Use of Stem Cell Mobilizer se2® as Part of Conventional Treatment on Ankle Injuries to Expedite Recovery in Professional Soccer Players

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ABSTRACT
Background: Ankle injury is common for soccer players. The number of peripheral blood stem cells (PBSC), is a key parameter in the extent of recovery. In animal studies, StemEnhance® shows accelerated muscle repair after induced muscle injury, and shown to trigger a significant increase in the number of PBSC. Determine whether SE2® could enhance the effectiveness of conventional treatment for ankle injuries. Methods: Twelve male soccer players were randomly assigned, to either experimental (SE2®) or control group. Both groups received conventional treatment. The experimental group received 12 capsules of SE2® daily for a month. The team’s doctor evaluated patients with soft tissue sonograms at days 1, 7, 14 and 21. The Karlsson Peterson Scoring for treatment for ankle injuries. Results: The acute ankle injury was similar in both groups. The participants were matched. The SE2® group experienced a significantly reduction in pain, range of motion and joint stability compared with control group. Recovery time was on average 17 days for the SE2® group versus 21 days for the control group. The use of the stem cell mobilizer SE2® in conjunction with conventional treatment reduced the recovery time from acute ankle injuries in male football players.

Keyword: SE2, Stem cells mobilizer, ankle injury, sport injury, stem cell, ligaments

INTRODUCTION
Soccer is one of the most popular sports worldwide with about 265 million players, both professionals and amateurs (Herrero et al., 2013). This popularity has massive financial implications especially when considering professional soccer. Extensive research has been done regarding types of injuries, with emphasis on professional players, since they have a greater exposure than soccer players at the recreational level. One of the most significant findings from the epidemiological studies of Woods et al. (2002, 2003) was the disproportionately high number of training injuries during preseason, and match injuries during the early stages of the season. Several reasons for this increased incidence have been suggested, including hard playing surface (Dragoo and Braun, 2010), high training intensity (Gabbett and Ullah, 2012), sudden change in training intensity from closed season to preseason, and short preseason preparation (Pontillo et al., 2014). The most common injuries are muscle and ligaments sprains, with muscle sprains being the first and most common of both injuries observed during preseason (Woods et al., 2002). It is crucial to the practice of sport medicine to find new ways of reducing the healing time and improving total recovery for these type of injuries and athletes.

Injuries to the skin, bones and muscles were shown to trigger mobilization of bone marrow-derived stem cells (BMSC) and their migration into the injured tissue where they participate to the process of tissue repair. (Matsumoto et al., 2008; Lee et al., 2008; Mansilla et al., 2006; Mace et al., 2009; Stout et al., 2007) It was documented that the speed and extent of tissue repair depends in part on the number of peripheral blood stem cells (PBSC) available to migrate into an injured tissue (Wu et al., 2007; Velasquez et al., 2007; Tomoda and Aoki, 2003). The stem cell mobilizer StemEnhance® has been shown in an animal study to accelerate muscle repair after induced muscle injury (Drapeau et al., 2010). StemEnhance® is a natural product containing an L-selectin blocker that works by interfering with the SDF-1/CXCR4 axis in the bone marrow, triggering stem cell mobilization (Jensen et al., 2007). Both StemEnhance® and its advanced formula SE2® have been shown to trigger a mild increase in the number of PBSC unfolding a great potential at the clinical level. This study was aimed at investigating the clinical potential of Endogenous Bone Marrow Stem Cell Mobilization (ESCM) using the stem cell mobilizer SE2®, when used along with conventional treatment for sport ankle injuries, in order to decrease recovery time and reduce the critical off match time for professional soccer players.

MATERIALS AND METHODS
Subjects:
A total of 12 male professional soccer players from the “Rayo Majadahonda” Team, in Spain, aged 18 to 22 years old, were randomly assigned to either experimental or control group. Athletes were in general good health and free of any health problems, including neurological, or systemic disorder that would
interfere with the results. All participants presented the same type of injury, consisting of ankle sprain Grade II with partial tearing of the ligaments, moderate pain, joint instability and swelling with bruising throughout the ankle and foot. None of the participant showed any fracture. Athletes with bilateral ankle sprain, ipsilateral knee injury, third degree sprain, and previous ankle sprain within 6 months were excluded from the study. The participants were pair-matched, considering age (20.0±1.4 vs 19.8±1.2), height (177.8±2.1 vs 178.3±3.1 cm), body weight (78.3±4.1 vs 79.2±3.2 kg), and extent of injury in control and experimental groups, respectively.

The Evaluations for each subject included global assessment, medical exam, soft tissue sonogram, and the Karlsson and Peterson Scoring System for Ankle Function (KAFS) for both groups at beginning of the study and each subsequent week for a total of 4 weeks. The KAFS is a validated disease-specific scale (0-100) that was developed to evaluate individuals with ankle injury. This scale measures eight parameters: instability, pain, swelling, stiffness, specific motion activities and need for support. Results are classified in four categories: excellent (90–100 points), good (80–89 points), fair (60–79 points) or poor (<60 points). Patients were evaluated by team’s doctors with soft tissue sonogram at days 1, 7, 14 and 21.

