Kidney Res Clin Pract 31 (2012) 257–258

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Letter and Reply

The use of tacrolimus in the management of minimal change disease

To the Editor:

Kim et al [1] showed interesting results that tacrolimus and low-dose prednisolone therapy induced complete remission rapidly and effectively in adult patients with minimal change disease (MCD). MCD has been regarded as an immunological disorder. Recent works, however, have dramatically enhanced the understanding of podocyte biology, which may be the mainstay involved in the pathogenesis of MCD, and many treatment options that were thought to work via immunosuppressive pathways are now known to have a direct nonimmunological effect on the podocyte [2]. Calcineurin inhibitors are frequently used to treat relapsing or resistant nephrotic syndrome [3]. There are several issues to be resolved, however, before taking tacrolimus as first-line therapy in adults with MCD.

Despite its recognized efficacy, there are still limited data on the renal histological changes that occur with tacrolimus therapy. Histological nephrotoxicity of tacrolimus has been well established in patients with nephrotic syndrome [4]. Previous studies suggested the lowest possible dose of tacrolimus be used in children with steroid-dependent or steroid-resistant nephrotic syndrome [5]. Kim et al treated patients with 0.05 mg/kg of tacrolimus as a fixed dose. Only one patient was treated with a lower dosage. The optimal dose of tacrolimus for inducing complete remission of adult MCD is the first question to be answered. There would be individual differences in the trough level of tacrolimus because of pharmacogenomics. To prevent toxicity, dose adjustment is necessary according to the trough level of tacrolimus [5].

Kim et al treated patients with 0.05 mg/kg of tacrolimus for 16 weeks. It is necessary to establish the ideal duration of tacrolimus therapy for the treatment protocol, addressing when its tapering begins. It is currently unknown whether complete discontinuance of all immunosuppressants is preferable to their long-term continuation at a low dosage. The ideal length of tacrolimus therapy is the second question to be answered [6].

Although this pilot trial included a small number of patients over a short period of time, tacrolimus produced a reliable, beneficial effect in adults with steroid-resistant or steroid-dependent MCD. Further investigations on a larger number of patients over longer follow-up periods are required to evaluate the clinical efficacy and effectiveness (including relapse rates and side effects) of tacrolimus in adult patients with MCD.

Bum Soon Choi
Department of Internal Medicine,
The Catholic University of Korea, College of Medicine,
Seoul, Korea
E-mail address: sooncb@catholic.ac.kr

References

[1] Kim YC, Lee TW, Lee H, Koo HS, Oh KH, Joo KW, Kim S, Chin HJ: Complete remission induced by tacrolimus and low-dose prednisolone in adult minimal change nephrotic syndrome: A pilot study. *Kidney Res Clin Pract* 31:112–117, 2012

[2] Oh J, Kemper MJ: Minimal change (steroid sensitive) nephrotic syndrome in children: new aspects on pathogenesis and treatment. *Minerva Pediatr* 64:197–204, 2012

[3] Oh J, Kemper MJ: Second-line options for refractory steroid-sensitive and -resistant nephrotic syndrome. *Expert Rev Clin Pharmacol* 3:527–537, 2010

[4] Morgan C, Sis B, Pinsk M, Tiu V: Renal interstitial fibrosis in children treated with FK506 for nephrotic syndrome. *Nephrol Dial Transplant* 26:2860–2865, 2011

[5] Butani L, Ramsamooj R: Experience with tacrolimus in children with steroid-resistant nephrotic syndrome. *Pediatr Nephrol* 24:1517–1523, 2009

[6] Roberti I, Vyas S: Long-term outcome of children with steroid-resistant nephrotic syndrome treated with tacrolimus. *Pediatr Nephrol* 25: 1117–1124, 2010

In Reply:

Thank you for your interest in our manuscript. First of all, the tacrolimus was not stopped after remission but the dosage was tapered down over various time-periods. As you mentioned, the adequate dosage and duration of tacrolimus for the treatment of minimal change lesion (MCD) are still being debated. We checked the trough level of tacrolimus during our study to monitor the toxicity as a protocol and got a mean level of 5.99 ± 2.63 (0.3–12.3) ng/mL, which was variable from patient to patient. The higher trough level did not give a guarantee of remission, and patients with a lower trough level also effectively achieved remission. In a small, open, prospective cohort study with tacrolimus for MCD patients, the authors maintained low-dose prednisolone (0.5 mg/kg/day)

http://dx.doi.org/10.1016/j.krcp.2012.10.003

and tacrolimus (0.05 mg/kg/day) for 24 weeks and followed patients for 23.0 months after cessation of tacrolimus [1]. During the observation period after the discontinuation of tacrolimus, 50% of patients (6/12 patients) remained in remission.

In this study, we did not plan to show the efficacy of tacrolimus to maintain remission in MCD and used a fixed dose of this drug. We cannot therefore suggest an appropriate schedule of tacrolimus for use in patients with MCD. We need well-designed clinical studies in the near future to determine the verified duration and dosage of tacrolimus to treat MCD.

Conflict of interest

None to declare.

Ho Jun Chin
Department of Internal Medicine
Seoul National University Bundang Hospital
Kyeongki-do, Korea
E-mail address: mednep@snubh.org

Reference

[1] Li X, Li H, Chen J, He Q, Lv R, Lin W, Li Q, He X, Qu L, Suya W: Tacrolimus as a steroid-sparing agent for adults with steroid-dependent minimal change nephrotic syndrome. *Nephrol Dial Transplant* 23:1919–1925, 2008

Available online 16 October 2012