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A prospective study of Autologous Growth Factors (AGF) in lumbar interbody fusion

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Abstract

BACKGROUND: Numerous preclinical and clinical studies have reported on the use of platelet concentrates to promote tissue healing. The results in spinal fusion applications are limited and controversial.

PURPOSE: The purpose of the current prospective clinical cohort study is to assess the effect of Autologous Growth Factors (AGF) on lumbar interbody fusion with specific attention paid to determination of clinical and radiographic outcomes.

STUDY DESIGN/SETTING: Prospective clinical study

PATIENT SAMPLE: Candidates for anterior-posterior lumbar fusion with diagnosis of degenerative disc disease and/or up to grade I spondylolytic spondylolisthesis based on positive provocative discography.

OUTCOME MEASURES: Clinical (visual analogue pain scale/functional outcome assessment) and radiographic outcomes (fusion on computed tomography at 6 months and plain radiographs at 12 and 24 months).

METHODS: Thirty-seven patients were assigned to standard anterior-posterior interbody fusion L2–S1 (single or two-level) using iliac crest bone graft (autograft group: 22 patients with 32 levels operated) or allograft combined with autogenous growth factors (AGF group: 15 patients with 25 levels operated). Radiographic outcomes were collected at 6 months postsurgery with computed tomography and at 12 and 24 months with plain radiographs. Pre- and postoperative clinical outcome measures included visual analog scores (VAS) for back and leg pain (0–10), SF-36 scores, and Oswestry disability determination. Average clinical and radiographic follow-up for the autograft group was 24.3+/−5.6 months (12–36 months) and AGF was 25.7+/−7.5 (6–40 months).

RESULTS: Fusion incorporation at each end plate was determined at 56% in both autograft and AGF (p=NS) patients based on computed tomography at 6 months with minimal subsidence noted and no direct correlation between the incidence or degree of cage subsidence and bone graft technique. The 12- and 24-month radiographic results confirmed an 85% arthrodesis rate for the autograft patients, whereas the AGF patients had an 89% fusion rate (p=NS). Clinical outcomes were similar for both groups and no significant differences were noted for pain or functional outcome improvements.

CONCLUSIONS: AGF combined with an allograft carrier is equivalent in radiographic and clinical outcomes to autograft in one- or two-level lumbar interbody fusion with supplemental posterior fixation and, thus, eliminates any morbidity from iliac crest bone graft harvesting. AGF combined with an appropriate carrier is a reasonable alternative to autograft and expensive bone induction technologies. Further research is still required to examine the optimum carriers, preparation and formulation, and platelet concentrations for this technology.

Keywords: Platelet concentrate; AGF; Lumbar interbody fusion; Outcomes

Introduction

A basic paradigm of healing after injury exists universally among all tissues. Platelets are a key component of the initial cellular response in tissue repair by migrating to the injury site and releasing a variety of growth factors.

FDA device/drug status: approved for this indication (Autologous Growth Factors).

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This early platelet-mediated activity induces formation of a structural, organized fibrin clot as well as chemotaxis of white blood cells and various noncommitted progenitor stem cells. Platelet degranulation and release of platelet-derived growth factor, transforming growth factor-beta, and vascular endothelial growth factor are among the known signaling substances to be important in fracture healing [1–4]. Tissue-specific differentiation and repair is then directed by other factors including bone morphogenic protein and transforming growth factor-beta.

This platelet-mediated wound healing response provides theoretical rationale for use in clinical practice [5–8]. Because platelets are a source of multiple growth factors, increasing their number and concentration to an injury site may lead to a synergistic effect on tissue repair. A platelet concentrate has several potential benefits in addition to enhancement of a tissue healing response, such as provision of a fibrin-based clot serving as a scaffold for cellular attachment and improvement of handling characteristics of a tissue-engineered graft.

Feasibility studies have been performed on the development of platelet concentrates for clinical use by means of centrifugation techniques [9–12]. Platelets can be sequestered from whole blood, leaving red blood cells and plasma (platelet-poor plasma). More advanced ultrafiltration methods result in *superconcentrated* plasma of up to 8–10 times that of whole blood. This proprietary platelet concentration system has been termed Autologous Growth Factors (AGF) (Interpore Cross, Irvine, CA).

Numerous preclinical and clinical studies have reported on the use of platelet concentrates to promote tissue healing. The results in spinal fusion applications are limited and controversial. Studies have described both beneficial effects of fusion incorporation as well as inhibitory reaction to platelet addition to autologous graft [13–17].

The purpose of the current study is to assess the effect of AGF compared with autograft iliac crest bone on lumbar interbody fusion, with specific consideration paid to determination of clinical and radiographic outcomes.

Materials and methods

Study group

Institutional review board approval was obtained for admission of human subjects into this study before the commencement of patient enrollment and informed consent. Two fellowship-trained orthopedic spine surgeons contributed patients deemed to be candidates for single or two-level anterior-posterior lumbar fusion to the study in a period from July 2000 through November 2002 and personally obtained verbal and written consent from each patient. Preoperative evaluation of the pain generator included the use of magnetic resonance imaging, radiographs, and provocative discography. Patients were assigned to standard anterior-posterior interbody fusion using iliac crest bone graft (autograft group; n=22) or allograft combined with autogenous growth factors (AGF group; n=15) based on availability of cell saver technology on the day of surgery.

Inclusion criteria included: at least 12-month history of low back pain with or without associated radiculopathy clinically determined to be localized to one or two disc spaces from L3 to S1 by radiographic evaluation including provocative discography; diagnosis limited to degenerative disc disease or spondylolisthesis (spondylolytic or degenerative) with less than or equal to 25% anterior vertebral body translation; exhaustion of a conservative, multidisciplinary treatment program including physical therapy, injection therapy, and oral pain medication when indicated lasting at least 6 months; age range from 20 to 60; and patient-derived visual analog score for back pain at least 7 on a scale of 0–10. Exclusion criteria included history of prior abdominal surgery requiring retroperitoneal exposure; previous spinal infection; greater than 25% spondylolisthesis; metabolic bone disease; and inability to comply with clinical follow-up regimen.

Operative procedure

An anterior retroperitoneal lumbar approach was initially performed in all patients. All interbody disc preparation was similar, with aggressive radical discectomy with preservation of the peripheral cortical end plates. Central end plate perforations were made with curettes or burr. Unilateral iliac crest graft was harvested via a 4–5-cm incision overlying the pelvis, with preservation of the inner and outer table of the ilium. Morselized graft was harvested and added to an ''upright'' titanium mesh cage (Harms Cage, DePuy Spine, Rayhnam, MA or Pyramesh, Medtronics, Memphis, TN) and inserted into the distracted disc space in the control group. Study patients had cancellous allograft ''chips'' combined with AGF (technique below) added to the cage and inserted into the disc space. Bone graft volume was standardized for each group and was measured at 15–20 cc/disc space. Device positioning was confirmed with intraoperative imaging studies. Each patient then underwent same-day posterior lumbar exposure and insertion of transpedicular instrumentation. Additional iliac crest graft was harvested from the posterior superior iliac spine with preservation of the inner and outer tables of the ilium in all control and study patients and added to the bilateral intertransverse process area to complete the 360-degree fusion procedure.

Standard postoperative management was employed for all patients, including initial pain control via intravenous narcotics, early mobilization, home exercises, and avoidance of nonsteroidal anti-inflammatory agents. All patients were educated and encouraged on nicotine cessation. Postoperative external bracing was not consistently prescribed or worn by patients.