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Research Article

Autologous Bone Marrow-derived Mesenchymal Stem Cell Transplantation in Sensorineural Hearing Loss Patients

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Abstract

Background: MSCs exhibit remarkable self-renewal capacity and the ability to differentiate not only into osteoblasts but even also into neurons *in vitro* and *in vivo* and therefore, MSCs have been successfully used in otorhinolaryngology.

Methods: Autologous human bone marrow mononuclear fraction (BMMF) was harvested and given to subjects with moderate to severe sensorineural hearing loss. The aim was to determine if bone marrow mononuclear fraction (BMMF) infusion causes any improvement in hearing.

Result: Out of 30 subjects 22 subjects did not showed significant improvement. 8 patients however showed significant improvement in PTA as well as clinically. The average improvement of 8 patients was calculated to be 15 db after 1 BM instillation. 2 patients also showed clinical improvement in their tinnitus which was an additional finding and needs to be evaluated further.

Conclusion: This review suggests that BMSCs are capable to migrate and survive into the cochlear tissues which them suitable to be used in transplantation as a strategy for regenerating inner ear and treatment of SNHL.

Keywords: Stem Cell; Sensorineural Hearing Loss; Neurons

Introduction

Sensorineural hearing loss occurs when the affected region is in the inner ear and/or auditory neurons and/or central auditory pathways. It is estimated that the number of patients with neuron-related hearing loss will rise to 630 million by 2030 [1]. Common causes for sensorineural hearing loss include genetic causes, noise-induced hearing loss, presbycusis and ototoxic drugs [2].

In mammals cells of Organ of corti lose their capacity for regeneration during postnatal maturation which may be the explanation for lack of regenerative capacity in cochlea [3]. This lack of regenerative capacity is the basis for use of stem cells in repairing damage to cochlea. Stem cells exhibit important ability for self-renewal and capacity to differentiate into mature cells of a particular tissue [4].

Multipotent mesenchymal stem cells are being used in otorhinolaryngology due to their ability to differentiate into neurons (*in vivo* and *in vitro*) and capacity for self-renewal [5]. Mesenchymal stem cells protect against excessive inflammation and help in regeneration of injured tissues [6-9].

Among the various types of stem cells, bone marrow-derived MSCs (BMSCs) are one of the most promising candidates for cell replacement therapy. MSCs can be induced to differentiate toward various types of cells including nerve cells [10,11]. It has been suggested that mesenchymal cells including fibrocytes of adult inner ear are derived from Bone marrow-derived mesenchymal stem cells and hence BMCs may be useful in recovery from injuries of inner ear [12]. BMSCs can differentiate into neuronal progenitor cells and therefore may represent a promising biological element

for treatment of inner ear disease, such as SNHL [13]. Furthermore, cells originating from bone marrow particularly those derived from hematopoietic stem cells (HSCs), seem to have the capability to engraft into the inner ear [14].

The aim of the present study was to determine if bone marrow mononuclear fraction (BMMF) infusion can improve hearing in patients with moderately severe to profound hearing loss.

Materials and Methods

Thirty patients with moderately severe to profound hearing loss were enrolled in present study after obtaining informed consent. The age group varied from 13 to 60 yrs. Autologous bone marrow was aspirated from iliac crest. The bone marrow aspirate was centrifuged at 1300 rpm/min, mixed with platelet rich plasma and instilled transtympanically via BPST point [15]. PTA was done before and 3 weeks after Bone marrow aspirate instillation. The average of pure tone thresholds from 250k-8k was calculated and compared pre and post BM instillation. Significant improvement was considered to be >10 db in PTA.

Results

In present study maximum number [21] of enrolled patients were in age group of 30-40 years (Range 13-60 years) (Figure 1). Majority of enrolled patients were male (60%). Seven patients had unilateral SNHL while twenty-three had bilateral SNHL.

