Manejo clínico neonatal del síndrome nefrótico congénito

7° Congreso Argentino de Nefrología Pediátrica
Sociedad Argentina de Pediatría

Dr. Javier Ruscasso
Servicio de Nefrología. Hospital Sor María Ludovica- La Plata.

Archives of Disease in Childhood, 1976, **51**, 344.

Congenital nephrotic syndrome of Finnish type

Study of 75 patients

NIILO-PEKKA HUTTUNEN

From the Children's Hospital, University of Helsinki, Finland

Huttunen, N-P. (1976). *Archives of Disease in Childhood*, **51**, 344. **Congenital nephrotic syndrome of Finnish type: study of 75 patients.** Seventy-five patients with congenital nephrotic syndrome of Finnish type were identified in Finland in the period 1965-1973, giving an incidence of $12 \cdot 2/10^5$. A large placenta and proteinuria from birth are the hallmarks of the disease.

About one-quarter of the patients had oedema and/or abdominal distension at birth and in all cases the full nephrotic syndrome was documented before 2 months. More than half of the patients died before 6 months and none lived longer than 2 years 3 months. A slight rise in blood urea nitrogen or serum creatinine levels occurred in 14 cases, but in none of these did a frank uraemia develop before death. Infection appeared to be the immediate cause of death in 31% of the cases; in 43% no cause of death other than congenital nephrotic syndrome could be shown. Thrombi in large vessels were found in 11 out of 58 necropsies.

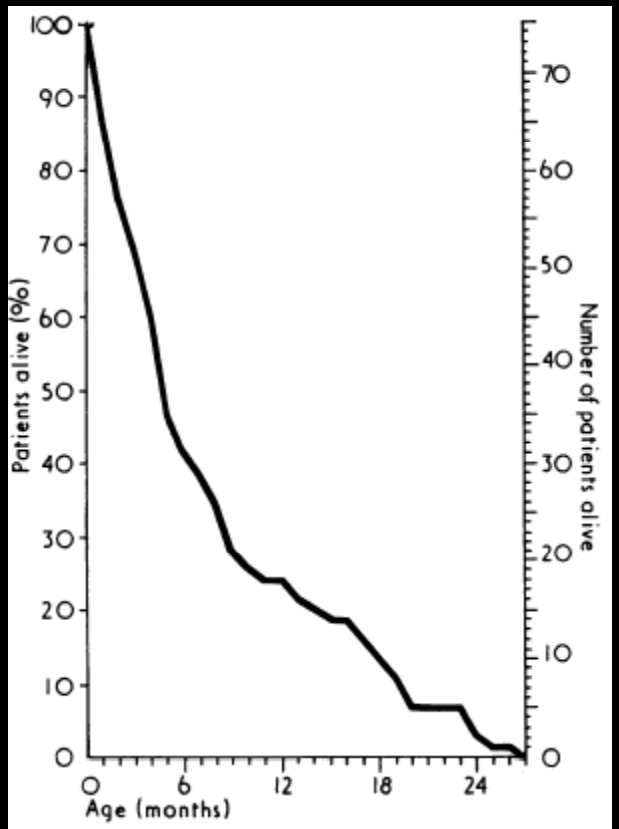


FIG. 3.—*Length of survival of 75 CNF infants*

Immediate cause of death of CNF patients. Diagnosis is based on clinical and necropsy findings in 58 cases and on clinical findings alone in 17

Cause of death	No. of cases	%
Infection	23	31
Sepsis	6	
Pneumonia	6	
Peritonitis	4	
Meningitis	2	
Other	5	
Transplantation trial	9	12
Thrombotic complication	4	5
Cerebral vein thrombosis	1	
Pulmonary artery thrombosis	1	
Pulmonary embolism	1	
Sagittal sinus thrombosis	1	
Miscellaneous	7	9
Aspiration	1	
Cerebral haemorrhage	1	
Interstitial occlusion	1	
Kernicterus	1	
Pulmonary haemorrhage	1	
Pulmonary atelectasis	1	
Subarachnoid haemorrhage	1	
CNF alone	32	43
Total	75	100

Pediatr Nephrol (1995) 9: 87–93

Pediatric Nephrology

Practical pediatric nephrology

Management of congenital nephrotic syndrome of the Finnish type

Christer Holmberg, Marjatta Antikainen, Kai Rönnholm, Marja Ala-Houhala, and Hannu Jalanko

Division of Paediatric Nephrology, Children's Hospital, University of Helsinki, Stenbäckinkatu 11, SF-00290, Helsinki, Finland

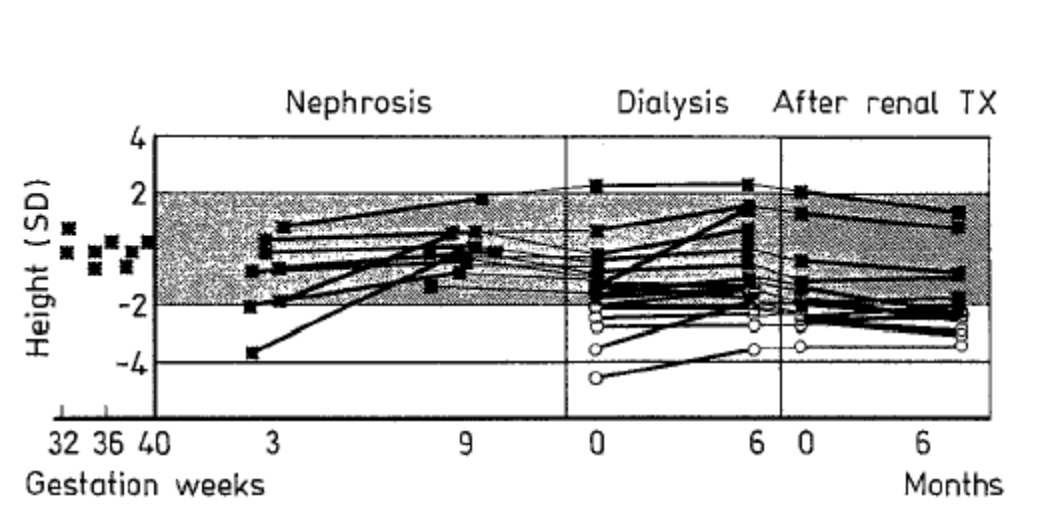


Table 1. Treatment recommendations for congenital nephrotic syndrome of the Finnish type (CNF) patients during their 1st year of life

