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## Cytotoxic therapy and side effect in childhood

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Some cytotoxic drugs are used in several chronic diseases in childhood. The effects of these drugs are often expected. On the other hand, we must observe the side effects of these drugs.

Steroid are the first choice drug with nephrotic syndrome which are popular of renal diseases in children. The majority of children with nephrotic syndrome will respond to steroid therapy with a clearing of proteinuria and hypoalbuminemia after 10 days.

Many investigators reported about the use of steroid in nephrotic syndrome. Some method of steroid which are given in every day for a long term, is questionable about frequent relapses and many side effects of the steroid therapy. After the reports about the use of steroid therapy of Lange et al(1953) and Soyka et al(1965), International Study Kidney Disease in Children are organized and started the definite use of steroid in the world in 1970. This method is as follows; Prednisone,  $60\text{mg}/\text{m}^2/24\text{hr}$  in 3 divided doses, is given daily for 28 days. The maximum dosage should not exceed  $80\text{ mg}/24\text{hr}$ . This is followed by intermittent therapy of prednisone,  $40\text{mg}/\text{m}^2$  in 3 divided doses, given on 3 consecutive days out of 7 for an additional 28 days. As a result, approximately 80% of patients with nephrotic syndrome will respond with a clearing of proteinuria, 64% will relapse in a 6 months period, and 39% will have 2 or more relapses within 6 months of the initial relapse. Recently, many clinic recommend the next follows as a participant in the International Cooperative Study Kidney Disease in Children. Prednisone,  $60\text{mg}/\text{m}^2/24\text{hr}$  in 3 divided doses, is given daily for 28 days. The maximum dosage should not exceed  $80\text{ mg}/24\text{hr}$ . This is followed by intermittent therapy of prednisone,  $40\text{mg}/\text{m}^2$  in 3 divided doses, given on every other day for an additional 28 days.

It is known to steroid toxicity as infection, diabetes mellitus, hypertension, psychotic disorder, steroid ulcer, cataract, glaucoma, osteoporosis, aseptic bone necrosis and so on. However these side effects gradually become rare by giving alternate therapy of prednisone, the patients with frequent relapser or steroid dependent nephrotic syndrome are given to much dose of steroid and may have these steroid toxicity.

Therapy in these patients may include the addition of cyclophosphamide, chlorambucil, recently ciclosporin or other immunosuppressant-cytotoxic drugs in order to decrease the dose of steroid. However these drugs are often effective, several untoward side effects of these drugs have been recognized and reported and preclude their use on a wider scale.

Short stature is one of the most important steroid side effects when the patients with nephrotic syndrome are given for prolonged use of steroid. The growth of 113 patients (79 boys and 34 girls) with idiopathic nephrotic syndrome were observed, and the relation between the dose of steroids and the growth velocity was assessed. In both boys and girls, growth development was normal until 9 year old, but retarded after 10 years of age. The final mean heights over 18 years in boys and girls were  $162.7 \pm 7.2$ cm and  $152.4 \pm 6.5$ cm, respectively. Of the patients whose final height was known, 63.6% were below -1SD; boys 66.7% and girls 58.8%. Four patients with long-term observation from the onset had a low growth rate between 10 and 13 years of ages without satisfactory growth after 14 years. It was observed that the growth velocity was excellent when 10-15 year old boys took a  $2.5\text{mg}/\text{m}^2$  of steroids and 9-14 year old girls took a dose under  $5\text{mg}/\text{m}^2$ . In regard to the growth of nephrotic children, the management between 10 and 14 years of age is very important and it is desirable to decrease the dose of steroids under  $2.5\text{mg}/\text{m}^2$  in boys and under  $5\text{mg}/\text{m}^2$  in girls, respectively.