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Willkommen
Bem Vindo
Selamat Datang
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Croeso
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Καλώς ήλθατε
Benvenuti

- The allograft is antigenic
- Host immune response → rejection
- Immunosuppression necessary

The need: risk assessment

- We recommend that immunosuppressive therapy is based on the transplant immunological risk and concerns with individual agents.

Immunological low risk:

- **1^{st} time transplant recipients OR repeat recipients not aggressively rejected a previous transplant**

Who have less than 20%* PRA and no DSA

The need: can change

- Highest early on
- Increased when DGF
- Increased during ± after rejection episodes
- Adaptive tolerance 3-6 Mo

The immune system is beneficial and indispensable

NEED

TOLERANCE

Prevent rejection

-Infection

-Malignancy

-Toxicity

GOAL:
maintain optimum level of IS

NEED

TOLERANCE

Prevent rejection

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GOAL:
maintain optimum level of IS

Difficult:

-Not measured

-Changing

-Induction
-Early
-Maintenance
-ttt of rejection
-reduced?

INDUCTION

- **We recommend that antibody induction therapy be used in all pediatric kidney transplant recipients.**

  The first dose should be given intraoperatively prior to declamping

- **IL2 receptor antibody (Basiliximab)**

is suggested for patients with low-intermediate risk; in a dose of:

- 20 mg x 2 doses (d 0 and 3-4) in recipients > 35kg

- 20 mg in 1-2 divided doses in recipients < 35kg

- **T cell depleting therapy**

(ATG; 5-9mg/Kg or thymoglobulin; 1.5mg/Kg/d x 5d)

is recommended for induction in high immunological risk transplants

and is not recommended in patients with increased risk of infection or malignancy

MAINTENANCE

Maintenance immunosuppression with

- a calcineurin inhibitor
  (Tacrolimus or cyclosporine)
- and mycophenolate
- with or without steroids

is recommended in most transplant recipients

MAINTENANCE

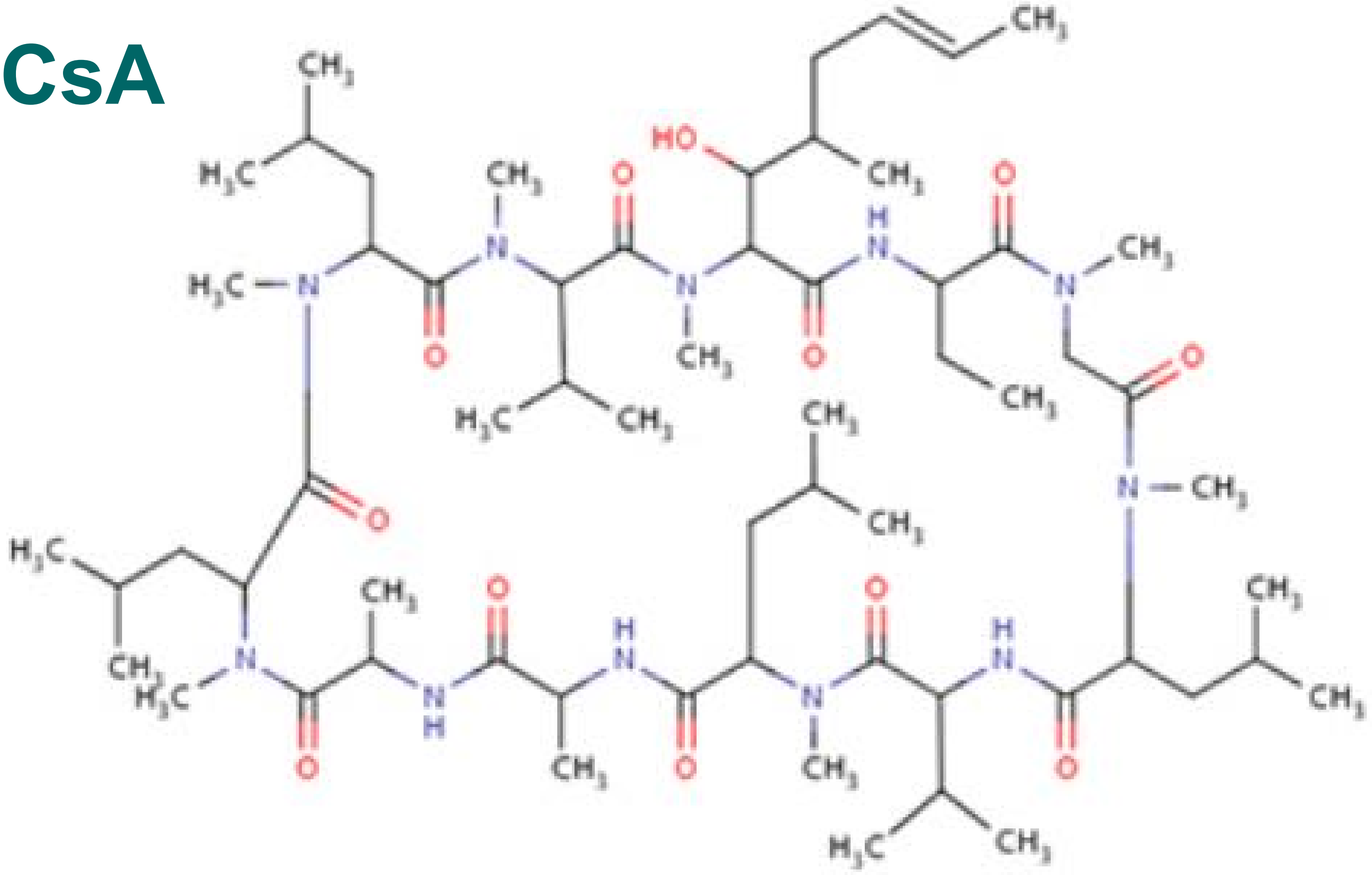
- In low risk transplants, steroid avoidance; with only perioperative steroids, tapered to elimination within the first week, may be used so long rejection has not occurred
- Azathioprine is generally less immunosuppressive than mycophenolate and may be used in individual patients/ situations
- We recommend NOT to use generic forms of immunosuppressive agents in KTRs