Albumin substitution	
	3–4 g/kg per day i.v. with frusemide 0.5 mg/kg (in four 2-h infusions during the 1st month and in one 6 to 8-h infusion later)
Nutrition	
	130 kcal of energy and 4 g protein/kg per day (in addition to i.v. albumin substitution) (10%–14% protein, 40%–50% fat and 40%–50% carbohydrate energy)
	15 ml rape seed oil and 2 ml fish oil
	fluids 100–130 ml/kg per day
	vitamin D_2 (2,000 IU/day), water-soluble vitamins (according to RDA), magnesium (40–60 mg/day) and calcium (500 mg <6. 750 mg 6–12 and 1,000 mg >12 months of age)
Additional medication	
	thyroxine (from birth, adjusted according to TSH)
	sodium warfarin (to keep PTT at 20%–30% of normal) (AT III 50 IU/kg i.v. 1 h before surgical or vascular procedures)
	prompt antibiotic therapy for septic infections

Pediatr Nephrol (1995) 9: 87–93

Management of CCPD after nephrectomy

Though normal growth can be achieved with the previously described therapy (Fig. 2), CNF children are still malnourished and have hypoproteinaemia [31]. To optimise treatment, we perform bilateral nephrectomy and start CCPD when a weight of 7 kg has been reached. The aims of this therapy are to end the proteinuria and correct the protein and lipid status prior to renal transplantation and to further improve the child's nutritional state. Thus, the conditions for successful renal transplantation will be met.

Pediatr Nephrol (1995) 9: 87–93

Pediatr Nephrol (2013) 28:2313–2321
DOI 10.1007/s00467-013-2584-7

ORIGINAL ARTICLE

Congenital nephrotic syndrome with prolonged renal survival without renal replacement therapy

William Wong · Maxwell Clarke Morris · Tonya Kara

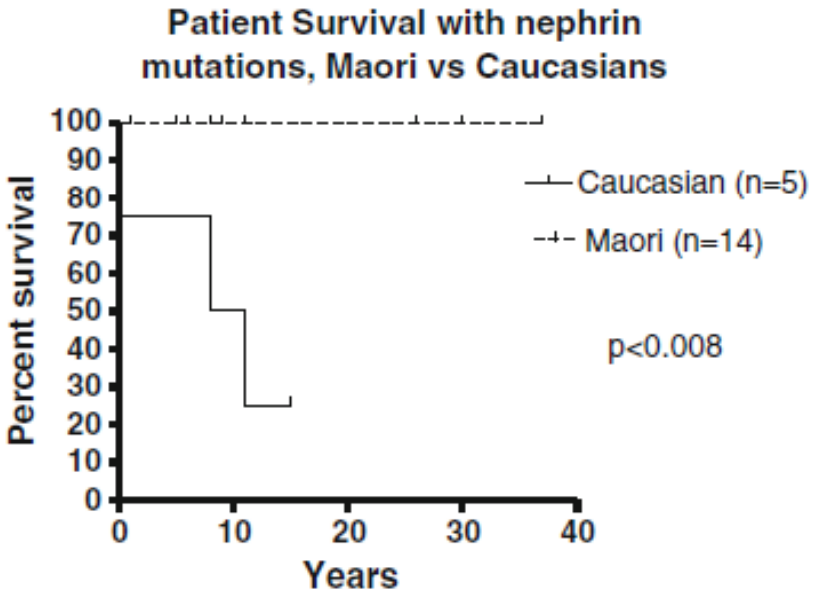
Abstract

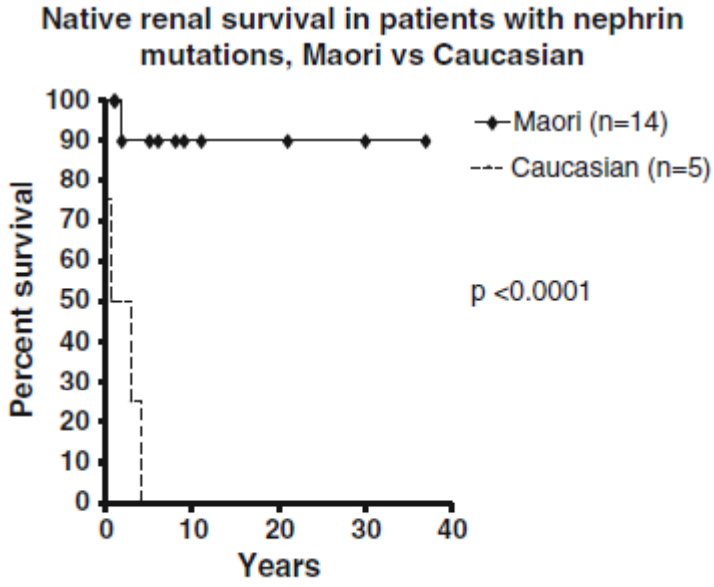
Background Infants with congenital nephrotic syndrome (CNS) develop severe nephrotic syndrome that is resistant to medical therapy, and bilateral nephrectomy is recommended toward the end of the first year of life followed by renal replacement therapy. CNS infants in New Zealand have been observed to exhibit a different course to those with the typical Finnish mutation.

