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A Preliminary Report of Percutaneous Craniofacial Osteoplasty in a Rat Calvarium

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ABSTRACT

Objective: To evaluate the potential for injectable, permanent bone augmentation by assessing the biocompatibility and bioactivity of subperiosteal hydroxyapatite (Radiesse) deposition in a rat model.

Methods: Fourteen adult Sprague Dawley rats were injected in the parietal skull with hydroxyapatite (n=10) or a carrier gel control (n=4), using a subperiosteal injection technique on the right and a subcutaneous injection technique on the left. At 1, 3, and 6 months, 3 rats (1 negative control, 2 variables) were sacrificed. At 12 months, the remaining 5 rats were sacrificed.

Results: The inflammatory response was limited in all specimens. Injectables were still present 12 months after the injection. New bone formation was only seen when the injection was located deep to a disrupted periosteum. The odds ratio could not be computed due to the zero count for the subcutaneous injections (95% CI (0.000, infinity), p < 0.001). The marginal effect of HA, however, was significant (carrier vs HA) on new bone formation, histologic data (95% CI (2.637, 3759.961), p = 0.002). The marginal effect of subperiosteal hydroxyapatite (HA) injections in 4 of 5 rats studied from the 1 month harvest (Figure 4), specimen 5 from the 3 month harvest, and specimens 12 and 14 from the 12 month harvest. Interestingly, mature lamellar bone was seen above the HA spherules in specimen 12, indicating osteointegration. (Figure 5)

Conclusion: This preliminary report of subperiosteal hydroxyapatite (Radiesse) injection in a rat model has verified the biocompatibility of injectable hydroxyapatite at the bony interface and suggests the potential for new bone formation.

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INTRODUCTION

Presently, calcium phosphate cements (CPC), such as hydroxyapatite (HA), are commonly used for the obliteration of bone defects. Favorable characteristics of CPC include customizability, isofromic setting, biocompatibility, and bioactivity (resorption is coupled with new bone formation). However, the chemical properties pertaining to setting, open exposure to tissue fluids, and the physical application of CPC is reserved for large defects, such as those that result from tumor extirpation or extensive trauma. How, however, bone grafts are often faced with smaller craniofacial defects that are of aesthetic concern to the patient but do not warrant the morbidity of open reconstructive surgery. In these cases, injectable materials are often used to fill in smaller craniofacial defects as well as the remaining 4 rats from the HA group. All specimens were stained with hematoxylin and eosin. Under low power magnification, the injectables were located and the surrounding tissue was examined. Proper identification of the injectables was confirmed by examining and comparing separate samples of the HA and carrier gel ex vivo (Figure 1). Polystain microscopy was used to distinguish new (woven) bone from mature (lamellar) bone.

Odds ratios, p values and 95% confidence intervals (CI) were calculated using Fisher’s conditional maximum likelihood estimation. P values < 0.05 were considered significant.

RESULTS

Histologic data are summarized in Table 1. While multinucleated giant cells were often present (Figure 2), only minimal mesenchymal cells were noted in the specimens. Seven (2 carrier, 5 HA) out of 13 subperiosteal injections were found to be deep to a disrupted periosteum, while the remaining 6 were noted to be in the subcutaneous layer with an intact periosteum beneath. Of note, HA spherules could not be found in the subcutaneous site or specimen 12 and at both injection sites for specimen 13.

In an attempt to analyze the effect of the injection plane (subcutaneous vs subperiosteal) and the injectable (carrier vs HA) on new bone formation, histologic data was re-organized as depicted in Table 2. Of note, injections that were intended to be subperiosteal but were found to be subcutaneous were excluded from the analysis. Because injections were considered “subcutaneous” (n=6) for the purposes of statistical analysis. Furthermore, any specimen without an identifiable injectable (subperiosteal injection site in specimen 12 and both sites in specimen 13) were excluded.

The odd of new bone formation in the subperiosteal HA injection group (4.944 times higher than the other 3 combinations in aggregate (95% CI (2.637, 3759.961), p = 0.03)). The marginal effect of subperiosteal injection was also significant, but a distant odds ratio could not be computed due to the zero-count cells in the subcutaneous groups (95% CI (0.000, infinity), p = 0.001). The marginal effect of HA, however, was not significant.

DISCUSSION

Minor deformities of the craniofacial skeleton can be quite bothersome aesthetically to patients. Radiesse provides an attractive alternative to implants as it is a biologic constituent, HA, has been used for over 2 decades for augmentation.3,4 Over the years, various studies have confirmed its safety, longevity and bioactivity (specifically the stimulation of new bone formation)5-7. Not surprisingly, off-label uses of Radiesse have arisen as well.11,12

To our knowledge, no one to date has examined the histologic effects of Radiesse injection at the bone level. We have now shown that Radiesse is biocompatible and long-lasting subperiosteally. In designing the study, we did consider the fact that the trauma of periosteal disruption could trigger osteoactivity and therefore confound results. We attempted to control for this with the carrier only injections; hypothesizing that new bone formation would be either absent or less pronounced without HA. Unfortunately, our histologic findings for periosteal disruption was only successful 54% of the time. Consequently, the numbers for truly subperiosteal HA and carrier injections were simply too low to demonstrate a statistically significant difference in the rate of new bone formation between the two. Notably, though, 4 of 5 odd of new bone formation in the subperiosteal HA injection group was significantly higher than the aggregate of all other combinations of injection plane and injectable. We also attempted to show that the plane of injection seems to be critical in any effort to induce osteoactivity as none of the subcutaneous injections resulted in new bone formation. Interestingly, our observations suggest that, regardless of the mechanism triggering new bone formation, injectable HA can be osteointegrated.

Refinements in the technique for subperiosteal injection are clearly necessary, and further study on a larger scale is warranted to better elucidate the stimulus for the osteoactivity we observed histologically.

REFERENCES


Figure 1. A multinucleated giant cell is depicted in this high power magnification view of a 1-mo hydroxyapatite injection

Figure 2. A multinucleated giant cell is depicted in this high power magnification view of a 1-mo hydroxyapatite injection

Figure 3. Under low power, hydroxyapatite spherules are seen to be embedded in new, woven bone in this 6-mo specimen

Figure 4. Under high power, new bone formation is seen just medial to the hydroxyapatite spherules in this 1-mo specimen

Figure 5. Under high power, hydroxyapatite spherules from this 12-mo specimen appear osteointegrated

Table 1. Summary of binary histologic data. The presence of periosteal disruption and new bone formation is indicated with (a). HA = hydroxyapatite (Radiesse)

Table 2. Summary of binary data for rate of new bone formation, grouped by all combinations of injection plane and injectable. SC= subcutaneous, SP=subperiosteal, HA=hydroxyapatite (Radiesse)