

# Stem Cell Research In The Management Of Complete Spinal Cord Injury In Bangladesh

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**Abstract-Objective:** Spinal cord injury, is certainly a debilitating and devastating condition in terms of its effect on a person's physical, mental, familial as well as social life. Spinal cord injury (SCI) causes sensory loss, motor paralysis and autonomic difficulties. Complete spinal cord injury with ASIA Grade A patients remains untreated and neglected in our country since long back. Here we describe an effective strategy for the treatment of complete spinal cord injury by autologous bone marrow derived stem cell.

**Method:** The study was conducted in the stem cell research unit in Neurosurgery department, Dhaka Medical College & Hospital, Dhaka, Bangladesh since January, 2015. The study population was 32 Patients with complete spinal cord injury (ASIA Grade-A). Total 60 ml of autologous bone marrow was aspirated and processed to prepare 6-7 ml of bone marrow aspirate concentrate (BMAC) which was transplanted at the site of cord injury. Bony alignment was done by decompression and stabilization. Post-surgical physiotherapy and regular follow up was given.

**Results:** Surgical outcome was assessed by ASIA Grading and subjective autonomic improvement. Among 32 patients, 16 patients (50%) improved by one grade, 10 patients (31.25%) improved by two grade, 5 patients (15.63%) improved by three grade, 1 patients (3.12%) did not show any improvement of any grade as because their follow-up period was less than 6 months. 31 patients (96.87%) noticed sensory/motor improvement, 25 (78.12%) patients noticed bowel improvement and 21 patients (65.62%) noticed bladder improvement by some extent.

**Conclusions:** Stem cell therapy is safe and effective. Steady and focused progress in stem cell research will open the door for many disable patients in the country like Bangladesh.

**Keywords—** *Spinal cord injury (SCI), Bone marrow aspirate concentrate (BMAC), American Spinal Injury Association (ASIA)*

## I. INTRODUCTION

Every year, around the world, between 250 000 and 500 000 people suffer a spinal cord injury (SCI). The majority of spinal cord injuries are due to preventable causes such as road traffic crashes, falls, violence, etc [1]. Bangladesh is a densely populated

developing country in Asia, with 964 persons per square km [2]. In Bangladesh, Most common causes of spinal injury were road traffic accidents (RTA) (50%), followed by history of fall and carrying loads on the head. 74.8% of the injured persons had been rescued from the accident site by local people but only 16.1% had been transported by ambulance. The spine board had never been used. More than half of the injured received initial treatment only at a sub-district or district hospital where none of the requisite facilities were available. While being transported from one hospital to the other, 10.7% experienced neurological deterioration to some extent [3]. Studies found that males (84%) are predominantly affected by TSCI. Three-fourths (75%) of the injured were in the economically productive age group of 15-45 year. As a result, SCI has a negative impact on families as well as the national economy of Bangladesh. Both age and gender have nearly the same distribution as seen in other studies on developing and developed countries [4]. Due to its profound impact on a person's overall quality of life and increasingly high incidence, injury to spinal cord due to any pathology is now considered as a morbid condition as well as a threat to both personal and national economy [5,6,7]. Spinal cord injury itself is a crippling condition, at the same time may lead to a variety of complications which can affect the life of the patient as it increases the treatment cost significantly and accelerate the disease process to early mortality [5, 7, 8]. The complex pathology of SCI may be divided into primary and secondary injury. The primary injury is induced by mechanical damage and resultant hemorrhage. Many factors contributing to secondary injury include: excitatory amino acid toxicity, oxidative damage, inflammation and autoimmune response, edema, ischemia. These combined injury mechanisms, leading to glial and neuronal cell death, demyelination and axonal degeneration, are manifested as a severe impairment in neurological function [9]. At the cellular level, mild contusion to the spinal cord causes massive neuronal and glial cell loss, demyelination, cavitation and glial scarring [10]. Resulting in loss of sensory perception, distal motor paralysis, and severe functional impairment. Functional improvement depends on the success of a combination of molecular, cellular and rehabilitative physiotherapy. Safe and effective therapies are clearly needed to enhance the quality of life for SCI patients. [11]. Stem

cell transplantation at the site of injury has emerged as a possible alternative therapy for severe spinal cord injury [12]. Human bone marrow-derived mesenchymal stem cells (HBMSCs), identified alongside hematopoietic stem cells and possessing tremendous capacity for self-renewal and differentiation, are a type of adult stem cell that have demonstrated positive effects in the treatment of SCI [13,14]. In the current study, we report on surgical outcome of autologous bone marrow derived stem cell transplantation in 32 patients of SCI treated in the stem cell research unit at Dhaka Medical College & Hospital, Dhaka, Bangladesh. In addition to BMAC transplantation in the cord, decompression and fixation of respective fragmented unstable vertebral column was done.

