Recombinant Human Bone Morphogenetic Protein-2

Controversy persists regarding Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) use in spine surgery.

Although numerous studies did not show statistically significant improvement in fusion rates with rhBMP-2 use, analysis of combined studies revealed significant improvement in fusion rate with rhBMP-2 in ALIF and PLF patients. Notably, even when pooling data from several studies, rhBMP-2 did not result in statistically significantly improved fusion rates in PLIF/TLIF. However, heterogeneity of rh BMP-2 dosing, surgical techniques, and quality of papers reviewed may limit the validity of conclusions drawn [1].

It has been hypothesized that the recombinant human bone morphogenetic protein-2 (rhBMP-2) amplification of the host inflammatory response interacts with nerves in the spine and contributes to the occurrence of new, postoperative complaints of radiculitis.

In a study, rhBMP-2/ACS did not appear to induce pain independent of grossly visible ectopic bone formation. At the earliest time points, rhBMP-2 appeared to have a neuroprotective effect as evidenced by decreased pain exhibited by the rhBMP-2-treated animals in the CCI cohort, but this effect diminished over time, and by Day 28, the pain behavioral responses in the rhBMP-2-treated group were comparable to those in the group in which saline was applied to the nerve. In the Sham cohort, there was a dose-independent induction of pain at later time points, presumably due to new bone formation mechanically irritating the nerve. Histological examination revealed nerve lesions that appeared to be caused by mechanical trauma associated with surgical manipulation of the nerve during placement of the ACS and/or CCI sutures [2].

RhBMP-2 at intermediate dosing may improve fusion rates with no increase in major complications in Adult Spinal Deformity surgery; however, HRQOL measures were similar between groups. Longer follow-up is needed to assess if fusion rates correlate with health-related quality of life (HRQOL) and revision surgery [3].

Case series

2016

Investigational patients (224) with single-level cervical degenerative disc disease underwent ACDF with rhBMP-2 at a dose of 0.6 or 1.05 mg and were compared with historical control patients (486) treated with allograft spacer and cervical plate.

At 24 months, improvement was significantly greater in the investigational group (37.1 points) than in the control group for Neck Disability Index (P=0.002) and arm pain (P=0.031). The overall neurological success rate was higher in the investigational group (P<0.001). Neck pain and general health status (SF-36 PCS and MCS) were similar. Fusion rate in the investigational group was higher than in the control group (99.4% vs. 87.2%, P=0.002).Cumulative adverse event rates at 24 months

were similar; however, higher rates of dysphagia (P=0.001), local swelling (P=0.024), oropharyngeal pain (P=0.013), neck pain (P=0.019), and foraminal stenosis (P=0.002) were observed in the investigational group. Heterotopic ossification was also higher in the investigational group.

At doses of 0.6 or 1.05 mg in a PEEK interbody cage, rhBMP-2 was effective in inducing fusion and improving Neck Disability Index and arm pain in single-level ACDF patients; however, higher rates of certain adverse events were observed in the investigational group [4].

1)
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2)
Zanella JM, Waleh N, Orduña J, Montenegro J, Paulin J, McKay WF, Wilsey J. Evaluating the effects of recombinant human bone morphogenetic protein-2 on pain-associated behaviors in a rat model following implantation near the sciatic nerve. J Neurosurg Spine. 2016 Aug;25(2):154-64. doi: 10.3171/2016.1.SPINE15891. Epub 2016 Mar 18. PubMed PMID: 26989976.
3)
Bess S, Line BG, Lafage V, Ames CP, Boachie-Adjei O, Burton DC, Hart R, Gupta M, Klineberg E, Mundis G, Hostin RA, Schwab F, Shaffrey CI, Smith JS. 151 Intermediate dosing of recombinant human bone morphogenetic protein-2 improves fusion rates with no increase in major complications but does not improve health related quality of life for adult spinal deformity at minimum 2 years: a prospective, multicenter analysis. Neurosurgery. 2014 Aug;61 Suppl 1:209-10. doi: 10.1227/01.neu.0000452426.29670.a5. PubMed PMID: 25032602.
4)
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