Autologus Haemopoitic Stem Cell Transplantation in Decompensated Cirrhotics via Portal Venous Route - Initial Experience from Bangladesh

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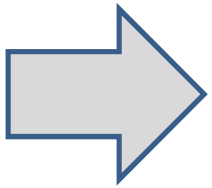
Introduction

Why We Need Induced Hepatic Regeneration?

- Extensive damage to hepatocytes
- Fibrosis of hepatic parenchyma
- Distortion of lobular structure
- Metabolic abnormality
- Synthetic impairment
- Excretory dysfunction

Normal regeneration

Overriding damage  Induced regeneration

Induced Regeneration

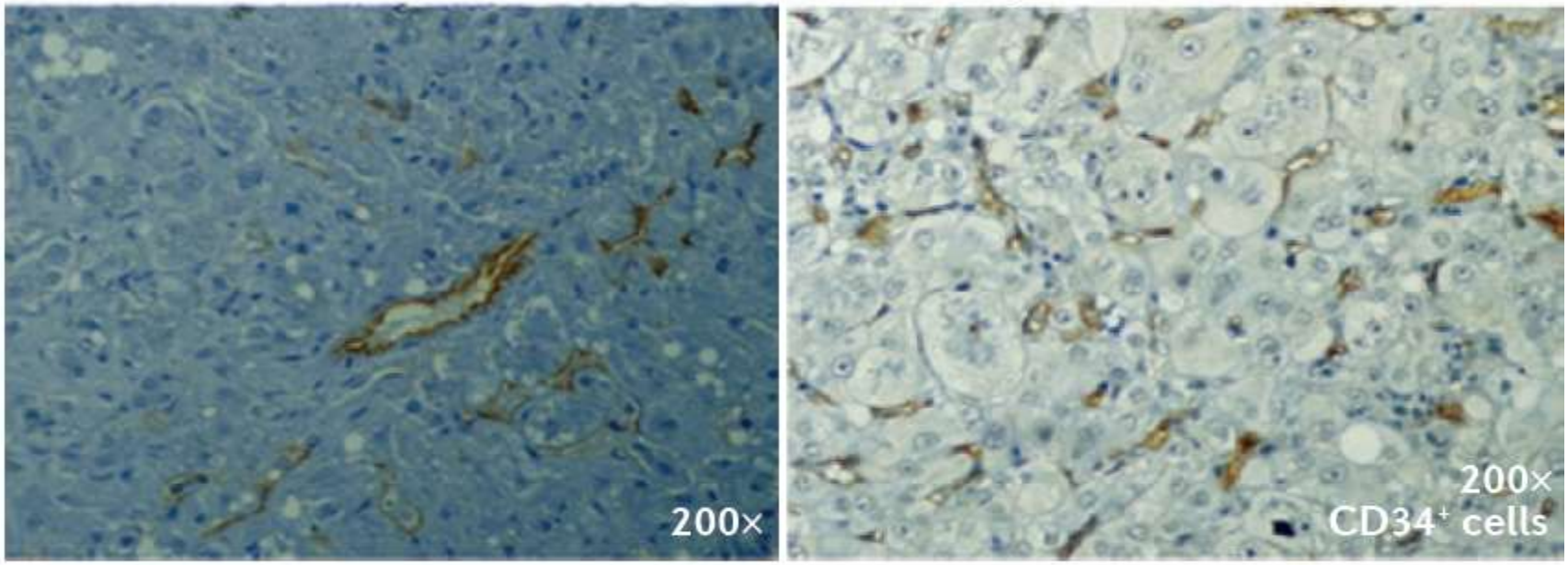
Regeneration by in vitro Procedure

Tissue Transplantation

Regeneration by in vivo Procedure

Stem Cell Transplantation

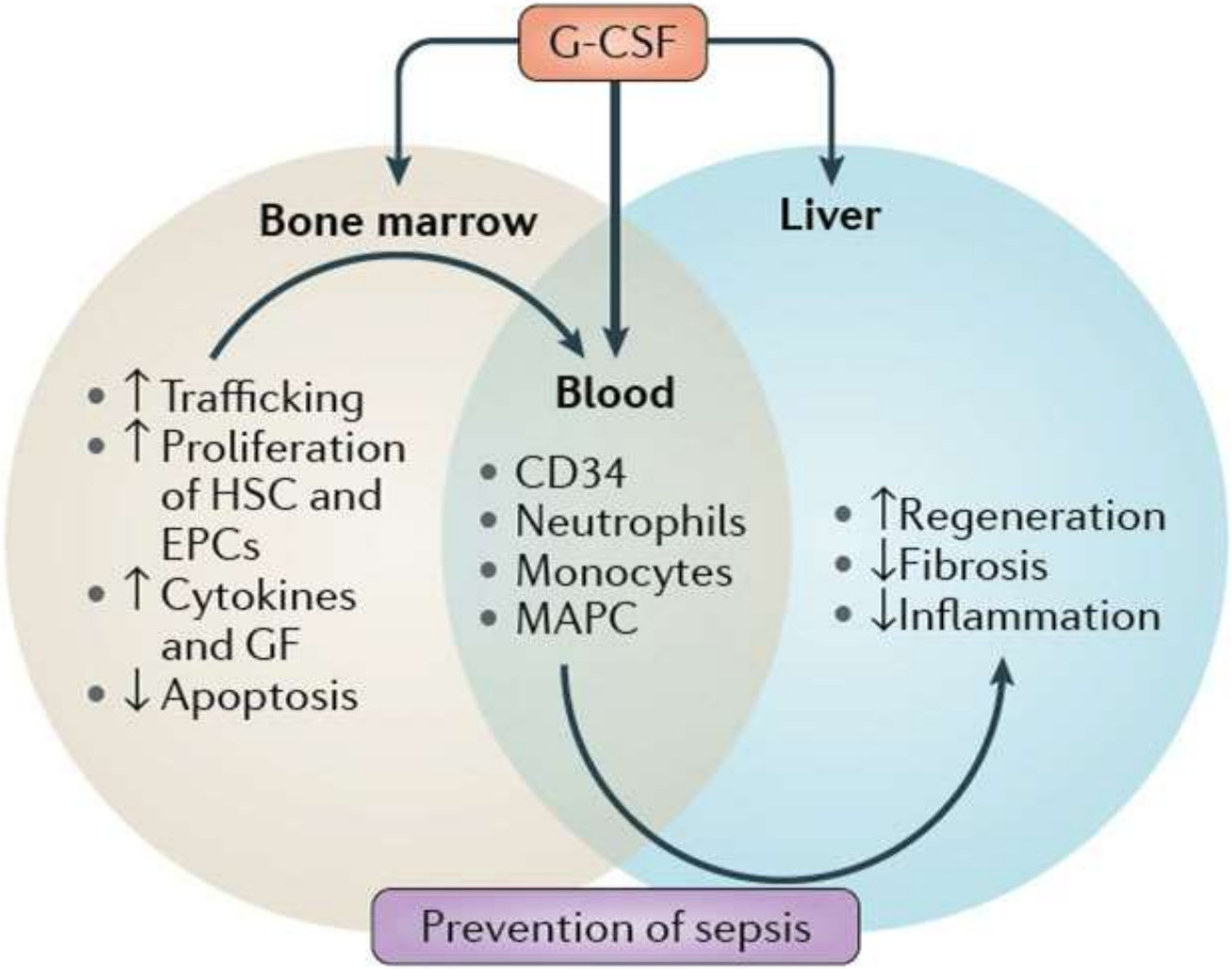
Mobilization of Stem Cells from Bone Marrow with G-CSF



30% pretherapy

70% post-G-CSF therapy

Kumar C et. al. Gastroenterol. 2015



Sarin, Chowdhury. Nat Rev Gastro Hepat. 2016

Table 2 Clinical Trials Assessing Cirrhotic Liver Disease.