Steroids

- Methylprednisolone IV: 5-10 mg/Kg (150-250 mg/m2) up to 250 mg per dose

  Day -1, induction, declamping, post-op, Day +1
- Gradually tapered, converted to oral when tolerated and dose is 2-3 mg/Kg/day
- Reduced targeting 15-20 mg/m2 by day 14
- 2.5-7.5 mg/ day 6-12 months.
- Further management is individualized
- Late discontinuation always carries a risk of AR

CsA



CNIs

- May be started before up to the morning after Tx
- Be aware of food and drug interactions
- **Starting doses:**

-Tacrolimus: 0.15mg/kg/day in 2 divided doses

-Cyclosporine: 8-10 mg/kg/day (250mg/m2/day) in 2-3 divided doses (3 in younger children)

- **Adjusted based on drug level monitoring:**

The suggested therapeutic target trough levels

- Tacrolimus: 10-15 ng/mL in the first month and 5-10 ng/mL later (higher in the first 3-6 months)

- Cyclosporine: 200-250 ng/mL in the first month, around 150 ng/mL up to 6 months and around 100 ng/mL thereafter

Tacrolimus is preferentially suggested: dyslipidemia, significant hirsutism & immunologically high risk

Cyclosporine	Tacrolimus
Suspension available Dyslipidemia Hirsutism	Once daily available More potent Diabetes Neurotoxicity

Mycophenolate

- Mycophenolate mofetil (MMF) or Mycophenolate sodium (MPS) may be used. Patients differ in tolerance
- Starting dose of MMF is 1200mg/m2 in 2 divided doses, starting 2 days preoperative

  -Lower doses 900mg/m2 may be used with Tacrolimus

  -Higher doses up to 1800mg/m2 may be used when needed (immunologically) & tolerated (hematologically & GIT)
- The starting dose of MPS is 900mg/m2 in 2 divided doses
- Mycophenolate should be separated from Tacrolimus or Cyclosporine by 2hrs

mTORi

- mTORi (sirolimus or everolimus) based protocols may be used in low immunological risk patients.
- They are not recommended in the first month
- Lower risk with malignancy and certain infections as CMV
- May cause/ increase proteinuria and dyslipidemia (dose-dependent)
- Everolimus allows reduction in CNI dose (60% with CsA and 40% with tacrolimus)

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- May cause/ increase proteinuria and dyslipidemia (dose-dependent)
- Everolimus allows reduction in CNI dose (60% with CsA and 40% with tacrolimus)
- The starting dose of everolimus is 0.6mg/m2/dose twice daily and target trough level is 3-8ng/mL
- Sirolimus:

-Loading dose: 3mg/m2 in those <40Kg, 6 mg in adults/ >40Kg

-Daily dose: 1mg/m2 --------- 2mg

-Doses are adjusted to a target trough level of 5-15ng/mL

-Induction

-Early

-Maintenance

-ttt of rejection

-reduced?