Methods A database of CNS children at our center was retrospectively examined. All cases diagnosed between 1975 and 2011 were reviewed. Demographic data, clinical features, genetic mutations, treatment, and outcome were extracted from clinical records.

Results Thirty-five patients with CNS, 23 children of Maori descent, and 12 Caucasians. Fourteen had died of either bacterial sepsis or intracranial thrombosis. Maori children had displayed a highly variable and protracted timeline to end-stage renal disease (ESRD) with median renal survival of 30 years versus 0.7 years in Caucasian patients. Mutation analysis of *NPHS1* showed a founder mutation in the Maori population.

Conclusions Congenital nephrotic syndrome in New Zealand Maori children exhibit a different clinical course to Caucasian children and have a mutation that was first described in this ethnic group.





Pediatr Nephrol (2013) 28:2313–2321

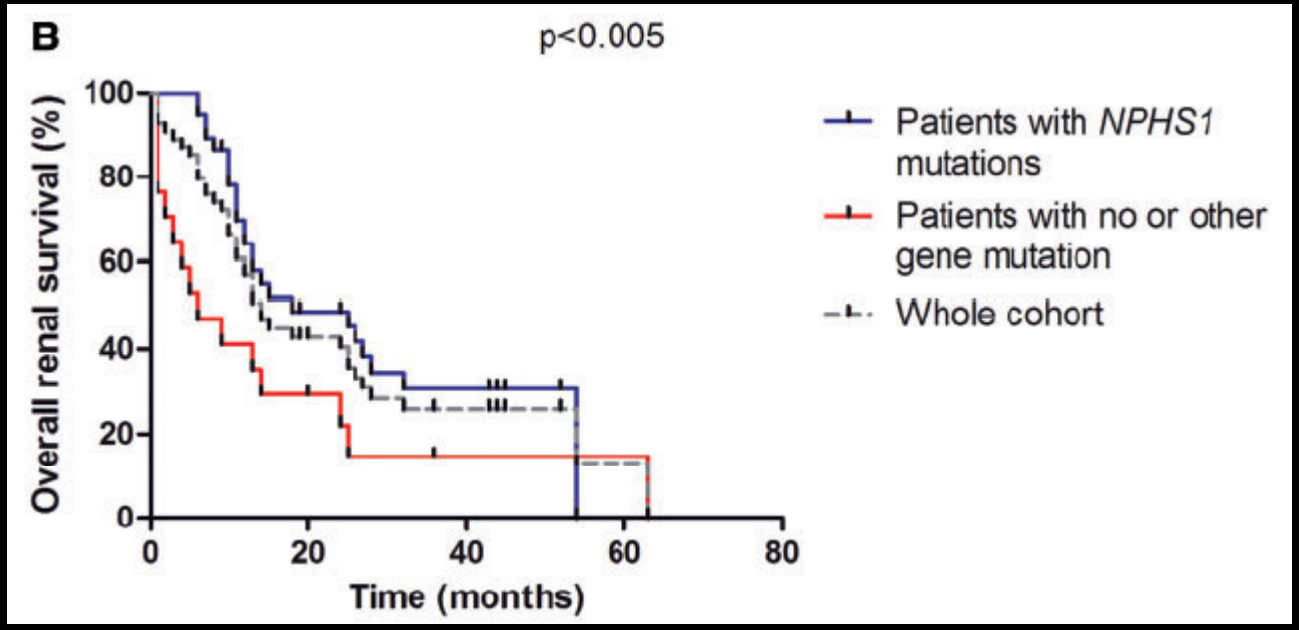
Nephrol Dial Transplant (2018) 1–10
doi: 10.1093/ndt/gfy015

ndt
Nephrology Dialysis Transplantation

Treatment and outcome of congenital nephrotic syndrome

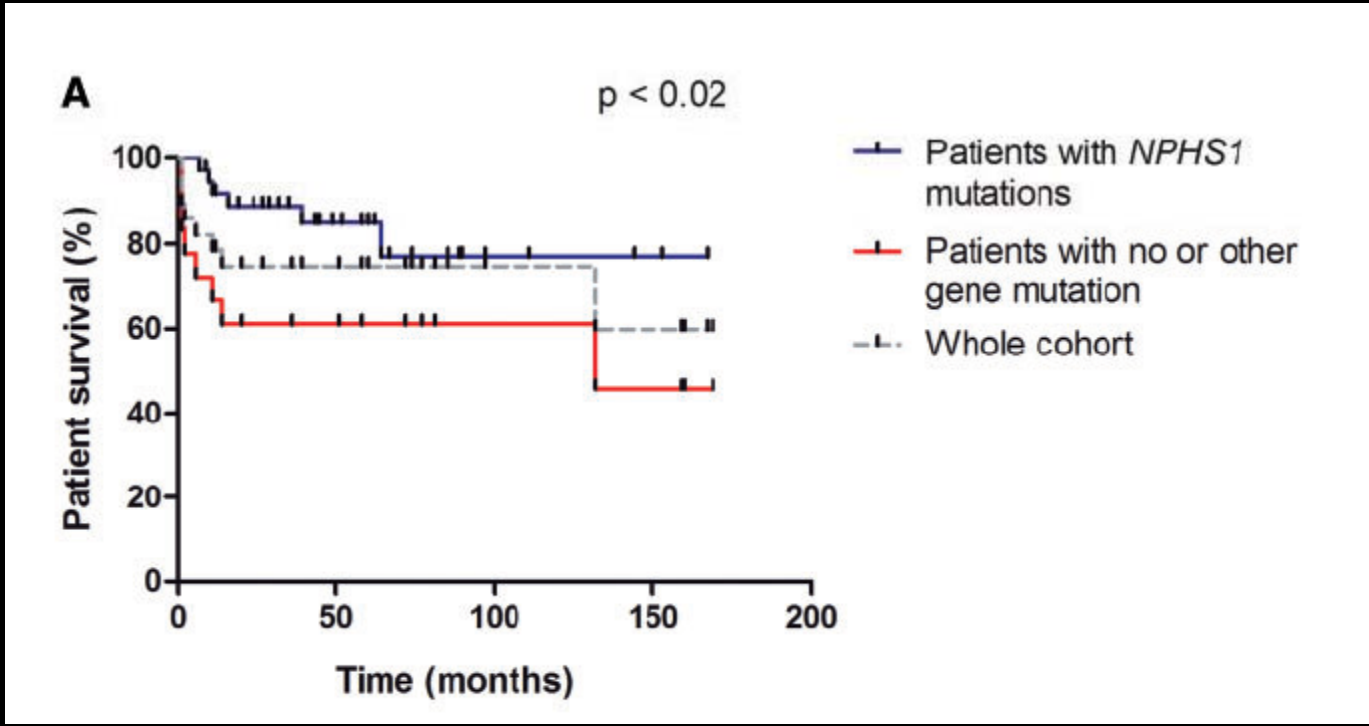
Sandra Bérody[1], Laurence Heidet[1,2,3], Olivier Gribouval[3], Jérome Harambat[4], Patrick Niaudet[1,2,3], Veronique Baudouin[2,5], Justine Bacchetta[6], Bernard Boudaillez[7], Maud Dehennault[8], Loïc de Parscau[9], Olivier Dunand[10], Hugues Flodrops[11], Marc Fila[12], Arnaud Garnier[13], Ferielle Louillet[14], Marie-Alice Macher[5], Adrien May[15], Elodie Merieau[16], Françoise Monceaux[17], Christine Pietrement[18], Caroline Rousset-Rouvière[19], Gwenaëlle Roussey[20], Sophie Taque[21], Julie Tenenbaum[12], Tim Ulinski[2,22], Rachel Vieux[23], Ariane Zaloszyc[24], Vincent Morinière[3], Rémi Salomon[1,2,3] and Olivia Boyer[1,2,3]

