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Letter to Editor

Expanded mesenchymal stem cell transplantation is safe in both local injection and vein transfusion

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More than 500 clinical trials are using mesenchymal stem cells (MSCs) in the world to treat some different diseases. The safety of expanded MSC transplantation is the most important thing to ensure that this therapy can become the routine treatment of human illnesses. More than five MSCs based stem cell drug products are approved in various countries demonstrated that expanded MSCs are safe in both local injection and transfusion. Moreover, some recent reports for six years followed-up clinical trials using expanded MSCs confirmed that there is not different tumorigenesis between the patients with and without expanded MSC transplantation. This letter aims to provide some evidence about the safety of expanded MSCs in clinical applications. However, the MSC quality should be strictly controlled during the in vitro MSC expansion.

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1. Dear Editor-in-Chief

In 2017, more than ten publications used expanded to treat some diseases in both local injection and infusion in Pubmed [1–10]. All publications showed expanded MSC transplantation was safe. Some studies followed-up 12 months, others followed up to 6 years. And some transplantations are autologous, and others are allogeneic. In the recent report, Bartolucci et al. (2017) infused allogenic expanded MSCs from umbilical cord tissue at the dose of 1×106 cells/kg to treat heart failure and follow-up to 12 months [1]. At 12th months, only UC-MSC treated group significantly improved the left ventricular ejection fraction. More importantly, there were no differences in mortality, heart failure admissions, arrhythmias, or incident malignancy between treatment group and placebo group [1]. In another study, Pang et al. (2017) reported the results of the clinical trial using the allogenic expanded MSCs from bone marrow for aplastic anemia treatment [8]. After the median follow-up of 17 months, the overall survival was 87.8%; there were 7/74 patients developed a mild headache and fever, no other side effects were detected. With these results, authors confirmed that allogenic BM-derived MSCs are safe in aplastic anemia [8].

In India, a four year-follow up study used autologous expanded MSC from bone marrow to treat chronic stroke [9]. In this study, 12 chronic stroke patients were intravenously infused with autologous expanded MSCs. All patients were followed up the 208th week without any cell related side effects [9].

For local injection, two clinical trials using expanded MSCs with one clinical trial followed up six years were reported. Centeno et al. (2017) lumbar degenerative disc disease-associated radicular pain with autologous expanded MSCs. In this study, thirty-three patients injected with their expanded MSCs and followed up to 6 years post-treatment. There was no any severe side effect such as death, infection, and tumor in the patients related to MSC transplantation. Particularly, up to 85% patients had a reduction in disc bulge size with average reduction size of 23% post-treatment [2].

I also found another report about safety and efficacy of Cx601 products in the treatment of complex perianal fistulas in Crohn's disease [3]. This study was funded by TiGenix to investigate the effectiveness of Cx601 – a stem cell drug containing allogenic adipose tissue-derived stem cells. The patients would be intralesionally injected with 120 million of Cx601 cells with the single injection. Patients were followed up to 52 weeks post-treatment. The results showed that 17% of patients treated with Cx601 and 29% patients in the placebo group had side effects included anal abscess and proctalgia [3].

By these reports, I initially concluded that autologous and allogenic expanded MSC transplantations are safe in both local injection and vein transfusion. However, more studies with longer time follow-up are essential to perform the meta-analysis review about the safety of expanded MSC transplantation.

2. Open Access

3. List of abbreviations

BM: Bone marrow; **MSCs**: Mesenchymal stem cells; **UC**: Umbilical cord

4. Ethics approval and consent to participate

Not to be applied

5. Competing interests

The authors declare that no competing interests exist.

6. Funding

Not to be applied

7. Authors' contributions

Both authors equally contributed in this manuscript, from preparing idea, looking references and writing. All authors approved the final manuscript.

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