Recommendation for use of rhBMP-2 in spinal interbody fusions

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To the Editor,

Miyazaki et al. [8] conducted a Medline search using various combinations of keywords, such as spinal fusion, bone morphogenetic protein, etc. Inclusion criteria for clinical studies were: studies that well describe the evaluating efficacy and rates of fusion by use of a particular material, surgical procedure and grafting technique, evaluation technique for fusion well described; number of patients more than ten. Grades of recommendation were done using Guyatt criteria [10]. However, we have to ask the authors a few clarifications related to inclusion of the studies of osteoinductive growth factors and gradation of recommendation for their use.

Khan et al. [4] analyzing 100 original randomized clinical trials reported in 5 leading orthopedic journals over 2 years found strong and significant ($P < 0.001$) positive association between industry funding and favorable outcome. These authors have suggested that large, prospective, multicenter collaborative trials that involve hundreds of patients and critically evaluate treatments are ultimately the goal for orthopedic clinical research [4]. So, was the number of patient set to be more than ten [8] in order to

include the study of Boden et al. [1] who evaluated 11 patients in investigational group, or is there some reasoning, supported by the literature, for inclusion of studies with the number of patients? It should be emphasized that the study of Boden et al. [1] was sponsored by the industry.

It is clear that different investigators would write this review differently. That is why we will not present in detail several studies that reported adverse effects of rhBMP-2 use in lumbar interbody fusions (LIF) [2, 5, 7, 12, 13] and which were overlooked by the authors, but we have to ask the authors [8] why there was no mention of the study of Haid et al. [3]? It was a prospective, multicenter, non-blinded, randomized, 2-year pilot study, in which 67 patients underwent a single-level posterior LIF using two paired cylindrical threaded titanium fusion devices. The FDA halted the study after ectopic bone formation into the spinal canal was observed in 24 of 32 patients who received rhBMP-2. That study was ignored by some of the authors previously because none of the cited studies at the time were able to correlate this finding with clinical symptoms [11]. As this is not the case anymore [14], we would like to know why it was ignored this time?

Miyazaki et al. [8], after presenting the studies of McClellan et al. [6] and Pradhan et al. [9], stated that those results suggest that the careful use of rhBMP-2 for anterior LIF is more beneficial than the use of allografts, although further clinical studies are required. It should be emphasized that Pradhan et al. [9], after preliminary results became available (nonunions were diagnosed in 5 of 9 patients who received rhBMP-2), stopped the practice of stand-alone anterior LIF with femoral ring allografts. They concluded that the use of rhBMP-2 soaked in absorbable collagen sponges and placed inside the graft does not increase the fusion rate and, in fact, may cause more nonunions [9]. Accepting all the above-mentioned

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information, we are interested to learn how Miyazaki et al. [8] would grade the recommendation for use of rhBMP-2 for LIF now?

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