Sobrevida renal general: con mutación NPHS1 vs. otras o ninguna mutación.

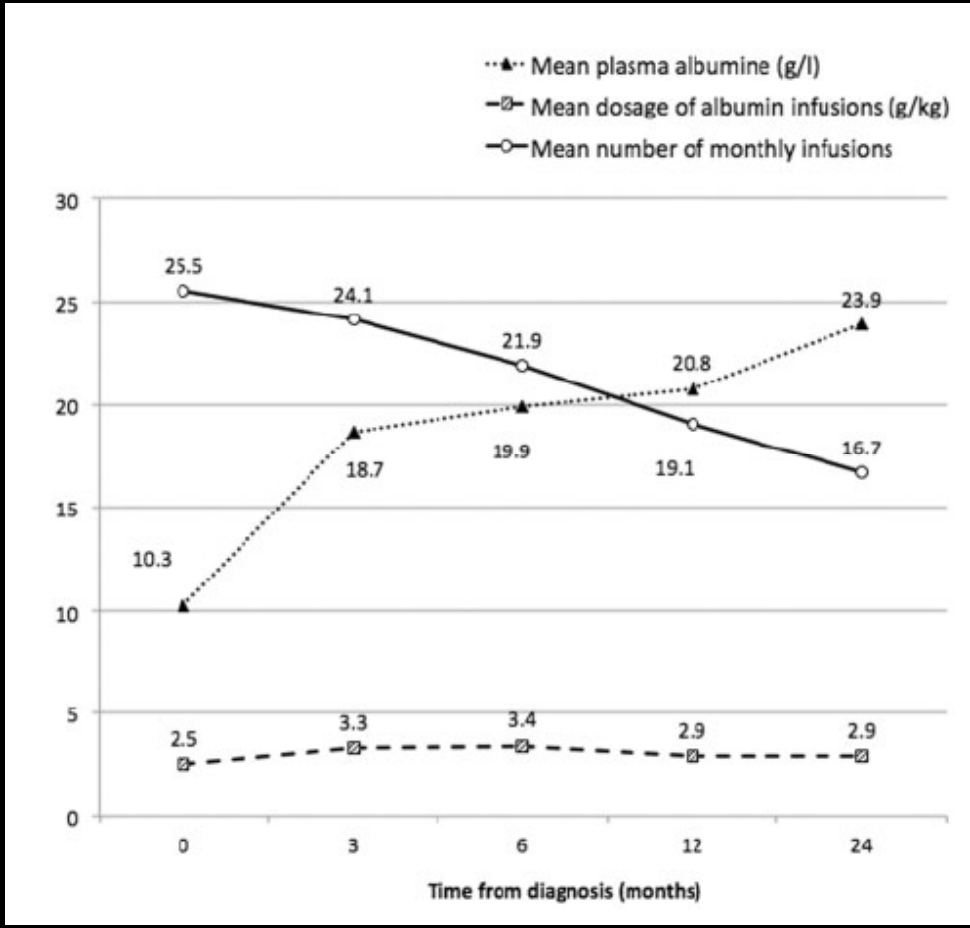


Nephrol Dial Transplant (2018) 1–10

Sobrevida del paciente: con mutación NPHS1 vs, otras o ninguna mutación.



