Role of Stem Cells In Treatment of Atrophic Non-Infected Nonunion

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By
MOHAMED MOSTAFA MOHAMED
M.B,B.CH

Under Supervision Of

Prof. Dr. Khaled M. Emara
Ass. Professor of Orthopedic Surgery
Faculty of Medicine, Ain Shams University

Dr. Hisham S. Shalaby
Lecturer of Orthopedic Surgery
Faculty of Medicine Ain Shams University

Faculty of Medicine
Ain Shams University
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Introduction

Introduction

Fracture repair continues to be widely investigated both clinically and on the fundamental research level, in part due to the fact that 5% to 10% of fractures results in either delayed union or nonunion, depending on duration of incomplete healing. Beyond the temporal delay in repair , nonunion share the same unifying characteristic: all periosteal and endosteal repair processes have stopped and the fracture will not heal without surgical intervention {1}.

Recent progress in human embryonic and adult stem cell research is a cause for enthusiasm in orthopedic surgery. Stem cells have therapeutic potential in the realm of orthopedic surgery because of their capacity to self renew and differentiate into various types of mature cells and tissues, including bone {2}.

Because nonunion remain a clinically important problem there is interest in the use of cell based strategies to augment fracture repair, such strategies are being investigated with variation in the model system, sources of stem cells, methods of applications and enhancement of osseous healing including genetic modification and tissue-engineering {3}.

This study clarifies the role of utilization of stem cells in promoting fracture healing in atrophic non infected nonunion.

Chapter 2
Aim of the work

Aim of the work

The aim of this study is to clarify the role of stem cells utilization in treatment of atrophic non infected nonunion and to simplify their mechanisms of action. A review of relevant literatures is presented together with their published results.

استخدام الخلايا الجذعيه لعلاج عدم التئام كسور العظام الضامر الغير مايكروبي

رسالة
توطئة للحصول على درجة الماجستير فى جراحة العظام

مقدمة من

الطبيب / محمد مصطفى محمد
بكالوريوس الطب و الجراحة

تحت اشراف

أ.د / خالد محمد عماره
أستاذ مساعد جراحة العظام
كليه الطب- جامعةعين شمس

د. / هشام سامح شلبى
مدرس جراحة العظام
كلية الطب – جامعة عين شمس

كلية الطب
جامعة عين شمس
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المحتويات

الهدف من الدراسة

الهدف من هذه الدراسه هو القاء الضوء على استخدام الخلايا الجزعيه كطريقه بيولوجيه لعلاج عدم التئام كسور العظام الضامر الغير مايكروبي وتوضيح اسلوب عملها واستعراض بعض النتائج الأكلينيكيه لها .

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المقـــدمـة

لا يزال عدم التئام كسور العظام الضامر الغير ميكروبي قيد البحث سواء كان علي المستوى الأكلينيكي او كان على المستوي البحثي خاصة مع بروزحقيقه هامه ان من ٥%الى١٠%من كسور العظام تتعرض لتأخر او عدم الألتئام (١).

ويتم تشخيص عدم التئام كسور العظام الضامر ليس فقط بتأخر التئام الكسر بل ايضا بتوقف جميع عمليات الألتئام الحيويه وحينها لن يتم التئام الكسر دون التدخل الجراحي (٢).

شهدت الفتره السابقه تقدما غير مسبوقا في مجال الخلايا الجذعيه سواء البالغه منها او الجنينيه وكان هذا وراء الحماس الشديد لأستخدامها في مجال جراحات العظام ، فالخلايا الجذعيه لها قدره علا جيه جائزه في جراحات العظام لقدرتها علي التجدد والأنقسام للعديد من الخلايا والأنسجه بما فيها العظام،ولأن عدم التئام الكسور الضامر الغير مايكروبي لا يزال مشكله اكلينيكيه مهمه لذا فهناك اهتمام لأستخدام الخلايا الجذعيه لتحفيز التئام الكسور.

من ثم يتم دراسة استخدامها بمختلف النماذج الحيوانيه ومختلف مصادر الخلايا المبدئيه وطرق التطبيق وطرق تحفيز الألتئام العظمي ومنها التعديل الوراثي (٣).

وفي هذه الدراسه نلقي الضوء علي بعض اليات عمل الخلايا الجذعيه في تحفيز التئام الكسور في مرض عدم التئام الكسور الضامر الغير مايكروبي ونستعرض بعض النتائج الأكلينيكيه لأستخدامها.

Chapter 3

Pathology of atrophic non-infected nonunion

Pathology Of Atrophic Non Infected Nonunion

Fracture healing is a unique biological process regulated by a complex array of signaling molecules and proinflammatory cytokines. This process can be subdivided into three phases: *inflammatory*, *reparative*, and *remodeling*. The first phase begins immediately following fracture and is characterized by the formation of a hematoma, migration of mesenchymal cells to the fracture site, and the release of cytokines and growth factors from leukocytes and fibroblasts. Following the initial process of inflammation, new bone is formed by intramembranous ossification as well as endochondral ossification. These processes are predominately mediated by osteoblasts. This phase is followed by an extended period of remodeling involving osteoclasts that resorb the new woven bone and osteoblasts that replace this matrix with lamellar bone [(1)].

Fracture repair requires at least four events that initiate fracture healing. These events include *recruitment, induction, modulation, and osteoconduction*. Recruitment requires the transportation of systemic osteoprogenitor cells or inducible pro osteoblasts to the fracture site. In addition, communication with the local cell population occurs to stimulate their osteoblastic capabilities (induction). Modulation or activation of these multipotential cell populations then follows. In the final event, osteoconduction, collagen, and hydroxyapatite surfaces are used to direct bone production into a biomechanically advantageous three dimensional lattice [(2)].

The normal physiological reaction to fracture is the spontaneous initiation of a sequence of events, which includes initial inflammation followed by soft callus formation, hard-callus formation, and, ultimately, bone repair and remodeling. In 5% to 10% of fractures, however, this process is either delayed or does not occur in which case the fracture is termed nonunited. Beyond the temporal delay in repair, nonunion fractures share one unifying characteristic: the fracture will not heal without intervention. In contrast to hypertrophic nonunion, where there is robust cellular activity at the fracture site but, due to poor orthopedic stability, the fracture does not heal, atrophic nonunions are marked by a cessation of all periosteal and endosteal repair processes, adding complexity to potential treatments [(3)].