The treatment of steroid sensitive nephrotic syndrome

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Introduction

The cause of steroid sensitive nephrotic syndrome (SSNS) remains unknown. Evidence suggests an immunological origin\(^1\). An abnormality in T cell function is also postulated\(^2\). Several immunosuppressive agents and levamisole, a drug known to alter T cell function have been used in the treatment of this condition.

Prednisolone was first used in the treatment of minimal change nephrotic syndrome (MCNS) in 1956 and is still considered the drug of choice, but a consensus has yet not been reached regarding the best treatment regime for the initial episode\(^3\). There have been some recent developments in the search that continues for the best treatment regime that induces a remission, prevents relapses and has minimum side effects.

Definitions

It is important to agree on standard definitions used before discussing the treatment options available.

**Steroid sensitive** - nephrotic syndrome is considered steroid sensitive (or steroid responsive) if there is response within 4 weeks of commencing a standard course of prednisolone.

**Steroid resistant** - Failure to respond to standard steroid therapy within 4 weeks.

**Response to treatment (Remission)** - Disappearance of proteinuria (negative or trace) for 3 consecutive days.

**Relapse** - Recurrence of proteinuria at ++ or greater for 3 consecutive days, or recurrence of proteinuria at any level with hypoalbunaemia and oedema.

**Frequent relapses** - 2 or more relapses occurring within 6 months of completing the initial course of treatment or if 3 or more relapses occur within any 12 month period.

**Steroid dependent** - Two or more consecutive relapses occurring during steroid treatment or within 2 weeks of stopping treatment.

**Steroid therapy of the initial episode**

The steroid regime arbitrarily chosen by the International Study of Kidney Diseases in Children (ISKDC) in 1967 is still widely used for the treatment of the first episode of nephrotic syndrome. There is increasing evidence now, to suggest that this regime is not the best.

Studies done over the past 2 decades have demonstrated a significant increase in the number of children in remission in the first 6-24 months of follow up after receiving 3-6 months of prednisolone for the initial episode when compared with children receiving the standard ISKDC regime\(^7,9,10\).

**ISKDC Regime**

- 60 mg/ m\(^2\) / day - in 2-3 divided doses x 4 weeks and not exceeding 80 mg /day
- 40 mg / m\(^2\) / day - given as a single dose for 3 consecutive days out of 7 x 4 weeks

*Now modified to*

- 40 mg / m\(^2\) / 48h - given as a single dose on alternate days x 4 weeks

as it was proven to be more effective than treatment given on consecutive days\(^4\).
WHAT WE NOW KNOW

- There is yet insufficient data to suggest that other steroid preparations are superior to prednisolone in inducing or maintaining remissions.
- A single morning dose of prednisolone given daily is as effective as divided doses given daily, in inducing a remission⁵.
- A single dose given in the morning has an added advantage of minimizing pituitary adrenal axis suppression.
- The number of relapses occurring in the first 6 months is highly predictive of the subsequent course of the disease⁶.
- The duration of steroid therapy of the first episode of disease has an influence on the subsequent course of the disease⁷,⁸,⁹,¹⁰.
- A longer duration of treatment is more important than the total dose of prednisolone in reducing the risk to relapse⁸,¹¹.

What then is the best initial steroid regime?

A recently concluded meta-analysis of all randomized controlled trials on steroid therapy of nephrotic syndrome has concluded that children in their first episode should be treated for at least 3 months, with an increase in benefit being shown up to 7 months of treatment¹¹.

The steroid regime that appears to be most favoured at present is

60mg/m²/day - given as a single morning dose for 4 weeks

40mg/m²/day - given on alternate days for 4 weeks

Reduction of dose by 25% every month over next 4 months

Treatment of relapses

Prolonged and intensified treatment of a relapse has no influence on the subsequent relapse rate⁴,¹². Therefore the standard treatment of relapses should continue.

The standard relapse treatment is -

60mg/m²/day - given as a single morning dose and not exceeding 80mg/day until response occurs

40mg/m²/48h - given as a single morning dose every other day for 4 weeks.

Relapses are best treated early before the onset of gross oedema. This helps to minimize the risk of complications.

References


