunoglobulin vs standard of care for the treatment of chronic active antibody-mediated rejection in kidney transplant recipients

kidney
INTERNATIONAL



Cohort/Methods

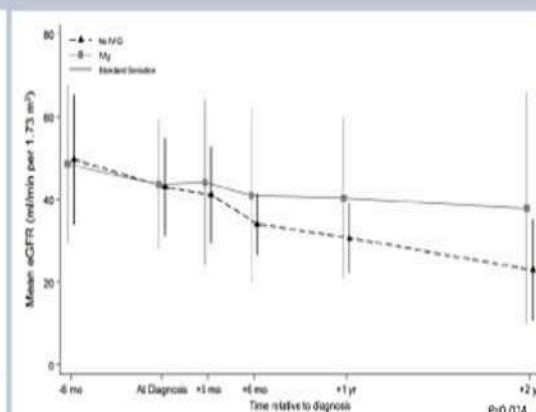
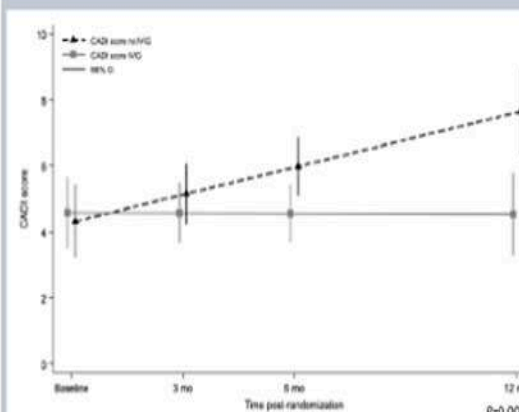
- Kidney transplant recipients with chronic active antibody mediated rejection were randomized 1:1 to intravenous immunoglobulin (IVIg) or standard of care.



Endpoints:

- Primary** – chronic allograft damage index (CADI)
- Secondary** – estimated glomerular filtration rate (eGFR), donor specific anti-HLA antibodies (DSA), allograft & patient survival and intra-graft mRNA expression.

Findings:



- IVIg stabilized histological damage
- IVIg stabilized eGFR
- IVIg did not reduce donor specific antibodies or proteinuria
- Patient and allograft survival was similar at 12 months
 - At 5 yrs, 0 deaths in IVIg and 5 deaths in no-IVIg group
- IVIg stabilized/reduced intra-graft gene transcripts – particularly B-cell, T-cell, NK-cell and fibrosis associated transcripts.

CONCLUSION: In kidney transplant recipients with chronic active antibody mediated rejection, IVIg therapy stabilized allograft histology, function and intra-graft gene transcripts.

IV IG in post transplant infections

- Treating Parvovirus B19, Polyoma BK virus and Cytomegalovirus (CMV).
- **Mechanisms:**
 - Broad-spectrum neutralizing antibodies against viruses.
 - Complement inhibition (\downarrow MAC, \downarrow C3 convertase activity).
 - Anti-inflammatory modulation of immune responses in infected tissues.
- In BKN : - Combining immunosuppression reduction with IVIG therapy showed the most significant benefit for viral clearance.
- Parvo –B19 :- IVIG therapy contains neutralizing antibodies against HPV-B19 .Dose: IVIG 2 g/kg over 2–5 days

Complications of IVIG

Adverse effect	Predisposing factors
Flu-like symptoms	High dose, rapid infusion rate, accompanying infection, previous adverse effects
Dermatological adverse effects	High dose, rapid infusion rate, accompanying infection, male patients with chronic inflammatory demyelinating polyneuropathy
Arrhythmia and hypotension	History of heart disease
Transfusion-related acute lung injury	Rapid infusion rate
Thrombotic events	High dose, rapid infusion rate, advanced age, being bedridden, diabetes mellitus, hypertension, dyslipidemia, prior/current thrombosis, preexisting atherosclerotic disease, elevated serum viscosity, oral contraceptive use, hereditary hypercoagulable state, idiopathic thrombocytopenic purpura
Aseptic meningitis	High dose
Renal impairment	Rapid infusion rate, advanced age, renal insufficiency, nephrotic syndrome, diabetes mellitus, dehydration, sepsis paraproteinemia, nephrotoxic drugs, hemolysis, sucrose-containing preparations
Hemolysis	High dose, rapid infusion rate, non-O blood group, underlying inflammatory state