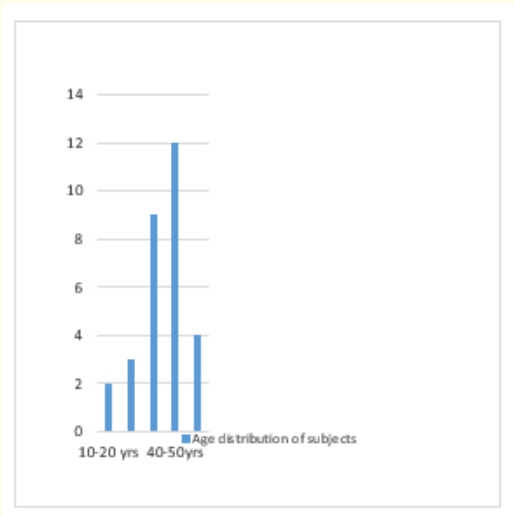

Figure 1: Age distribution of patients.

Out of 30 subjects 22 subjects did not showed significant improvement. 8 patients however showed significant improvement in PTA as well as clinically. The average improvement of 8 patients was calculated to be 15 db after 1 BM instillation (Figure 2). 2 patients also showed clinical improvement in their tinnitus which was an additional finding and needs to be evaluated further.

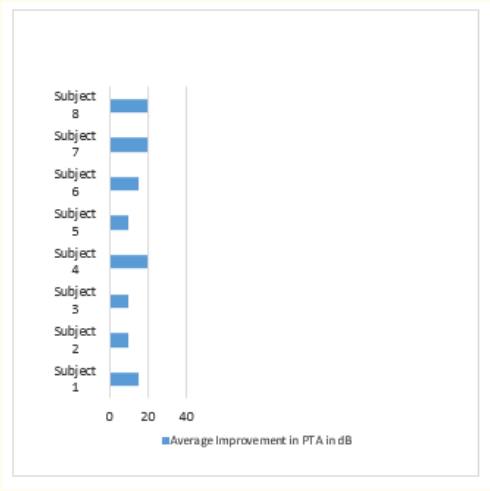

Figure 2: Average improvement in pure tone thresholds in decibels.

Maximum improvement was seen around 2000-8000 Hz (Figure 3).

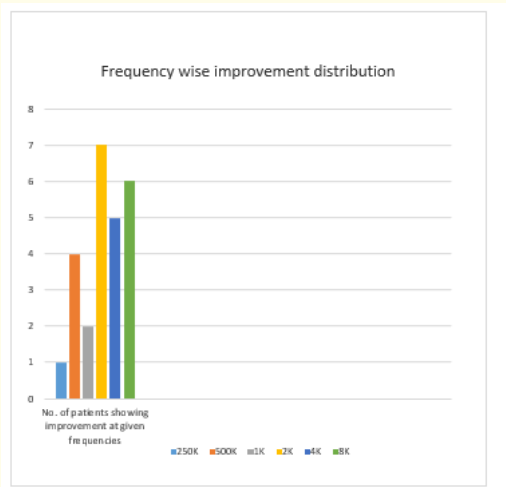

Figure 3: Number of patients showing improvement as per frequency.

Two patients also showed clinical improvement in their tinnitus which needs to be evaluated further.

Discussion

Among MSCs, BMSCs have been widely studied and are comparably more practical [17]. Various studies indicate potential of BMSC to deliver therapeutic molecules and restore cochlear cells.

Mesenchymes SC of bone marrow are easy to obtain and also generate neurons in their differentiation process. Together with produced neurotrophyns, they would increase the number of neurons and would provide support to spiral ganglion, with potential improvement of the cochlear implant efficiency [18].

Considering the potential of MSCs to differentiate into neural type cells, these cells would be good candidates for regenerative cell-based therapies [19-23].

According to ISSCR (International Society for Stem Cell Research), ASCs or tissue-specific stem cells exist in completely formed organs or tissues. As they retain the capacity for self-renewal and differentiation into cells from the same tissue or organ in which they are located, they are classified as multipotent. Despite this limitation, adult stem cells are considered valuable because (i) they are easier to extract from tissue samples, (ii) face fewer ethical issues than human ESCs Aand (iii) are good candidates for use in cell therapy, since they can be obtained from adult patients in treatment, reducing risks of immunological rejection [24].

Conclusion

Human bone marrow stem cells can be delivered to cochlea by systemic route, i.e., intravenously or locally infused in the round window, scala tympani or scala media, or direction injection into the modiolus. Lee H S., *et al*. used intravenous route to deliver BMSC in two patients without any side effect but no improvement was observed [16]. In present study BMSC were injected locally. Improvement in eight out of thirty patients warrants further studies to establish the role of BMSC in improvement of SNHL.

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