Higher Dosages of BMP-2 in Alveolar Cleft Repair Result in Higher Rates of Postoperative Nasal Stenosis

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INTRODUCTION

A former surgeon at our institution preferentially used bone morphogenetic protein-2 (BMP-2) instead of autograft for alveolar cleft repair. Clinically, his patients who received BMP-2 appeared to have higher rates of postoperative nasal stenosis. To determine if this relationship was dose-dependent, a content analysis was performed comparing different dosages of BMP-2 in alveolar cleft repairs.

Methods and Materials

BMP-2 had six levels of concentration depending on the size of kit used in the alveolar cleft (mg): 0, 1.05, 2.1, 4.2, 8.4, 12. Postoperative outcomes were examined by content analysis of clinical notes. Nasal stenosis was defined as any mention of clinical signs of stenosis, and indeterminate responses were counted as no stenosis. Patients with nasal stenosis prior to their primary alveolar repairs were excluded.

Results

60 consecutively enrolled patients underwent 115 surgeries that met criteria: surgeries involving BMP-2 (BY) 48%, those without BMP-2 (BN) 52%. The average age at surgery (years): BY 3.53, BN 3.43, $P = 0.890$. The incidence of postoperative nasal stenosis: BY 61.8% (34/55), BN 30.0% (18/60), $^{***}P < 0.001$. Some surgeries involved a concurrent nasal repair: BY 69.1%, BN 31.7%, $^{***}P < 0.001$. Using the predictor variables BMP-2 status, concurrent nasal repair status, and their interactive effect, a logistic regression indicated that only BMP-2 status was a statistically significant predictor of postoperative nasal stenosis: OR 3.49 (95% CI = 1.06, 11.46) $^{*}P = 0.04$. BMP-2 concentration was then used as a predictor variable with 6 continuous levels in a logistic regression, adjusting for concurrent nasal surgery. The regression indicated that BMP-2 dose level was a dose-dependent predictor of postoperative nasal stenosis with an odds ratio of 1.244 (CI = 1.030, 1.503), $^{*}P = 0.023$.

Conclusion

In patients who received BMP-2 during alveolar cleft repair by a former surgeon at our institution, higher rates of postoperative nasal stenosis were observed as greater doses of BMP-2 were used. A logistic regression showed that the effect of BMP-2 on nasal stenosis is dose-dependent and statistically significant, whereas concurrent nasal surgery is not a significant predictor. Possible etiologies include BMP-2 exacerbating septal deviation or leading to hypertrophic bone deposition, and both need to be investigated further. These results suggest that BMP-2 has a dose-dependent effect with certain clinical outcomes, such as postoperative nasal stenosis.