

**INTERVENTIONS FOR
IDIOPATHIC STEROID-RESISTANT
NEPHROTIC SYNDROME IN CHILDREN
(Cochrane review)**

**Khoa Thận - Nội tiết
BV Nhi Đồng 2**

Objectives

To evaluate the benefits and harms of interventions used to treat **idiopathic steroid-resistant nephrotic syndrome** (SRNS) in children

Methods

Types of studies:

- all RCTs and quasi-RCTs,
- aged 3 mths to 18ys, with idiopathic SRNS.

Methods

Types of participants:

- aged 3 mths to 18ys with SRNS,
- renal biopsy diagnoses of MCD, MesPGN, FSGS.

Exclusion criteria:

- congenital NS, H-S nephritis, SLE
- membranous glomerulopathy,
mesangiocapillary glomerulonephritis

Methods

Types of outcome measures:

- number in complete, partial remission during and following therapy
- number reaching end-stage kidney disease
- adverse effects of therapy...

Results

In this 2010 update, this systematic review includes **14 studies** involving 449 evaluable patients.

These studies examined 09 therapeutic regimes for SRNS.

Definition of steroid resistance

- 6 studies: as persistent proteinuria of $>4\text{mg}/\text{m}^2/\text{h}$ after 4 wks (Lieberman 1996), 5 wks (Kleinknecht 1979), 6 wks (APN 2008), 8 wks (Bagga 2004, ISKDC 1970, 1974)
- 3 studies: as persistent proteinuria $>40\text{mg}/\text{m}^2/\text{h}$ after 5 or 8 wks of prednisone (Garin 1988, ISKDC 1996)
- 2 studies: proteinuria $>2\text{g}$ (Choudhry 2009) or $>1\text{g}/\text{m}^2/\text{d}$ (Mantan 2008) after 4 wks of daily prednisone
- 1 study: no response after 8 wks (Yi 2006)
- 2 studies did not define steroid resistance (Chongviriyaphan 1999, Elhence 1994)

Cycloporin vs placebo/no treatment

{3 studies (Garin 1988, Lieberman 1996, Ponticelli 1993a), 49 children:
RR 7.66, 95% CI 1.06 to 55,34.

Grade of evidence: low quality, small patient numbers}

- **significantly increased** the number of children
complete remission
- All renal pathologies, follow-up 3-12mths

Cycloporin vs placebo/no treatment

(2 studies, 33 patients: RR 5.83, 95% CI 0.75 to 45.09

Grade of evidence: low quality, small patient numbers)

In the subgroup of children with FSGS,

the summary estimate **was similar** to that for the analysis for all renal pathologies

CsA vs IV cyclophosphamide

1 study (APN 2008), 32 children: RR 3.40, 95% CI 1.12 to 10.28

Grade of evidence: low quality, small patient numbers,
follow-up for only 12wks.

significantly increased the number with complete
or partial remission

Oral cyclophosphamide + prednisone vs prednisone alone

2 studies (ISKDC 1974, ISKDC 1996), 84 children: RR 1.06, 95% CI
0.61 to 1.87

or in those with FSGS: 2 studies, 63 children: RR 1.01, 95% CI 0.43
to 2.37)

There was **no significant difference**

IV vs oral cyclophosphamide

1 study (Elhence 1994) 11 children RR 3.13, 95% CI 0.81 to 12.06.

Grade of evidence: very low quality, small patient numbers, large loss to follow-up

There was **no significant difference**.

Although 7/7 children with MCD received IV cyclophosphamide achieved complete remission compared with 1/4 children given oral, but small numbers of children studied

IV cyclophosphamide vs oral cyclophosphamide + IV dexamethasone

1 study (Mantan 2008), 49 children: RR 1.13, 95% CI 0.65 to 1.96

Grade of evidence: very low quality, small numbers of events)

There was **no significant difference** at 6 mths

Tacrolimus vs cyclosporine

1 study (Choudhry 2009), 41 children: RR 0.86, 95% CI 0.44 to 1.66

Grade of evidence: low quality, small patient numbers,
no blinding)

There was **no significant difference** at 6 mths,
12 mths.

Azathioprine + prednisone vs prednisone alone

1 study (ISKDC 1970), 31 children: RR 0.94, 95% CI 0.15 to 5.84

There was **no significant difference**.

ACEi

2 studies (Bagga 2004: 25 children; Yi 2006: 55 children).

Grade of evidence in the fosinopril: low quality, small patient numbers and short follow-up.

ACEi (Enalapril and fosinopril) significantly **reduced proteinuria** in children with SRNS

Enalapril: high vs low dose

- **Low dose enalapril** (0.2mg/kg/d) reduced median urinary albumine/creatinine ratio from 3.9 to 2.3, but the difference was not significant.
- **High dose enalapril** (0.6 mg/kg/d) reduced median urinary albumine/creatinine ratio from 5.2 to 2.5, but the difference was not significant.

(Bagga 2004, 25 children)

Enalapril

- The urinary albumin/creatinin reduction between the beginning and end of treatment **was significantly lower with low dose enalapril compared with high dose enalapril**
- These results were not able to be meta-analysed

Mycophenolate mofetil (MMF)

- MMF** is also used to treat SRNS with variable results
- The results of the NIH sponsored study comparing **MMF vs IV methylprednisolone + CsA** in children and adults with FSGS are awaited

Rituximab

The anti CD-20 monoclonal antibody, rituximab, has been used in some children with SRNS and FSGS resistant to other therapies with **variable results** (Prytula 2010)

Conclusions

1/ CsA may increase the number of children who achieve complete remission in SRNS.

2/ ACEi significantly reduce the degree of proteinuria.

Quality of the evidence

Studies included in this systematic review were small, often of poor quality and addressed several different therapeutic regimes, which limited the opportunities for meta-analysis