Nephrol Dial Transplant (2018) 1–10



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Nephrology Dialysis Transplantation

Treatment and outcome of congenital nephrotic syndrome

- Conclusiones:

1- Sobrevida libre de IRCT en 2/3 de los pacientes al año de vida y la mitad a los 2 años,

2- Una significativa reducción o aún discontinuación de las infusiones de albúmina permitiendo un cuidado ambulatorio en un subgrupo de pacientes

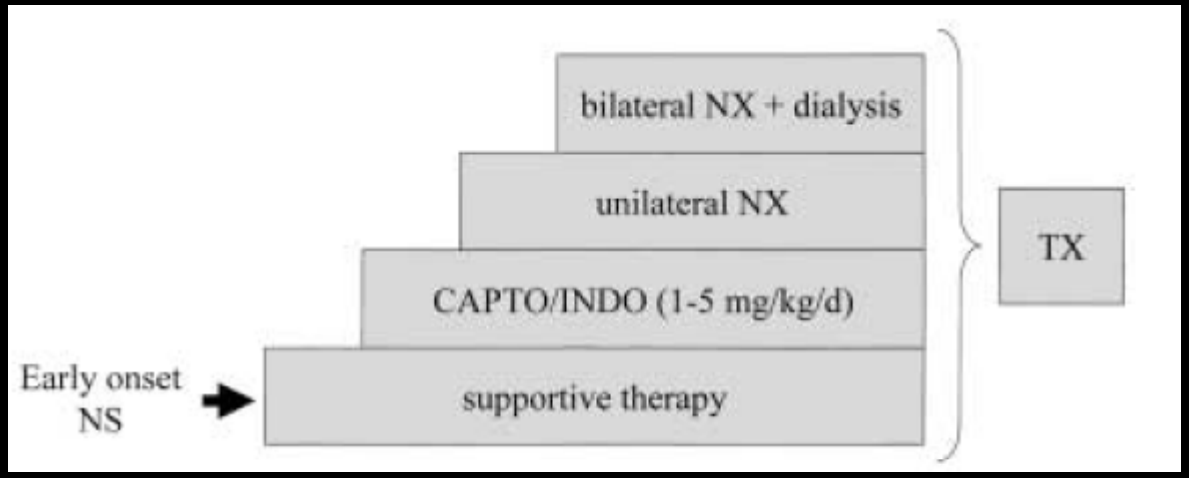
Estos resultados subrayan la necesidad de nuevas guías terapéuticas para pacientes con SNC.

Pediatr Nephrol (2000) 14:1077–1082

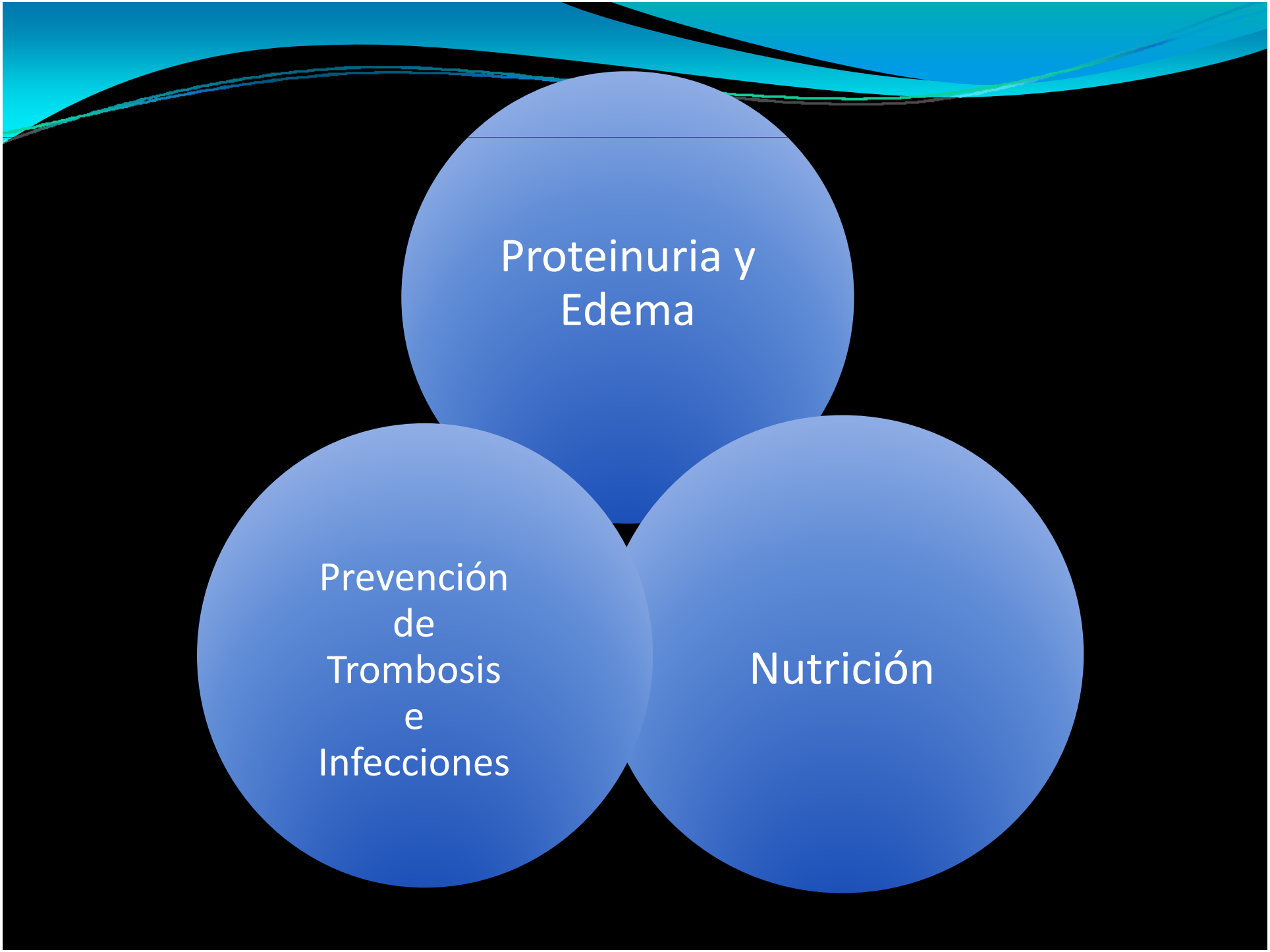
CLINICAL NEPHROLOGY / ORIGINAL ARTICLE

Christoph Licht · Frank Eifinger · Mostafa Gharib
Gisela Offner · Dietrich V. Michalk · Uwe Querfeld

A stepwise approach to the treatment of early onset nephrotic syndrome



El objetivo de las decisiones terapéuticas es llegar al trasplante renal.


