

Stem Cell Therapy in Chronic Leg Ulcer and Avascular Necrosis (Bone) Due To Sickle Disease (SCD)

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ABSTRACT:

BACKGROUND: Impeccable magnitude of Haemoglobinopathy in Western odisha involving 1 out of 10 persons in vulnerable community needs innovative approach to address the challenges.

STEM CELL THERAPY : Stem Cell therapy in chronic leg ulcer and Avascular necrosis, the twin complications of SCD, was contemplated. It is promising in the former where as lack of sufficient data has not permitted the formulation of reliable recommendation in the later group.

KEY WORDS: Sickle cell disease (SCD), Stem Cell Therapy, Chronic leg ulcer, Avascular Necrosis.

INTRODUCTION:-

Chronic leg ulcer and Avascular necrosis (AVN) are severe complication of sickle cell disease (SCD),^(1,2). Its treatment is not standardized. Chronic leg ulcer refer to a defect in the skin below the level of knee and above the foot persisting for at least 6 or more weeks⁽³⁾. AVN is a condition of Non traumatic ischemic bone necrosis⁽⁴⁾, both share the common aetiopathophysiology of interruption of vascular supply due to sickle disease⁽⁵⁾. Haematopoietic stem cell transplantation (CHSCT) is a commonly used method for improving human health by restoring cellular and organ function damaged by disease or injury on the principle of break- through strategies for tissue engineering “ Repair and Regeneration”⁽⁶⁾. This study was undertaken to asses wound healing capacity, effectiveness and safety of exogenously applied / infiltrated autologous mesenchymal stem cell on both chronic leg ulcer and AVN due to sickle cell disease. The result so obtained were compared with control group, analyzed and put forth along with review of literature.

MATERIAL AND DESIGN

Centre for research – Sickle cell Research Centre& Department of Surgery, VSS Medical College, Burla. Out of 60901 homozygous sickle cell disorder (Hb ss) registered in the centre from April 2010 to 31st to March 2013, 1121 subjects were recruited in the study.

Illustration-I

Total	N 6901	Age Group 1-75	Mean age in year 18.3± 12.05	Male 4170(60.43%)	Female 237 (39.37%)	Children 2467 (35.57%)
Recruited Group	1121	—	22 + 11.6	—	—	—
Chronic leg ulcer	21	1.9%	-do-	21	Left leg-06	right leg-14
AVN	216	19.3%	-do-	201	15	Both-1
						Femoral head-201 Humeral head-15

Source:- Patel D.K. Clinical aspect of sickle cell disease, 5th brazillican symposium of sickle cell disease and hemoglobinopathies available with // www.cehmob.org.br/symposiathtual

Illustration-II .

These 21 case with chronic leg ulcer further categorized into two groups on the basis of size 5-9cms(4) and 10-12cms(17). The entire 10patients belonging to the later group were taken up for stem cell therapy remaining 5 of this group sub-served as control, 2 lost to follow up.

Design

Type	Dose	Route	Frequency
Autologous Messenchymal stem cell	10-15ml	External / infiltrated (nonsystemic)	Once
Observation period	Complete wound healing	Incomplete wound healing	--
8-10weeks	8	2	--

Source: Prof Sribatsa Mohapatra, Prof & HOD Surgery, VSS Medical College and Adviser Department of Tissue Engineering, NIT, Rourkela (Fig- A & B)- CD enclosed.

Stem cell therapy in AVN due to SCD is still in infantile state and passing through litmus test for the reason mentioned below.

DISCUSSION

Tissue engineering is based on the principle that progenitor cells, committed to the desired lineage placed on a supportive carrier can regenerate any tissue in the human body⁽⁷⁾. The strategy is to isolate stem cell from the patient (autologous) and seed the committed cell on the site of interest, here chronic leg ulcer.

This advance has led into isolation of many morphogenetic protein like recombinant human bone **morphogenetic protein** (Rh BMP-2) used in bone regeneration, transforming **growth factor- beta** (TGF- β) used in regeneration cartilage, **vascular endothelial growth factor** (VEGF) used to stimulate blood vessel formation to guide the differentiation, commitment and maturation of stem cell⁽⁸⁾

Stem cell local application is an innovative versatile technology probably a new and original approach for chronic leg ulcer. It is effective, 8 of 10 having complete wound healing, and safety, then time consuming, tedious text book approach⁽⁹⁾. The principle is based on niche theory –osteoblastic niche, in both the occasions the stem cells are applied locally /infiltrated (non systemic) & in contact with the defective tissue, endo-osteal or osteoblast in AVN and a wound surface in chronic leg ulcer for repair and regeneration. The application of stem cell therapy in AVN is an widely accepted concept⁽¹¹⁾. The novel treatment has no bleeding or scar formation as the process does not involve surgery. Patient has to visit hospital for a day in a week for each of the four injection. Hospital stay is very short, but currently, it is costly almost 3-4lakhs, hence unaffordable and in accessible for a common man. This is an entirely different approach⁽¹¹⁾, vis-à-vis to the current series, where AVN is due to vascular interruption as result of sickle cell disease where repeated osteonecrosis to even regenerated tissue can not be ruled out, as SCD has conspicuous tendencies for recurrent vaso-occlusive crisis.

Besides alternative modalities of non inflammatory, osteograting and resorbable and generation bone graft (biograft) with faster healing device have been work out⁽¹²⁾, it is affordable, accessible, relatively cheaper and not amenable to vaso-occlusive crisis.. however more studies are needed to better evaluate the effectiveness of both.

CONCLUSION:-

Autologous stem cell external application on the area of interest is a promising and proved safety and effective. Its role in AVN due to SCD vrs biograft conjectural, both need large scale studies to find out the best.

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Illustration-II

A data of 1121 sickle cell anemia patients (HbSS)

Presentation	% of total cases
Mean Age	22.0 ± 11.6 yrs
Asymptomatic cases	6.7%
Painful crisis	86.6%
Mod & Severe Anemia (Hb<10g%)	64.2%
Hemolytic jaundice	54.4%
Infections	36%
Presentation	% of total cases
Splenomegaly	50.8%
Avascular necrosis	19.3%
Cholelithiasis	27%
Chronic renal failure	17%
CNS (Stroke)	2.6%
Leg Ulcer	1.9%
Priapism	0.3% (3 pts)
Mortality	4.7% (53 pts)

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Chronic leg ulcer



Figure- A before stem cell therapy



Figure- B after stem cell therapy



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