Biologic Treatment for Intervertebral Disc Degeneration

Summary Statement

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In past decades, the biomechanics of intervertebral disc degeneration have received much attention. More recent research efforts have focused on understanding the biology of the disc degenerative process. The ability to manipulate disc architecture and biology by direct application of growth factors or by gene therapy techniques may present an opportunity to halt or slow disc degeneration. Preliminary studies using these strategies have confirmed their ability to replenish essential disc matrix components that are known to decrease with disc degeneration.

The opportunity to slow or reverse intervertebral disc degeneration with biologic manipulations is an exciting area of research. The first article reports the ability of direct injection of stimulatory proteins into the disc to promote a reparative process. However, the duration of any effect is limited by the relatively short half-lives of the injected proteins, which may limit their usefulness for the in vivo treatment of chronic disc degeneration. The ability to up-regulate extracellular matrix production with BMPs, in combination with the tissue engineering techniques described, may offer the potential to repair disc deficiencies such as anular defects that may be exacerbated and/or created with surgical discectomy or those occurring with disc herniations. This strategy will require biointegration of the engineered tissue into the disc and also favorable biomechanical behavior of the implant.

Gene therapy strategies offer the opportunity for sustained expression of synthetic proteins in the disc. The authors of the second article have reported that the intervertebral disc seems to be relatively “immuno-privileged,” allowing for expression of virally transfected genes for at least 1 year. The authors continue to search for specific genes that will be optimal for this application.

Unfortunately, most current animal models of disc degeneration involve an artificial physical or chemical injury to the disc, which may not necessarily replicate the biology seen in human disc degeneration. This limitation makes it difficult to directly apply the results of biologic strategies to replenish the disc matrix reported in animals to human disc degeneration. A number of research groups are exploring techniques and models that might allow for the study of disc repair under conditions that more closely mimic human disc degeneration.

When considering future applications of these technologies, we must appreciate the fine line between physiologic disc aging and disc “disease” that may be the cause of a patient’s symptoms. Even if we have the technology to halt disc degeneration and replenish the matrix by biologic means, this may not be appropriate in the “treatment” of the normal disc aging process. More likely, these techniques will be applied in the treatment of a “painful” disc relatively early in the degenerative cascade. Only clinical trials can determine if replenishing the disc matrix and restoring lost disc height will reduce discogenic pain.

Before these strategies are considered for clinical trials, the potential toxicity of the proteins or genes to be used in the disc must be rigorously studied. This may be particularly relevant with gene therapy techniques for which long-term expression of the end product is likely. In addition, the effects of these products on the neural elements should be evaluated before consideration for clinical use. The past experience with intradiscal chymopapain treatment, in which a potentially useful technique was brought into disrepute by relatively few disastrous cases, emphasizes the importance of clearly understanding the potential for complications with intradiscal injection therapies.

The innovative biologic approaches described in this section offer the potential to retard or reverse disc degeneration using techniques that should be associated with minimal patient morbidity. A thorough understanding of the biologic response and toxicity profiles of the agents used is mandatory before proceeding with clinical trials.