Study	Author year	Sample size	Methodology	Stem cell	Author conclusions
1	Gaia et al,[23] 2006	Active Treatment: 8 (5 male) Healthy donors: 40	Mobilization using G-CSF	HSC	Safe and feasible. Increase in cell count with potential regeneration
2	Khan et al,[29] 2010	Active Treatment: 4	Infusion of human fetal stem cells	hHPC	Significance decrease in patient MELD score. may be used as supportive treatment
3	Terai et al,[24] 2006	Active Treatment: 9 (8 male)	Infusion of BM taken from ileum	MNC	Improvement of liver function
4	Kharaziha et al,[28] 2009	Active Treatment: 8 (4 male)	Infusion of BM taken from iliac spine	MSC	No increase in morbidity or mortality. May improve liver function
5	Mohamadnejad et al,[25] 2007	Active Treatment: 4 (1 male)	Infusion of BM taken from iliac crest	MSC	Safe and feasible. Some improvement in liver function
6	Mohamadnejad et al,[26] 2007	Active Treatment: 4 (2 male)	Infusion of BM taken from iliac crest	HSC	Infusion not safe through hepatic artery due to side effects
7	Nikeghbalian et al,[31] 2011	HSC Treatment: 3 (1 male) MNC Treatment: 3 (2 male)	Infusion of BM taken from iliac crest	HSC MNC	Safe and feasible. No significant difference between HSC and MNC
8	Lin et al,[32] 2012	Active Treatment: 38 Placebo Treatment: 16	Infusion of cells derived from umbilical cord	MSC	Safe and has potential to improve quality of life of patient
9	Zhang et al,[3] 2012	Active Treatment: 30 Placebo Treatment: 15	Infusion of cells derived from umbilical cord	MSC	Safe and feasible. Can improve liver function
10	Salama et al,[30] 2010	Active Treatment: 90 (78 male) Placebo Treatment: 50 (38 male)	Mobilization using G-CSF followed by infusion from iliac crest	HSC	Safe and tolerated. HSC transplantation can be used as supportive treatment.
11	Pai et al,[27] 2008	Active Treatment: 9 (6 male)	Mobilization using G-CSF followed by infusion	HSC	Safe and feasible. Improvement in liver function

Review Article

JOURNAL OF CLINICAL AND EXPERIMENTAL HEPATOLOGY

Could Stem Cell Therapy be the Cure in Liver Cirrhosis?

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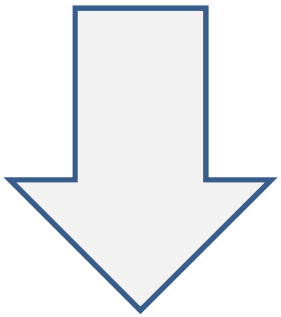
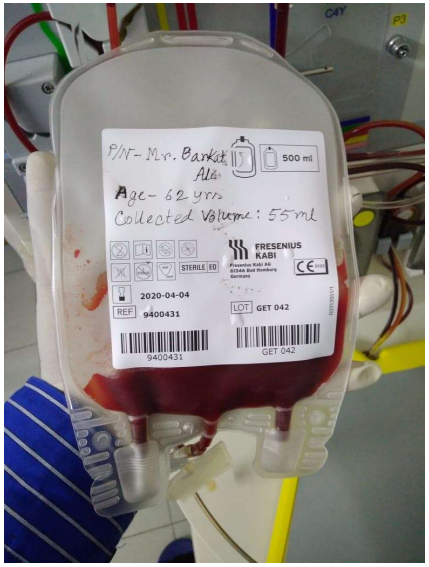
- **11 clinical trials analyzed stem cells therapy in treatment of liver cirrhosis**
- **Primary aim to determine safety of this therapy**
- **Concluded that infusion of stem cells through either the hepatic artery or portal vein was safe**

