TACROLIMUS IN NEPHROTIC SYNDROME RESISTANT TO FIRST LINE THERAPY IN ADULTS: A PROSPECTIVE STUDY

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Objectives:

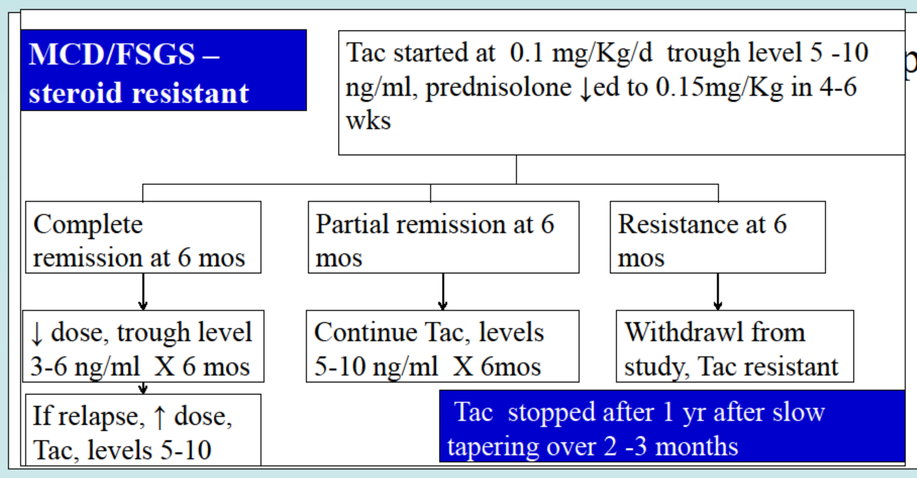
- Management of steroid resistant (SR) minimal change disease (MCD), FSGS and modified Ponticelli regimen (alternating monthly cycles of steroids and cyclophosphamide for 6 months) resistant membranous glomerulopathy (MGN) is a challenging task.
- Is Tacrolimus (Tac) effective in this situation without serious adverse effects ?
- This prospective study was done to to assess the response to Tacrolimus therapy and toxicity of the drug at end of 1 year of Tacrolimus.

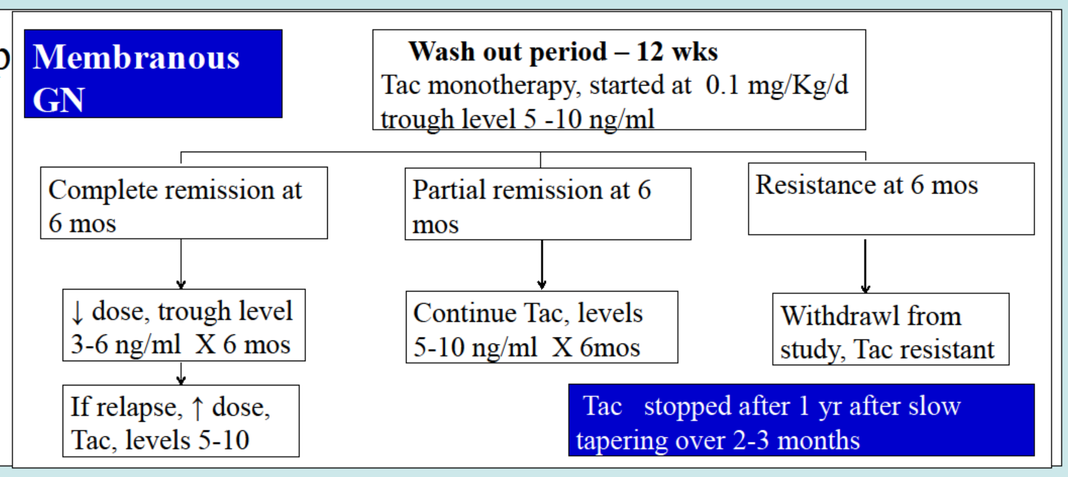
Methods:

