Biomedical Data Mining

Extended Abstract

Peripheral blood hematopoietic progenitor cells correlate with clinical outcome of trauma haemorrhagic shock

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Abstract

Background: Haemorrhagic shock (HS) accounts up to half of early injury passings. Hematopoietic disappointment has been seen in test creatures and human after stun and injury. One of the features of bone marrow disappointment is different organ brokenness disorder and is generally found in patients recuperating from serious injury and haemorrhagic stun. Bone Marrow (BM) brokenness is related with activation of hematopoietic forebear cells (HPCs) into fringe blood. Present investigation investigated the relationship of fringe blood hematopoietic ancestor cells (HPCs) with mortality in injury haemorrhagic stun patients (T/HS).

Materials & Methodology: Planned accomplice investigations of patients introducing inside 8 hrs of injury with T/HS in the Department of Emergency Medicine, Jai Prakash Narayan Apex Trauma Center, All India Institute of Medical Sciences were enrolled. Fringe blood tests were gathered in every patient for estimation of fringe blood HPCs. Fringe blood ancestor cell (PBPC) measurement was performed by estimating HPCs tallies utilizing the hematology analyzer (Sysmex XE-2100). Clinical and research facility information were tentatively gathered after assent. Moral endorsement was taken and information was dissected by Stata 11.2.

Results: 39 patients with T/HS and 30 typical solid controls were enrolled. HPCs were fundamentally higher ($P<0.001$) in the T/HS when contrasted with control. Among study gathering, 14 patients passed on inside 24 h at the clinic confirmation, and discovered HPCs fixations were exceptionally critical ($P<0.001$) in non-survivors (n=14) when contrasted and survivors (n=25) among T/HS patients.

Conclusions: Our studies propose the fringe blood HPCs might be early prognostic marker for mortality among patients who gave injury haemorrhagic stun on confirmation. Be that as it may, the specific sub-atomic system and flagging pathway engaged with the difference in the conduct of bone marrow microenvironment is as yet hazy.

Introduction

Severe trauma and hemorrhagic shock is the leading cause of mortality in individuals between 5 and 44 years. Hematopoietic failure has been observed in experimental animals and human following shock and injury. One of the facets of bone marrow failure is multiple organ dysfunction syndrome and is commonly seen in patients recovering from severe trauma and haemorrhagic shock.

Bone marrow (BM) is composed of after stromal cells, fibronectin, proteoglycans and hematopoietic stem cells (HSCs) niche in mammals. Previous studies demonstrated that impaired growth of hematopoietic progenitor cells (HPCs) and stromal cells associated with bone marrow failure in T/HS. Shah et al. (2009) reported in severe trauma, initial mobilization of HPCs from BM to peripheral blood into injured or inflammatory tissue, is beneficial for wound healing and maintaining immune response. Increased peripheral blood HPCs were associated with BM dysfunction. There is paucity of literature regarding the HSCs behavior and its correlation with outcomes following T/HS.

The present study explored the role of circulating Haematopoietic progenitor cells and its correlation with outcomes in T/HS. It also focuses on technique to study HPCs.

Materials and Methods

Study design: Prospective cohort study

Study group

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Inclusion criteria
Trauma victims with hemorrhagic-shock
Age group > 18, <60 years
Systolic blood pressure of ≤90 mmHg.
Patients or proxy must be willing to provide informed consent
Patients presenting within 8 h injury to the Emergency Department.
Exclusion criteria include
Age group <18, >60 years
Systolic blood pressure >90 mmHg
Patients already resuscitated with colloids or crystalloids before reporting to the emergency department.
Patients had a history of haematological diseases or pre-existing anaemia, liver or renal failure
Cardiogenic shock
Head injury
Hematologic diseases or preexisting anemia, had active HIV infection, or had a history of renal or liver failure
Septic shock
Neurogenic shock
Control group: Healthy control

Result

39 T/HS patients, between 18-60 yrs, with 31 males and 8 females and 30 controls were recruited for the study. Results from the samples collected from 25 T/HS who had survived were compared with the data from the non-survivors of T/HS.

In T/HS, the levels of peripheral blood HPCs were elevated when compared to normal healthy volunteers ($P < 0.001$) [Table 1]. Subgroup analysis showed increased peripheral blood HPCs levels among non-survivors ($n = 14$) compared to survivors ($n = 25$, $P < 0.001$).

Elevation in peripheral blood HPCs is also observed in non-survivors patients with ISS score 17.0 (9, 50) vs. 12 (4, 50) $P < 0.05$) [Table 2], creatinine (1.2 ± 0.3 vs. 1.0 ± 0.40), $P < 0.05$), PT (24.2 ± 9.5 vs. 20.5 ± 10.3) $P < 0.05$) APTT (45.3 ± 22.9 vs. 31.9 ± 11.1), $P < 0.05$), pH (7.0 ± 0.2 vs. 7.29 ± 0.1), $P < 0.05$, pO2 (88.2 ± 5 vs. 135.1 ± 8), $P < 0.05$, pCO2 (74.93 ± 9 vs. 29.7 ± 12), $P < 0.05$ when compared to the non-survivors.