Treatment of AR

- We recommend that all AR episodes be initially treated with pulse methylprednisolone (250 mg/m2 – 10 mg/Kg for three successive days).
- We recommend that subclinical AR be treated
- We suggest that first responsive AR episodes be followed by rapid tapering of oral steroids to or just above the maintenance dose, with optimizing trough CNI levels
- We suggest that increased immunosuppression be considered for patients with rebound, recurrent, difficult or antibody-mediated ARs

Treatment of AR

- AR is considered steroid resistant if there is no response 5-7 days after the first dose
- We recommend T cell depleting therapy in all steroid-resistant acute T cell mediated rejections,

  and suggest its use in very early, severe (Banff IIb or above) or rebound cases

Options for ABMR include steroids, plasma exchange, Rituximab and IVIG:

- **PE** is suggested at:

  -1.5 plasma volume daily x3 → 1 PV 3/wk to complete 8

  -Additional treatments may be indicated based on condition

  Replacement with 5% albumin unless plasma is otherwise indicated (coagulopathy, possibly within 48h of kidney biopsy)
- **IVIG** may be replaced at 100 mg/kg/dose/PE, 400 mg/Kg after the 3rd PE and/or be given in a total of 1-2g/Kg. The latter dose should be given after, not before, PE
- The recommended dose of **Rituximab** is 375 mg/m2/ dose for 2-4 doses at weekly- 2wk intervals.

  The first dose may be given after the third PE session; however, wait for a min 24 hrs (ideally 48 hrs) before next PE
- **We suggest intensifying baseline immunosuppression after treatment for ABMR**

Reduction of IS

-Induction
-Early
-Maintenance
-ttt of rejection
-reduced?

- Serious or life-threatening infections
- Infections resistant to treatment
- Certain infections eg EBV and BK
- Malignancy

Measures for infection prevention are equally important

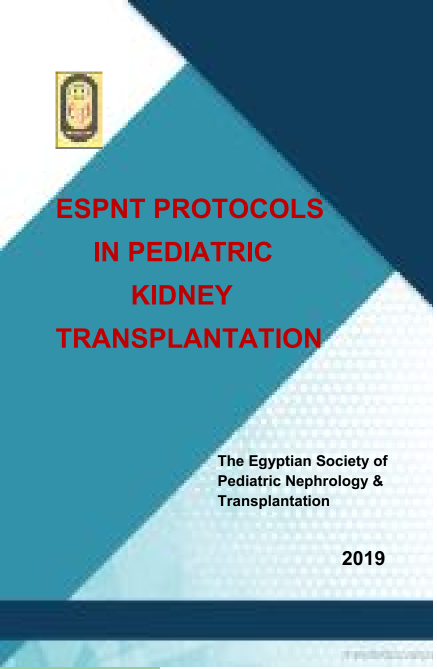
- General hygiene
- Minimize exposure
- Active immunoprophylaxis
- Chemoprophylaxis
- Early recognition and treatment

- **We recommend that reconsideration of immunosuppression be considered a part of the management of KTRs with malignant or premalignant conditions.**

Reduced quality of life from graft loss must be balanced against the potential for prolonging survival by reducing immunosuppression.

The future?

- Assessment of immur
- Protocols promoting t
- Bioartificial organs
- Gene-edited xenograf



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SURGICAL GUIDELINES

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KDIGO transplantation guidelines

Canadian guidelines: clinical guidelines for kidney transplantation (Vancouver coastal health, Providence heath care, BC transplantation)

British transplantation society and The renal association, UK guidelines
ERA-EDTA guidelines

Cochrane database of systematic reviews (Steroid withdrawal and CMV infection)

UpToDate (general principles of kidney transplantation in children, evaluation of recipient, evaluation of living donor, HLA matching, differential diagnosis of graft dysfunction, infections)

Nottingham children's hospital protocol

Lau K et al. Management of children after renal transplantation: highlights for general pediatricians (Review article). Transl Pediatr. 2012;1:35-

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Article Text

Article info

Original research

Guideline adaptation: an approach to enhance efficiency in guideline development and improve utilisation

PDF

B Fervers[1], J S Burgers[2, 3], R Voellinger[4], M Brouwers[5, 6], G P Browman[6, 7], I D Graham[6, 8, 9], M B Harrison[6, 10], J Latreille[6, 11, 12], N Mlika-Cabane[13], L Paquet[6, 11], L Zitzelsberger[6], B Burnand[4], The ADAPTE Collaboration*

Q1. A reduction in immunosuppression is recommended

A early after transplantation

B when there is high panel-reactive antibody

C during treatment of rejection

D in cases with BK virus infection

Q2. T-cell depleting antibodies

A are better avoided in transplants with a high immunological risk

B are the first line therapy for cell-mediated acute rejection

C are associated with fewer drug reactions than Basiliximab

D are associated with an increased risk of malignancy

Q3. Tacrolimus

A. is the preferred calcineurin inhibitor in those with impaired glucose tolerance

B. is the preferred calcineurin inhibitor with steroid minimization/ avoidance protocols

C. is preferrably given with mycophenolate at the same time of the day

D. dose should be increased when using mTORi

Thank You