Animal Model of Chronic Perforation Is Best for Eardrum Regeneration Using Biological Materials

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We would like to address the manuscript entitled “Effects of Cell-Based Therapy for Treating Tympanic Membrane Perforations in Mice,” by Goncalves et al.1 The authors suggested that topical application of bone marrow–derived exogenous mesenchymal stem cells enhanced the healing of tympanic membrane perforations (TMPs) in the mice animal model of acute TMPs and could be a promising alternative to tympanoplasty.1 Their work is interesting. However, we consider the study design to be inappropriate.

1) This study used an animal model of traumatic TMP. It is well known that traumatic TMPs tend to heal spontaneously. Although large perforations of >50% of the intact membrane usually fail to close within 3 months following injury, some recent studies demonstrated that the topical application of an agent solution alone significantly improved the closure rate of large human traumatic TMPs and shortened the closure time.2 Therefore, a bioscaffold would seem to be unnecessary. In addition, clinical study found that a bioscaffold did not improve the closure rate of traumatic TMPs when compared with spontaneous healing.3

2) It is important that novel biological materials are mainly used to repair persistent TMPs with chronic suppurative otitis media (CSOM). The authors stated, “Generally, the surgeon refires the edges of the wound to initiate the inflammatory cascade with hopes of an enhanced healing after the placement of the graft. Here we use an acute mouse model of TMPs that presents similarities with the refreshed wound.”3 Excision of the perforation margin is a confounding factor because it induces an acute inflammatory response that potentially restarts the acute wound-healing process.4 Nevertheless, although the surgeon refires the edge of the perforation, the essence of acute TMP and TMP with CSOM is different. Previous studies suggested that chronic TMPs did not lead to a decrease in the level of growth factors but, rather, a rise in the level of metalloproteinase activity. A clinical study showed that the topical application of epidermal growth factor on human traumatic TMPs was effective, but it was ineffective in human chronic TMPs.2,5 Similarly, fibroblast growth factor 2 was effective in the regeneration of human traumatic TMPs,2 whereas no evidence was found that the topical application of fibroblast growth factor 2 alone facilitated the closure of human TMPs with CSOM. Thus, a comparison of the various studies of bone marrow–derived exogenous mesenchymal stem cells with or without a scaffold is needed to demonstrate the treatment effect in an animal model of TMPs with CSOM that is clinically relevant in the future.

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Disclosures

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References