Proteinuria y Edema
Prevención de Trombosis e Infecciones
Nutrición

Proteinuria y Edema

Medicación antiproteinurica

- ACE inhibidores/ARA II
- Indometacina

Medicación antiproteinurica

- ACE inhibidores/AT II
- Indometacina

Clinical and laboratory observations

Successful treatment of Finnish congenital nephrotic syndrome with captopril and indomethacin

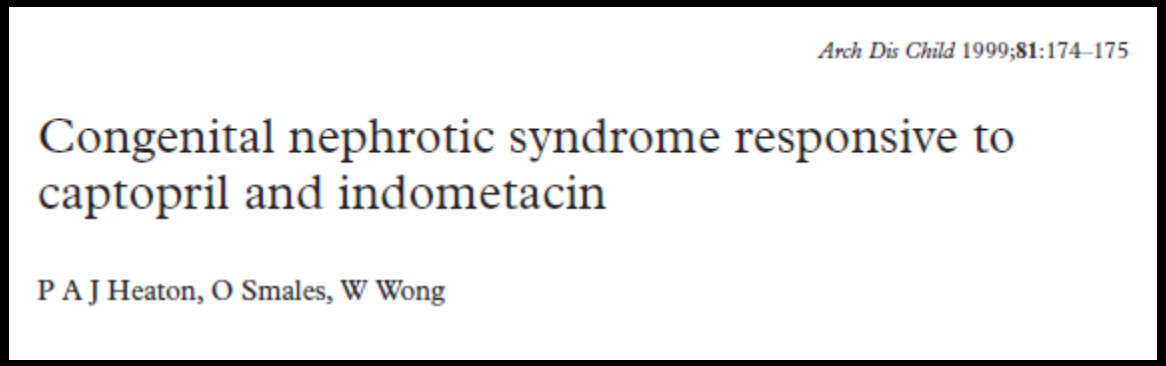
A. Pomeranz, MD, B. Wolach, MD, J. Bernheim, MD, Z. Korzets, MBBS, and J. Bernheim, MD

From the Departments of Nephrology, Pediatrics, and Pathology, Meir General Hospital, Kfar Saba, and the Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

Two infants with biopsy-proven microcystic Finnish congenital nephrotic syndrome (onset at birth) were treated with a combination of captopril and indomethacin for 2½ and 2 years, respectively; they had a marked reduction of urinary protein excretion without further need for albumin infusions. One infant has end-stage renal disease; the other infant's glomerular filtration rate has remained within normal limits. (J PEDIATR 1995;126:140-2)

Medicación antiproteinurica

- ACE inhibidores/AT II
- Indometacina



Arch Dis Child 1999;**81**:174–175

Congenital nephrotic syndrome responsive to captopril and indometacin

P A J Heaton, O Smales, W Wong

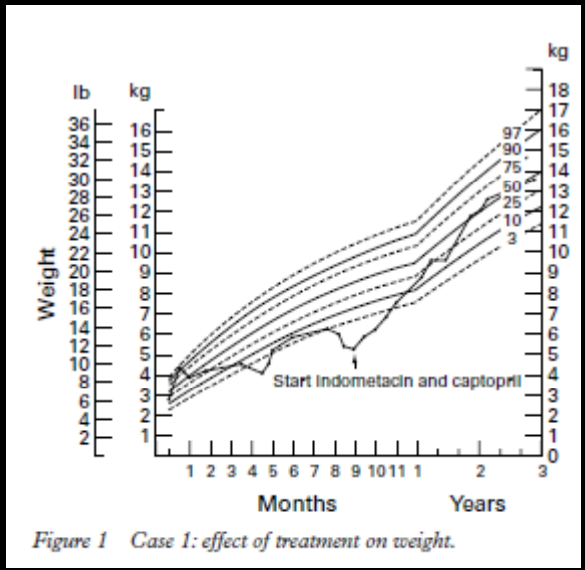


Figure 1 Case 1: effect of treatment on weight.

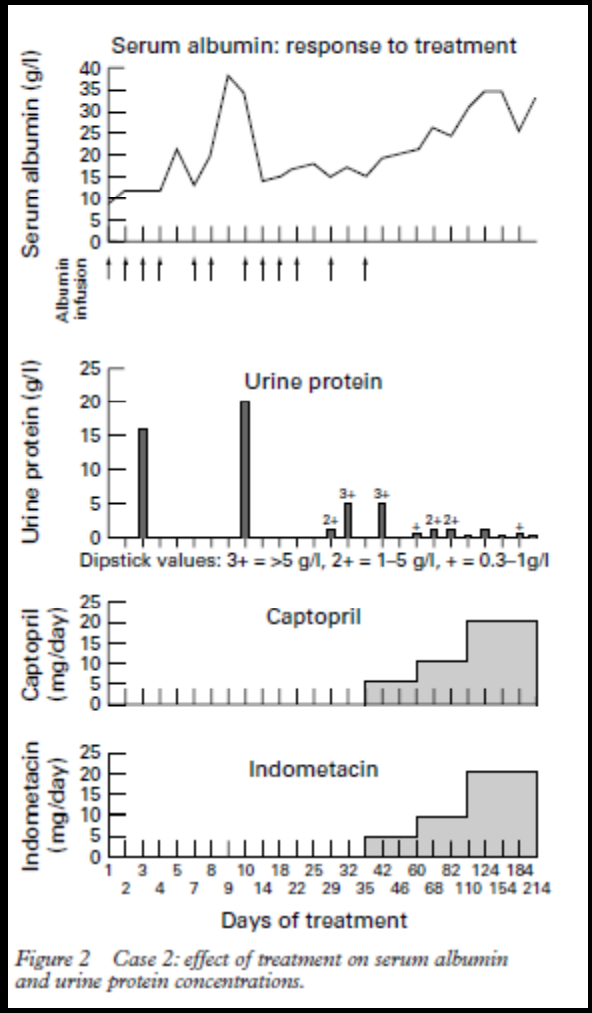


Figure 2 Case 2: effect of treatment on serum albumin and urine protein concentrations.

