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The alkaloid sinomenine in rat transplant models: and yet it does move

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Sir: We read with interest a recent letter to the editor by Schuurman et al. [6] in this journal, which refers to an earlier publication of ours on the efficacy of the alkaloid sinomenine in the rat cardiac transplant model [1]. Intrigued by the synergistic effects of sinomenine with low-dose cyclosporine, Schuurman and collaborators attempted to reproduce our observations, but failed to confirm our findings. Therefore, they suggest that no further studies on this compound as a potential immunosuppressant in clinical transplantation are warranted. Having performed our previous investigations with great care and under reproducible circumstances, we cannot agree with Dr. Schuurman's conclusions for several reasons.

First, the authors of the letter did not use the same experimental conditions as we did. The protocols differ with regard to the route of administration of cyclosporine (intramuscularly vs orally); the route of administration of sinomenine (intraperitoneally vs subcutaneously); the use of solvent for sinomenine (normal saline vs distilled water); the strain combination used (ACI-to-Lew vs DA-to-Lew); and, finally, also the supplier of the compound sinomenine (Shanxi Institute vs Aldrich). Schuurman and coauthors acknowledge some of those differences without, however, accounting for them in their conclusions. While some differences may be of minor significance, the route of drug administration, for example, is certainly not.

Second, our study was supported by in vitro assays showing a synergistic effect of sinomenine with cyclosporine in terms of its antiproliferative ability on thymocytes. Furthermore, we showed by immunohistochemistry that combined treatment with sinomenine and cyclosporine resulted in markedly reduced intragraft mononuclear cell infiltration along with a reduction of inflammatory cytokines.

Third, other investigators, in particular the group of the pharmacologist Dr. Kaever who collaborated on our paper, have demonstrated in a series of independent studies the immunomodulatory properties of sinomenine both in vitro and in vivo [2, 3, 4, 7]. Though it may not be scientifically recognised in the western world, the wide use of sinomenine preparations in China for treatment of arthritic symptoms may also suggest that the drug has immunomodulatory effects.

Fourth, follow-up experiments by one coauthor of this letter (WM) indicate that sinomenine was effective as an adjunct to cyclosporine in significantly reducing the extent of myointimal proliferation in a rat model of chronic cardiac allograft rejection. Again, the dominant feature related to a marked reduction in mononuclear cell infiltration [5].

Given those considerations, we think that it would be inappropriate to discard sinomenine from the list of immunomodulatory agents for potential future use in transplantation. In particular, the antiproliferative properties of sinomenine warrant further studies in the context of chronic allograft rejection.

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