## II. MATERIALS AND METHODS:

### A. Patient Selection

A total of 32 SCI patients were enrolled in our study at Dhaka Medical College Hospital, Bangladesh from January, 2015 to January, 2020. There were 24 male patients (75%) and 8 female patients (25%), aged ranged from 11-67 years, with an average age of 33.5 years. According to the American Spinal Injury Association's classification of SCI (ASIA impairment scale) all the 32 cases were of grade A. Among all SCI patients, there were 7 cases involving the cervical region, 17 cases involving the thoracic region, 8 cases involving lumbar region. When divided into the etiology of SCI, there were 19 cases caused by RTA and 13 cases are of fall from height. Written informed consent were obtained from all participants before intervention.

### B. Transplantation Method

Under aseptic conditions, 60 ml of bone marrow was aspirated from the posterior superior iliac crest and placed immediately into a sterile bag containing 4 ml of ACD solution. Then the aspirate was filtered from the bag and placed in a container and centrifuged for 14 min at 4000 rpm at room temperature. The supernatant plasma, Buffy coat were discarded, and the nucleated cells which were precipitated are collected in a special syringe and transplanted at the site of injury immediately. Before transplantation in the cord, decompression and bony fusion of the vertebral column was done. After adequate decompression by laminectomy, partial corpectomy and discectomy followed by stabilization with transpedicular screw and rod was done, durotomy at the site of injured spinal cord was done. The contused cord elements, fibrin debris, haematoma was sucked out and the site of injured area was prepared for transplantation, then the CSF pathway was made established. Then the centrifuged BMAC stem cell was transplanted at injured site and in the surrounding place. Then water tight closure of dura was done. A total of 6 ml BMACs were injected into each SCI patient.

## III. RESULTS

### A. Assessment of Neurological grading by ASIA impairment scale:

Our analysis of the 32 SCI study patients receiving autologous BMAC transplantation was notable for all patients exhibiting improvement in sensory and motor function. Of the 32 SCI study patients, 31 individuals (96.87%) improved by one or two or three grades as measured by the ASIA impairment scale where 16 (50%) of those 32 patients improved by one grade, 10 (31.25%) of the 32 patients improved by two grade and 5 (15.63%) of those 32 patients improved by three grade. 1 (3.12%) patients did not shown any improvement (Table I). The prognosis of SCI patients appears to be dependent on the stage of SCI, the cause(s) of SCI and patient's age. Considering the multiple characteristics of our study patients, we compared the therapeutic effects of autologous BMAC transplantation on SCI patients according to the variables in Table II.

### B. Assessment of urinary and bowel function:

Of our 32 individuals (100% of the total SCI study subjects) suffering from urinary dysfunction in the form of acute retention. Patient recovery information is shown in Table III. 32 patients (100%) present to us with acute urinary retention requiring catheterization. Of the 32 SCI individuals suffering from urinary dysfunction, 65.62% (21/32) experienced post-stem cell transplantation improvement in urinary function to varying degrees.

Of the 32 individuals (100% of the total SCI study subjects) suffering from bowel dysfunction, in the form of dry stool. Patient's recovery information is listed in Table IV. Of the 32 individuals, 25 cases (78.12%) experienced post-stem cell transplantation improvement in bowel function to varying degrees.

## IV. DISCUSSION

A series of animal experiments [15, 16] and clinical trials [17, 18] have previously demonstrated that stem cells have beneficial effects for SCI. Our study demonstrates that motor and sensory dysfunction, urinary and bowel functional disorders may improve significantly following stem cell transplantation. A study using Human Bone Marrow Mesenchymal Stem Cell (HBMSC) transplantation for the treatment of SCI [17] demonstrated that 29.5% of patients in the acute stage (<2 weeks) experienced an improvement in ASIA impairment rating from grade A to either B or C. Additionally, 33.3% of patients in the subacute stage (2-8 weeks) experienced an improvement in ASIA impairment rating from grade A to either B or C; while no improvement in ASIA impairment scale occurred in the chronic (>8 weeks) group. In our current study, (31) 96.87% of SCI patients experienced an improvement in ASIA grading, with the majority of these patients receiving stem cell transplantation and adequate decompression after 2 weeks of SCI with the exception of one patient who was in the chronic (after 1 year) SCI stage by laminectomy and removing soft tissue. Stem Cell therapy appears to have been more