Arch Dis Child 1999;**81**:174–175

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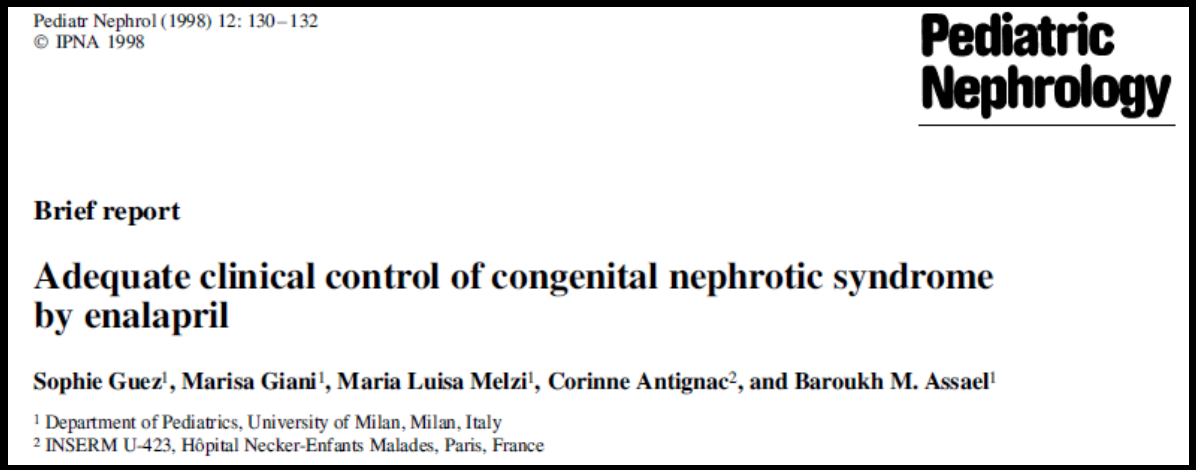


Pediatr Nephrol (1998) 12: 130–132

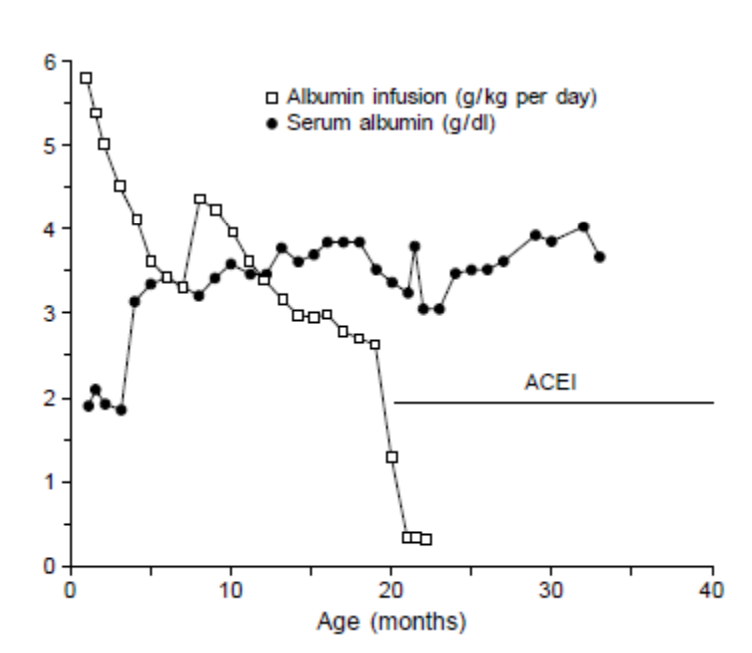
Pediatric Nephrology

Brief report

Adequate clinical control of congenital nephrotic syndrome by enalapril

Sophie Guez[1], Marisa Giani[1], Maria Luisa Melzi[1], Corinne Antignac[2], and Baroukh M. Assael[1]

[1] Department of Pediatrics, University of Milan, Milan, Italy
[2] INSERM U-423, Hôpital Necker-Enfants Malades, Paris, France



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Pediatric Nephrology

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Proteinuria y Edema

Albumina

- Infusión de albúmina al 20%.
- 3-4 gr/kg/día en casos de SN severo.
- 1-3 infusiones diarias (utilizar catéteres venosos profundos colocados a las 2-3 semanas de vida).
- Furosemida (0,5 mg/k) junto con la albúmina.

Nutrición

- Elevada ingesta energética: 130 kcal/kg/día.
- Elevada ingesta proteica: 3-4 gr/kg/día. Adición de caseína a la leche..
- Suplemento de Vitamina D o Calcidiol.
- Polivitaminicos.
- Calcio y magnesio.
- Sonda nasogastrica.

Prevención de Trombosis e Infecciones

- Anticoagulación: warfarina/aspirina.
- Antibióticos profilácticos: penicilina (controversial)
- Gamaglobulina EV (controversial)

Terapia accesoria

- Tiroxina.
- Eritropoyetina.
- Vacunas: luego de la nefrectomía.

Nefrectomía unilateral o bilateral

- Reducción de la necesidad y frecuencia de infusiones de albúmina.
- Cuando existen pérdidas masivas (<100 gr/l) se plantea nefrectomía bilateral.

