Author's response to reviews

Title: A Multi-center, Randomized, Clinical Study to Compare the Effect and Safety of Autologous Cultured Osteoblast Injection to Treat Fractures

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Author's response to reviews: see over
Reviewer's report

Title: A Multi-center, Randomized, Clinical Study to Compare the Effect and Safety of Autologous Cultured Osteoblast Injection to Treat Fractures

Version: 5 Date: 2 October 2008

Reviewer: Jennifer Westendorf

Reviewer's report:

Kim and colleagues have submitted a revised manuscript that describes the results of a multi-center randomized clinical trial that compared the safety and efficacy of autologously cultured osteoblasts on fracture treatment. In the revised manuscript, the authors addressed all the previous concerns; however, they were only partially successful in answering them adequately. The lingering compulsory issues are:

1. Figure 4 is a new figure. Are the data from each time point statistically significant between the control and treated groups?

➔ After two months, the data were statistically significant. But at one month, the data were not statistically significant. I inserted this fact in the result section.

2. The fracture healing data was separated into age groups as requested and added as Figure 6. The authors state that there was no statistical difference between the two groups. Which two groups? How do the 20-29 year olds compare to each of the other groups? They seemed to respond the best.

➔ There was no statistical difference in the osteoblast injection response between the younger age patient group and the older age group (p=0.71); also, when we compared the 20-29-year-old patient group with other groups, there was no statistical difference. (Fig. 5)

3. The control group was untreated and did not receive fibrin injections. On page 12, the authors provide a nice discussion of the potentially beneficial effects of fibrin on growth factor recruitment and retention. Given these potentially positive effects, the authors should add a sentence stating that they cannot conclude that the fibrin did not have an effect in this study.

➔ As perhaps the sentence on page 12 caused a misunderstanding about fibrin, we changed it. We intended to communicate that fibrin just acts as a carrier when we attempt to apply a cell or growth factor to a certain area as fibrin does not induce growth factor recruitment. Injection only fibrin to fracture site is ethically problematic. The injection procedure involves some stress, time, and patient inconvenience, and no patient will agree a treatment that is ineffective for them.
4. There are still some confusing sentences. Incorrect comma usage is a common error, especially at the beginning of the manuscript. The patient enrollment numbers cited in the text on page 8 are confusing and do not agree with the numbers in Figure 2.

➔ As you pointed, there were some incorrect numbers on page 8. We corrected the figures, comma usage, and the confusing sentences.

Discretionary Revisions:
1. Figures 3 and 4 could be combined into parts A and B.
➔ We changed it to Fig 3a, b

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.

1. 그림 4 의 값이 각각 통계학적으로 유의하나?

Independent T-test 를 이용한 각 visit 별 두 그룹간의 분석 결과 이식 후 1 개월에서는 유의한 차이를 나타내지 않아 가بول혈청수변화량의 차이를 보이지 않았고(p-value=0.196), 동재기와 이식 후 2 개월에서는 유의한 차이를 나타내어 가بول혈청수변화량의 차이를 나타내었다(p-value=0.023, p-value=0.003).

2. 20~29 세 사이와 다른 연령대를 비교한 결과

ANOVA (analysis of variences) test 를 이용한 시험군내에서 연령군간 가بول혈청수변화량의 차이는 없는 것으로 나타났다(p-value=0.7110). 따라서 20~29 세군을 포함하여 모든 연령대군에서의 가بول혈청수변화량은 같다.

확인하시고 궁금한 사항 있으시면 연락 주십시오.

건강히 잘 지내시고, 담에 연락하도록 하겠습니다.

감사합니다.