Can Cyclophosphamide Pulse Therapy Change the Natural Course of Idiopathic Glomerulopathy Resistant to Steroids?

D.		Grekas
H.		Kalekou
N.		Tsakalos
A.		Tourkantonis

First Medical Department, Renal Unit, University of Thessaloniki AHEPA Hospital, Thessaloniki, Greece

D.M. Grekas, Ass. Prof. in Nephrology, University Hospital AHEPA, Thessaloniki 546 37 (Greece)

Dear Sir,

The efficacy of steroids and immunosuppressive agents in the treatment of idiopathic or systemic glomerular disease remains controversial. The use of corticosteroids in the treatment of lupus nephritis is now standard, even though there is no controlled evidence that survival or morbidity have really improved [1]. Whether the addition of cytotoxic agents improves survival and morbidity is more controversial [2]. Cyclophosphamide is a cytotoxic immunosuppressive and anticancer drug that has been used to treat a large variety of human disorders. Since cyclophosphamide can suppress immune responses mediated by both B and T cells, many physicians have turned to this drug as a last resort for patients with various nonmalignant inflammatory diseases. Daily cyclophosphamide treatment puts the patient at a continuous risk with regard to bladder complications, infections and chromosomal abnormalities which may lead to lymphoma or leukemia. In contrast, treatment with intermittent boluses of cyclophosphamide limits the risk of such complications. These data, based on animal studies as well as on studies of patients with lupus erythematosus, suggest that it may be possible to improve the current forms of therapy [3].

To our knowledge, cyclophosphamide pulse therapy has not yet been tested in patients with idiopathic membranous nephropathy (IMG). We have therefore tried this treatment in 2 male patients with IMG and nephrotic syndrome. At first, both patients were given oral 1–2 mg/kg body weight methylprednisolone daily. The dosage was then slowly reduced during the next 2 months. Due to the absence of any positive response, the patients were also given pulse methylprednisolone treatment (1 g daily for 3–4 consecutive days). Both patients then developed resistance to steroid treatment, and we decided to continue the pulse therapy with 1 g cyclophosphamide per month. After 5–6 sessions of this treatment, the 2

Table I. Clinical and laboratory findings of 2 patients with IMG and nephrotic syndrome

OP = Oral prednisolone; BP = bolus prednisolone; BC = bolus cyclophosphamide.

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patients showed a dramatic reduction of proteinuria to near-normal levels (less than 1 g/24 h), and their renal function was again within normal limits (table I). At the follow-up 24 months after treatment, both patients were in complete clinical and laboratory remission. The therapy was well tolerated, and we did not observe any side effects.

Whether the apparently positive results achieved in our 2 patients with IMG by intermittent cyclophosphamide treatment can be maintained is as yet unknown. It is important to note that with this mode of therapy, the incidence of complications attributable to daily long-term cyclophosphamide treatment could so far be avoided. However, it is not clear yet whether the risk of malignant disease will also be decreased after intermittent bolus treatment with cyclophosphamide [4].

The preliminary results of our 2 cases suggest that this mode of treatment is more successful in retarding the immune-mediated destruction than therapy with oral or bolus methylprednisolone. Nevertheless, pulse therapy with cyclophosphamide should still be considered experimental, and more randomized clinical trials are needed to confirm its efficacy.

References

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