Study design: Prospective observational
Study period: Jan 2011- Dec 2012
Inclusion criteria: Adult (18-60 yrs) steroid resistant biopsy proven MCD/FSGS, modified ponticelli regimen resistant MGN
Exclusion criteria: Secondary nephrotic syndrome
eGFR < 70 ml/mt
Abnormal liver function tests, DM
Earler therapy with CyA, MMF
Who did not undergo kidney biopsy

Definitions: **Nephrotic syndrome:** Proteinuria (>3.5g/day) ,hypoalbuminemia (<3.5g/dl), hyperlipidemia and oedema
Steroid-resistant FSGS/MCD- Persistence of nephrotic syndrome despite prednisone 1 mg/kg/d or 2 mg/kg every other day for >4 months.
Modified ponticelli regimen resistant IMGN: Persistance of nephrotic syndrome at the end of 6 months of therapy with alternating cycles of steroids and cyclophosphamide.
Complete remission - Reduction of proteinuria to <0.3 g/d and normal serum creatinine and serum albumin >3.5 g/dl .
Partial remission- Reduction of proteinuria to 0.3–3.5 g/d and stable serum creatinine (change <25%) or decrease>50% from baseline, and stable serum creatinine
Tac related nephrotoxicity : > 25% rise in serum creatinine from baseline

Outcomes
Primary outcome: Complete / partial remission at the end of therapy
Secondary outcome: Drug toxicity including nephrotoxicity





Results:

❖31 pts (M:F 21:10) completed 12 months (FSGS/ MCD=24, MGN=07)
❖Mean age 26.7 10.5 and 43.1 8.9 yrs in FSGS/MCD & MGN respectively
❖Response rate: 09 (29%) complete remission and 05 (16.1%) partial remission in FSGS/MCD + MGN
❖ Mean duration to remission: 16 6.9 weeks (12-24 weeks)
❖ ***All pts of MCD responded to Tac***
❖**FSGS variants**: FSGS-NOS 16, Cellular FSGS 04, Collapsing 01, Tip 01
❖FSGS variants response: Comp / partial remission - FSGS NOS: 7 (43.7%) , Cellular: 1(25%) , Tip variant 1 (100%)

	FSGS/MCD (n=24)	MGN (n=7)
24 hr U proteins (gm/day) (baseline)	3.55 2.67	6.85 3.94
24 hr U proteins (gm/day) (at 6 mos)	2.0 1.2	2.09 2.67
24 hr U proteins (gm/day) (at12mos)	1.68 1.35	3.8 5.7
S creatinine (mg/dl) (baseline)	0.91 0.27	0.88 0.16
S creatinine (mg/dl) (post treatment)	0.95 0.43	1.11 0.29
S albumin (gm/dl) (baseline)	2.57 0.81	1.97 0.48
S albumin (gm/dl) (post treatment)	3.3 0.61	3.33 0.58

	FSGS/MCD (n=24)	MGN (n=7)
Complete remission	08 (33%)	01 (14.2%)
Partial Remission	03 (12.5%)	02 (28.5%)
Resistant	13 (54.1%)	04 (57.3%)
Time to respond (weeks)	17.3 4.7 (12-24)	16.6 7.3 (12-24)
Relapse within 3 months after stopping Tac	06 (25%)	01 (14.2%)

	FSGS/MCD (24)	MGN (7)
Reversible nephrotoxicity	05 (21%)	01 (14.2%)
Impaired glucose tolerance	01 (4.1%)	02 (28.5%)
Neurotoxicity (tremors/headache)	02 (8.3%)	01 (14.2%)
Diarrhoea	01 (4.1%)	00 (00)
Infection	02 (8.2%)	01 (14.2%)
Worsening HT (≥20 mm Hg↑ in SBP or DBP)	04 (16.4%)	01 (14.2%)
Cosmetic (hirsuitism, gum hyperplasia)	02 (8.4%)	00(00)

Conclusions:

Tac is effective in FSGS,MCD & MGN patients resistant to first line therapy. However it needs strict kidney function monitoring due to its potential nephrotoxicity.