beneficial for the patients in the current study than for those in the study by Yoon et al, in theory, the higher the grade, the greater the improvement; however, our data suggests an inconsistency with this theory as because our all samples were complete spinal cord injury with lowest grading. In addition, while our study followed-up patients for more than six months, Yoon et al continued for 10.4 months. May be this two factors are the causes of difference of the results. In our study among 32 SCI patient 16 patients improved one grade, 10 patients improved two grade and 5 patient improved three grade and 1 patients does not improved yet at all but patient may improve in subsequent follow up. Normal urinary and bowel function make a significant contribution to quality of life. Of the 32 SCI patients (100% of total) reporting urinary dysfunction, 21 patients (65.62%) experienced improved micturition following stem cell transplantation. In the study by Kishk et al [19] where no patients experienced complete recovery in urinary function, but in our study five patients experienced a return to normal function and other with dribbling urine prior to stem cell therapy. All 32 patients having bowel dysfunction in the form of hard stool, 25 patients (78.12%) experienced an improvement in function following stem cell therapy; this result is commensurate with the results from the study by Kishk et al. In addition to aiding the functional integrity of autonomic nerves for normal urinary and bowel function, the return of intestinal secretions following stem cell transplantation may have ameliorated a significant factor in the bowel dysfunction in certain patients. Although limitations exist, bone marrow derived stem cell transplantation has demonstrated its effectiveness for the treatment of SCI. The majority of our patients clearly benefited from transplantation with notable improvements in sensory, motor and autonomic function. The mechanisms by which stem cells benefit SCI patients, however, are not fully clear. Currently, the mechanisms by which stem cells are believed to repair damaged tissue include the secretion of neurotrophic factors, the ability to re-wrap injured nerve fibers suffering demyelization and the formation of neural circuitry by transplanted cells that are able to differentiate into neurons [20- 21]. However, despite steadily accruing evidence in support of the therapeutic benefits of stem cell transplantation, universal consensus regarding the mechanisms of action does not yet exist. Additional studies of autologous bone marrow derived stem cell transplantation for the treatment of SCI remain a critical pursuit.

**Table 1:** ASIA grading before and after cell transplantation

ASIA rating before transplantation	Initial cases (n)	ASIA Grading Improvement 6 months after transplantation					Number of cases presenting improvement
		A	B	C	D	E	
A	32	1	16	10	5	0	31 (96.87%)
<b>Total</b>	<b>32</b>	<b>3.12%</b>	<b>50%</b>	<b>31.25%</b>	<b>15.63%</b>	<b>0%</b>	<b>31 (96.87%)</b>

**Table 2:** Different variables impacting the efficacy of stem cell transplantation.

Factors	Initial cases (n=25)	Cases improved 6 months after cell transplantation (n=25)
<b>Cause of injury</b>		
Trauma		
RTA	19	19
FALL	13	12
Non-trauma	0	0
<b>Site of injury</b>		
Cervical vertebrae	7	6
Thoracic vertebrae	17	17
Lumber vertebrae	8	8
<b>Gender</b>		
Male	24	24
Female	8	7

**Table 3:** Recovery of urinary function in spinal cord injury (SCI) patients

Types	Initial cases (n=25)	Cases improved 6 months after cell transplantation (n=25)
Acute Urinary retention	32	21

**Table 4:** Recovery of bowel function in spinal cord injury (SCI) patients

Types	Initial cases (n=25)	Cases improved 6 months after cell transplantation (n=25)
Hard stool	32	25

Fig 1: Pre-operative MRI of SCI



Fig 2: Per operative view with fixation

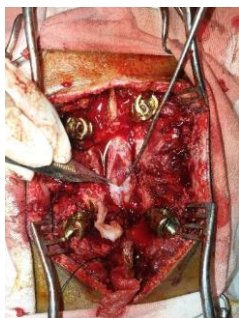


Fig 3: Various stages of preparation of bone marrow aspirate concentrate (BMAC)

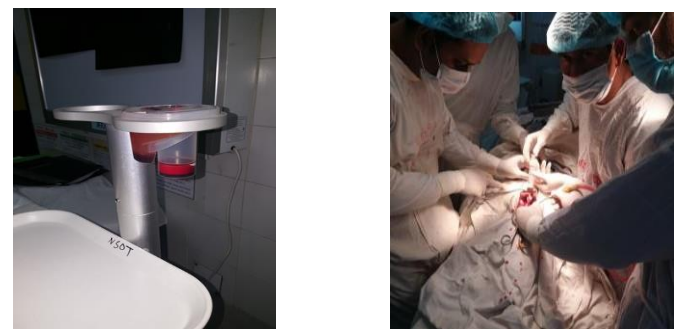
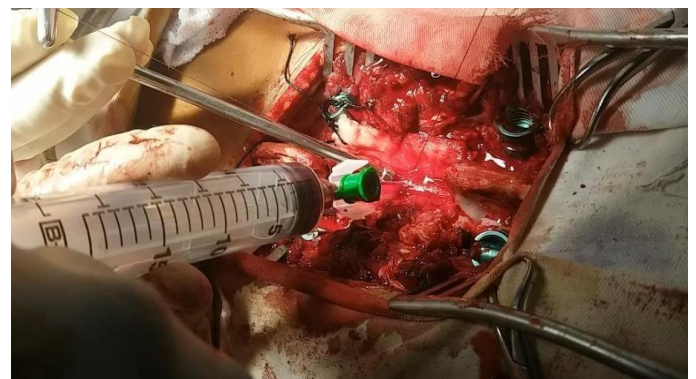


Fig 4: Stem cell placement at the site of injured cord.



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