Discussion

Trauma hemorrhagic shock cause tissues hypo perfusion and consequent cellular hypoxia, hypoglycemia and metabolic damage. It leads to organ dysfunction by suppressing the immune system and elevation of inflammatory response. Previous studies reported that in severe injury and HS, mobilization of HPCs from BM to peripheral blood are associated with BM dysfunction. Therefore, we evaluated the circulating peripheral blood HPCs and its correlation with outcome.

We found increase in peripheral blood HPCs with T/HS when compared to healthy control. In study group, peripheral bloods HPCs were higher among non-survivors as compared to survivors. Previous study showed that when peripheral bloods HPCs were grown in methylcellulose media; it increased in severely injured patients versus control (15 ± 26 vs. 3 ± 1, <0.05). This study only recruited severe injury group and did not correlate with outcomes. Our study correlated with ISS and outcomes in terms of survival or death.

Baranski et al. showed two times increase in HPCs mobilization into peripheral blood and plasma G-CSF levels at three hours following lung contusion and hemorrhagic shock (LC/HS).[9] Kollet et al. reported T/HS induced stress condition and activation of osteoclast results in mobilization of progenitor cells into peripheral blood, when compared to myocardial infarction and stable angina.

In severe trauma, initial mobilization of hematopoietic progenitor cells from BM to peripheral blood, is beneficial for wound healing and maintaining immune response. Fonseca et al. reported that in severe trauma induced stress condition, increased urine nor-epinepherine level versus control (139 ± 59 mcg/day vs. 35 ± 9 mcg/day) promoted BM dysfunction and hematopoietic failure in human. Excessive release of inflammatory cytokines leads to sustained elevation of catecholamine concentrations.

Elevated catecholamine levels alters the regulation of signaling pathways (CXCR4 and SDF1) resulting in suppression of bone marrow HPCs and continued mobilization of HPCs into peripheral blood leading to persistent anemia. Similarly, stress condition induced by catecholamine is also seen in burn injuries. Previous studies showed Granulocyte colony stimulating factor (G-CSF) as one of potent stimulator of hematopoietic

mobilization, in BM dysfunction following severe trauma and haemorrhagic shock.
Sifri et al. showed BM suppression among GM-CFU and BFU-E colony in castrated male and male rats after T/HS.[18,19] There were 60% decrease in all BM HPCs colony growth, including CFU-GEMM, BFU-E, and CFU-E, when compared to unmanipulated control (UC) at 3h (12 ± 1*, 26 ± 1*, 31 ± 1* vs. 36 ± 1, 65 ± 1, 73 ± 1*P < 0.05) in lung contusion following by hemorrhagic shock.

BM derived stem and progenitor cells have a capacity for self-renewal, differentiation, survival, migration, proliferation and mobilization; which are regulated by extrinsic and intrinsic signal provided by their microenvironment. BM HPCs are thought to be located within specific stroma niches. This specific microenvironment provides soluble factors and cellular interaction required for HPCs proliferation and differentiation. As HPCs differentiate, they may move for one niche to another.

Peripheral blood HPCs quantification was done by sysmex XE 2100 automated haematology analyser in the present study. This is a quick (90 second), user friendly, low cost alternative method for quantification of peripheral blood HPCs. Flow cytometry is the recommended for hematopoietic stem cell count with (monoclonal antibody) MoAb anti – CD34: This however requires skilled personal and expensive procedure and is a time consuming. Sysmex XE2100 does not require MoABs and it can also be used for measurement of complete blood count (CBC) count and leukocyte differential (LDS) count.

Basic principle of Sysmex XE-2100 automated haematology analyzer has immature myeloid information (IMI) channel which are used for quantification of HPCs per microliter of blood. The IMI channel of the Sysmex system lyses mature and erythropoietic cells by means of a special lyse reagent.

Cells in the area of low volume and a reduced plasma/nucleus relation are detected as HPCs and analyzed using a special HPCs software program. HPCs like all immature cells, are resistant to the lytic reagent and are located within a specific gated area of the scattergram.

Limitations

HPCs were assessed only once in T/HS. HPCs were not measured in trauma patients without HS. Further studies may evaluate the peripheral blood HPCs at different time point and its correlation with outcomes following T/HS. The role of signaling pathways involved in HPCs mobilization needs attention and design new therapeutic target to reactivate BM.

Conclusion

Peripheral blood haematopoietic progenitor cells increased after trauma hemorrhagic shock. The peripheral blood HPCs were elevated among non-survivors. Peripheral blood HPCs may be explored as an early marker for mortality among T/HS patients.

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