Can Vitamin C Prevent Complex Regional Pain Syndrome in Patients with Wrist Fractures?

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To The Editor:

In the article "Can Vitamin C Prevent Complex Regional Pain Syndrome in Patients with Wrist Fractures? A Randomized, Controlled, Multicenter Dose-Response Study" (2007;89:1424-31), Zollinger et al. studied the prophylactic effect of vitamin C on the prevalence of complex regional pain syndrome in 416 patients with a wrist fracture. They concluded that vitamin C is indeed effective, and they recommended giving 500 mg of vitamin C daily for fifty days to each patient with a wrist fracture to prevent complex regional pain syndrome.

Some limitations of this study mentioned in the article include a large selection bias (416 of 2137 eligible patients were enrolled) and a low event rate due to an unexpected low prevalence of complex regional pain syndrome (4.2% compared with 22% in the authors’ previous study1). This means that only eighteen patients (eight of the 328 in the treatment group and ten of the ninety-nine in the placebo group) fulfilled the criteria for complex regional pain syndrome. In one patient with fractures of both wrists, complex regional pain syndrome developed on one side, where the fracture turned out to be badly reduced, and the other side healed without complications. This example reveals dramatically how this study demonstrates a strong confounder: although the number of fractures needing reduction was equal in both groups, the quality of the reduction was not mentioned.

Open reduction and internal fixation of wrist fractures generally achieves a better reduction than closed reduction with application of a cast. Retrospective studies of surgically treated wrist fractures have therefore demonstrated a lower incidence rate of complex regional pain syndrome, of around 3.5%2. To my knowledge, no prospective study has ever demonstrated an association between the incidence of complex regional pain syndrome and the quality of reduction, but pain
syndromes in general occur more frequently when fractures are not adequately reduced.

Much scientific effort has been put in attempts to achieve prophylaxis and treatment for complex regional pain syndrome with pharmacological means, but these efforts did not result in any clinical recommendations. Conservative physical therapy has provided some benefit for patients with complex regional pain syndrome. Since the introduction of functional and time-contingent "pain-exposure" physical therapy in children with complex regional pain syndrome by Sherry et al. in 1999, more reports on this approach are to be expected for adult patients as well.

A difference is therefore to be expected between patients with complex regional pain syndrome who are treated by a physical therapist and those who are not. The use of any form of physical therapy is not mentioned in this paper, introducing another possible confounder. This paper therefore does not provide support for the effectiveness of vitamin C in preventing complex regional pain syndrome.