Consumable:

Both groups received conventional treatment for the ankle injury consisting of NSAID medication (as needed), application of a cold pack, complete or partial immobilization (with cast, brace, or bandage), partial weight bearing and crutches (as tolerated), instructions on early ankle exercise, home exercises, and resumption of sports and daily activities.

The experimental group received 12 capsules of SE2® and 3 capsules of StemFlo® daily for 4 weeks. StemFlo® is a dietary supplement containing fibrinolytic enzymes and antioxidants aimed at optimizing blood circulation in the fine vasculature. Both SE2® and StemFlo® were provided by Stemtech International, Inc., Florida, USA.

The study was evaluated and approved by the Ethical Committee of Clinica Quantum (Spain). The protocol met all requirements established by the Conference of Helsinki for research on humans.

RESULTS

All 12 subjects completed the study.

The overall severity of acute ankle injuries was similar in both groups at the beginning of the trial. Subjects in the experimental group showed significant improvement in their physical examination and soft tissue sonogram after 12-14 days. KAFS Analysis evidenced a noticeable difference in the course of recovery between the two groups (Figure 1). The SE2® group experienced a significantly greater reduction in pain, range of motion and joint stability associated with their ankle injury compared with control group. The time to heal the acute ankle injury and go back to playing soccer was on average 17 days for the SE2® group compared to 21 days and over for the control group. After two weeks, the overall KAFS Median scores was 89 for the experimental group and 72 for the control group. The maximum difference was seen at Day 17 when the level of recovery based on the KAFS Median scores per group have classified the individuals in 2 different categories: good (80–89 points) for experimental group and, fair (60–79 points) for the Control group. (Figure 2)

Figure 1. Karlsson and Peterson Scoring System for Ankle Function (KAFS) before and 14 days after conventional therapy alone (Control) and conventional therapy accompanied along with the consumption of SE2® and StemFlo®. Incorporation of SE2® and StemFlo® to the treatment protocol significantly improved ankle pain and stability, activity and overall score 14 days after the injury.

Figure 2. KAFS Median scores for the Control and Experimental groups, measured weekly over a period of 4 weeks (mean ± SE). The Experimental group receiving conventional therapy and consuming SE2® and StemFlo® showed faster recovery and could return to play on average one week before the control group receiving only conventional therapy.

The study was intended only as a complementary protocol to expedite the recovery in athletes with this type of injuries. However, additional benefits were also revealed in the experimental group with regards to pain level. Individuals in the experimental group requested less anti-inflammatory and pain medication.

CONCLUSION

The development of protocols that not only efficiently treat sport injuries but also expedite the recovery is the cornerstone of the practice of sport medicine. In this scope, this study further documents the therapeutic potential of Endogenous Stem Cell Mobilization (Drapeau et al., 2012) in tissue repair, and more specifically in sport injuries.

This study documented that the use the stem cell mobilizer SE2® along with StemFlo®, a fibrinolytic product aimed at improving blood microcirculation, in conjunction with conventional treatment reduced the recovery time from acute ankle injuries in
male football players. The time to revert the acute ankle injury was on average 17 days for the SE2® group, and over 21 days for the athletes in the control group. Complete recovery was on average reduced by one week with the use of SE2® and StemFlo®.

StemEnhance®, a concentrate of the cyanophyta Aphaniizonemon flos-aquae that was documented to trigger bone marrow stem cell mobilization (Jensen et al., 2007) has been shown to significantly accelerate muscle repair after injection of cardiotoxin in the tibialis muscle of irradiated mice transplanted with bone marrow stem cells expressing green fluorescent protein (GFP) (Drapeau et al., 2010). In this study, muscle repair took place through the migration of circulating bone marrow-derived stem cells into the injured muscle and their subsequent differentiation into muscle cells, as shown by the incorporation of GFP-positive muscle cells in the regenerating muscle. StemEnhance® was also reported to promote tissue repair and significant improvements in single patient outcomes associated with a wide variety of health conditions (Drapeau et al., 2012).

Other studies have documented the healing potential of bone marrow stem cell mobilization (Velazquez, 2007). For example, Bozlar et al. (2005) injected the stem cell mobilizer G-CSF (25μg/kg/day) or 0.9% saline in rats that had been subjected to fracture of the tibiae. Radiological, histological and biomechanical assessment performed 3 weeks later revealed a significantly greater recovery in the G-CSF treated animals. Likewise, in mice subjected to burn and incision of the skin, animals treated with G-CSF showed greater recovery (Eroglu et al., 2004).

CD34+ stem cells collected from peripheral blood following mobilization by using G-CSF were locally injected along with atelocollagen in rats subjected to medial collateral ligament injury, and results were compared with a control group only treated with atelocollagen. Animals subjected to G-CSF and then injected with CD34+ stem cells showed much greater recovery, using macroscopic, histological, and biomechanical assessments (Tei et al., 2008). Greater tissue repair was at least in part due to enhanced neovascularization in the treated animals. Endogenous Stem Cell Mobilization and more specifically the use of the stem cell mobilizer SE2® therefore emerge as possible complementary protocols to support the effectiveness of conventional treatment for sport ankle injuries, thereby decreasing the recovery time and reducing the critical off match time for the professional soccer player. Further investigations should be done with a broader spectrum of sport injuries.

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