Methods

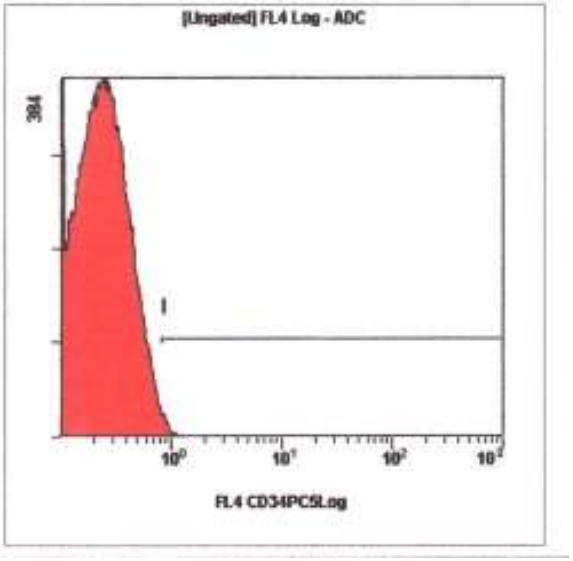
Pre-stimulation

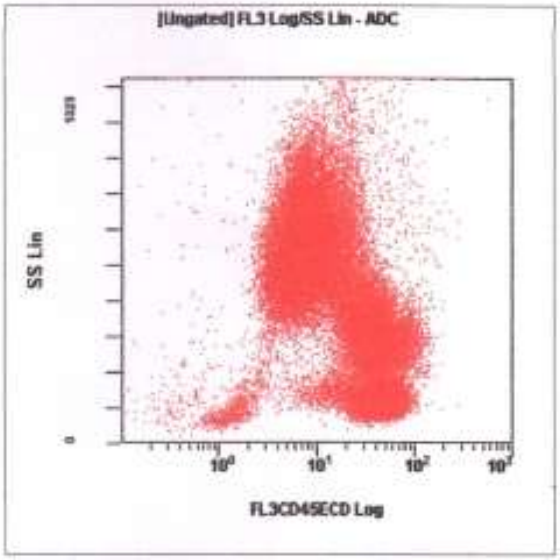


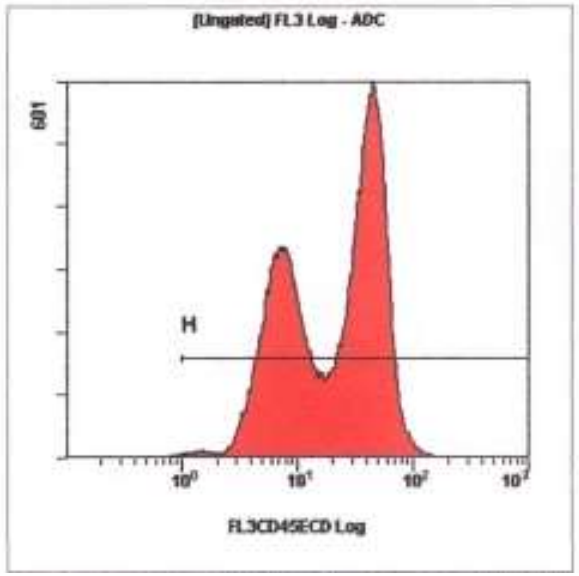
Stimulating Stem Cell Production by G-CSF in decompensated cirrhosis (30 IU daily for 6 days)


P/N- Mr. Barkat Ali
500 ml
Age- 62 yrs
Collected Volume: 55ml
FRESENIUS KABI
STERILE EO
2020-04-04
REF 9400431
LOT GET 042
9400431
GET 042