Diálisis

- Para casos severos se plantea realizar nefrectomía bilateral e ingreso en terapia de reemplazo renal (DP o HD) con peso cercano a los 7 kg.
- Colocar catéter de DP 2 semanas previas a la nefrectomía. Corregir hernias inguinales (comunes en estos pacientes).
- Modificar dieta y aportes (de paciente proteinurico a paciente urémico)

Medicación inmunosupresora

- Escasos estudios que evalúen el tema gran escala.
- Existen reportes de escaso pacientes con mutaciones NPHS1, NPHS2, WT1 y PLCE1 que muestran mejoría después de terapia inmunosupresora, de mecanismo desconocido.
- En general no está indicado.

Trasplante renal

- Pronóstico excelente.
- Recurrencia de SNC es excepcional (desarrollo de anticuerpos antinefrina después del trasplante). Utilizar plasmaféresis, ciclofosfamida o anticuerpos Anti CD20.
- A menudo se trasplantan con escaso peso.
- Procedimiento técnicamente dificultoso.
- Incremento del riesgo de eventos trombóticos.

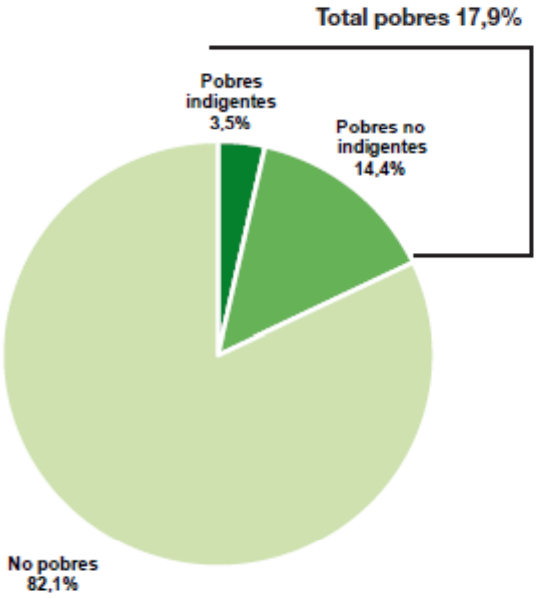
Aspecto social

Incidencia de la pobreza y de la indigencia en 31 aglomerados urbanos

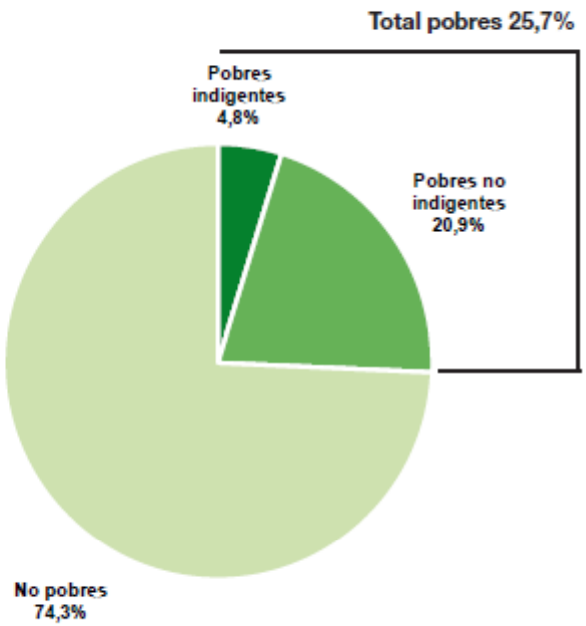
Segundo semestre de 2017

Gráfico 1. Resultados del segundo semestre de 2017

Incidencia de Pobreza e indigencia. Hogares



Incidencia de Pobreza e indigencia. Personas



Población en viviendas particulares por tipo de cobertura de salud, según grupo de edad y sexo. Total del país. Año 2010

Grupo de edad y sexo	Población en viviendas particulares					
	Total	Tipo de cobertura de salud				
		Obra social ([1])	Prepaga a través de obra social	Prepaga sólo por contratación voluntaria	Programas y planes estatales de salud	No tiene obra social, prepaga o plan estatal
Total	**39.671.131**	**18.410.964**	**4.192.827**	**2.029.716**	**722.942**	**14.314.682**
0-4	3.326.197	1.233.328	361.540	143.378	107.171	1.480.780

36%

44%

Conclusiones:

- La historia natural de los pacientes con SNC fuera de Finlandia tiene un curso evolutivo mas lento.
- Los requerimientos de albumina EV. disminuyen con el tiempo.
- El objetivo de las decisiones terapéuticas es llegar al trasplante renal
- Terapia escalonada.
- Las medidas para poder cumplir con este objetivo son control de:

1- Proteinuria y edema

Infusión de albúmina al 20%.

3-4 gr/kg/día en casos de SN severo. 1-3 infusiones diarias (utilizar catéteres venosos profundos desde la 2-3 semana de vida). Furosemida (0,5 mg/k) junto con la albúmina.

ACE inhibidores/AT II

Indometacina

2- Nutrición.

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Elevada ingesta proteica: 3-4 gr/kg/día. Adición de caseína.

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Suplemento de Vitamina D o Calcidiol. Polivitaminicos. Calcio y magnesio.

3- Prevención de trombosis e infecciones.

Anticoagulación: warfarina/aspirina.

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Gamaglobulina EV (controversial)

Conclusiones:

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  - Vacunas: luego de la nefrectomía.
- Nefrectomía unilateral o bilateral
- Diálisis
  - Para casos severos nefrectomía bilateral e ingreso en terapia de reemplazo renal (DP o HD) con peso cercano a los 7 kg.
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  - Procedimiento técnicamente dificultoso.
  - Incremento del riesgo de eventos trombóticos.

Primer día de Jardín de Infantes

Muchas Gracias