Stem Cell Count

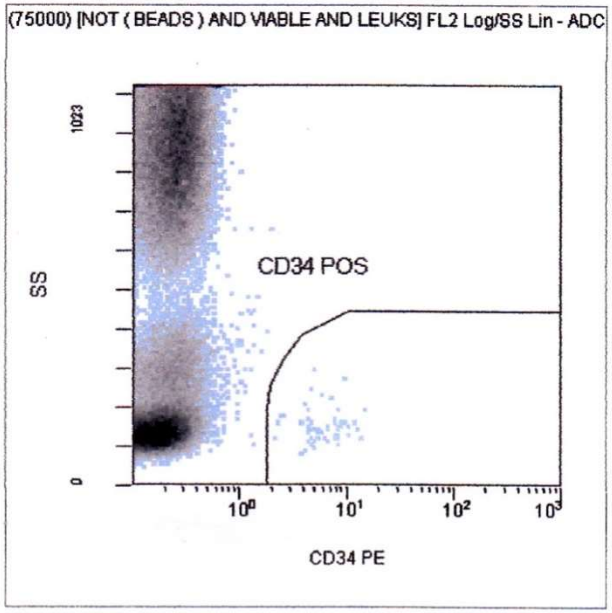




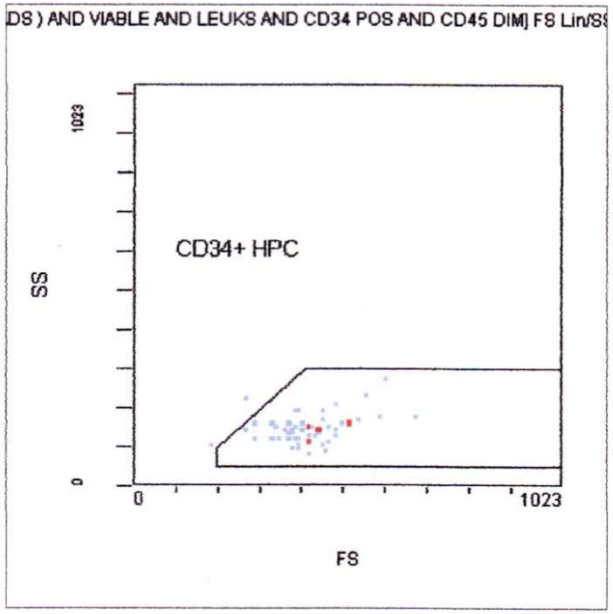


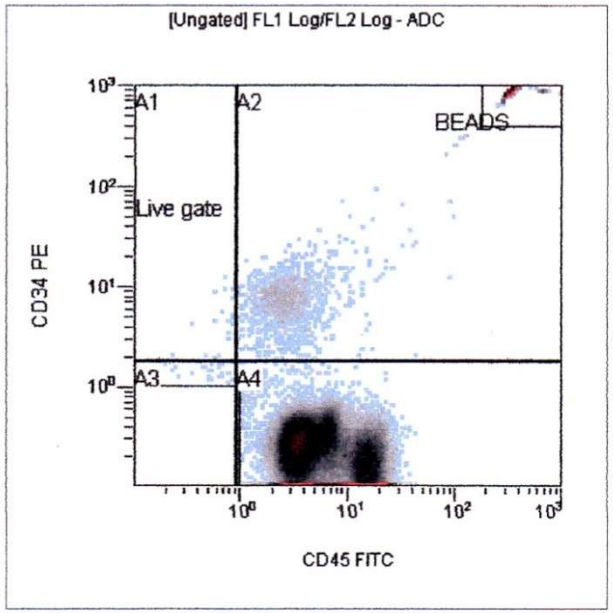
- CD34 HSC Count: by flow cytometry
- Count 7.5 x 10^5 /ml

Stem Cell Viability



- **CD34 HSC viability: using FC 500 Beckman Coulter 4 colour (CXP software)**
- **Kit: Stem cell single platform**





Results

Result [n=33]

	Baseline	At Day 30	At Day 90
Bilirubin	4.09	1.87	1.64
Albumin	3.08	3.15	3.40
PT	17.57	16.65	15.55
Ascites	9 (++/+++)	4 (++/+++)	1 (++/+++)

Death: 1

Mahtab et. al. HAEMATOCON 2019

Stem Cell Therapy for Cirrhosis of Liver in Bangladesh: Specific Design Compatible for Developing Country

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Table 1: Biochemical parameters of patients with liver cirrhosis at different time points

	Bilirubin	*SGPT*	*Albumin*	*INR*	*PT*	*Creatinine*
Basal	2.2±2.5	38±25	2.63±0.45	1.67±0.53	20.24±6.63	1.09±0.35
One month after start of therapy	1.81±1.55	35.55±14.3	3.03±0.48*	2.0±2.2	18.41±6.0	1.03±0.36
Three months after start of therapy	2.03±1.80	33.0±12.8	3.12±0.39*	2.02±2.39	17.58±6.0	1.04±0.37

SGPT, serum glutamic-pyruvic transaminase; INR, international normalized ratio; PT, prothrombin time $p < 0.001$

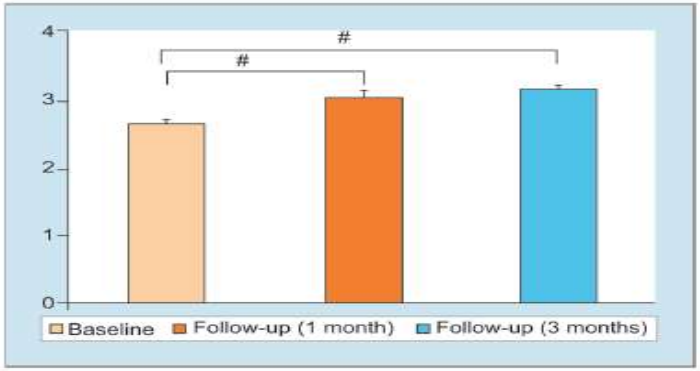

Fig. 1: Levels albumin at different states before and after stem cell therapy in patients with liver cirrhosis

Result [n=34]

	Baseline	At Day 30	At Day 90
WBC	6992 29444 (after GCSF)	-	-
CD34	4648790.08/ml		
Bilirubin	3.83	2.59	1.56
Albumin	2.69	2.96	3.24
PT	20.34	17.88	17.85
Ascites	14 (++/+++)	3 (++/+++)	-

Deaths: 11
Unrelated cause: variceal bleeding, MI: 7
Related cause: HE - 3, HRS - 1

Mahtab et. al. EJOHG 2018

Conclusion

- Autologous haemopoitic stem cell transplantation safe in decompensated cirrhosis
- No rise in AFP; no hepatic SOL
- Seems beneficial
- Further study to optimize outcome and treatment design

Thank You!