The favourable effects of Autologous Hematopoietic Stem Cell Transplantation on the immune system in patients with type 1 diabetes

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Objective

Autologous Hematopoietic Stem Cell Transplantation (AHSCT) is a promising treatment to reverse type 1 diabetes (T1D) in patients with significantly improved β-cell function. This study was designed to investigate the potential immunological mechanisms involved.

Methods

18 newly-diagnosed T1D were divided into two groups, the AHSCT group and the insulin therapy group. Blood mononuclear cells (PBMC) of the patients at the baseline visit and the 12-mon follow-up time was collected and cultured. Cell proliferation study was assessed by cell count kit 8 (CCK8), proportion of T cell subsets were analyzed by flow cytometry, and the concentrations of the cytokines in the cell culture supernatants was detected by Procarta Immunoassay Kit. The mRNA expressions of the cytokines were tested by real-time PCR.

Results

1) PBMC showed significant lower proliferation in the AHSCT group and the insulin therapy group compared to the newly-onset group, no difference was found between the two treatments; 2) The proportion of Th1 and Th17 cells decreased in the AHSCT group, but no change was found in the insulin therapy group compared to the newly-onset group; the mRNA expression of IL-2 and IFN-γ and the supernatants concentrates were significantly reduced in the AHSCT group, while the same levels were found in the insulin therapy group as the newly-onset group; 3) The proportion of Treg cells in the AHSCT group was close to the newly-onset group, while it changed less in the insulin therapy group, accompanied with the up-regulated mRNA expression and the increased supernatants concentrations of TGF-b in the AHSCT group compared to newly-onset group. No difference was found in the insulin therapy group.

Conclusion

Our results suggested that the AHSCT treatment has induced a favorable immune situation by reducing activity of PBMC proliferation, associated with skewing from Th1/Th17-dominated to increased Treg phenotypes. It might be important to normal immunity and disease control.

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Table 1. clinical characteristics of type 1 diabetic patients before and after undergoing AHSCT or insulin therapy

	insulin therapy		AHSCT	
	Insulin-0M	Insulin-12M	AHSCT-0M	AHSCT-12M
Age(year)	20.18±4.02		18.86±1.46	
Gender(F/M)	(6/4)		(5/3)	
BMI (kg/cm^2)	18.28±1.39		19.25±1.11	
FBG(mmol/L)	6.50±2.01	6.04±1.70	6.26±0.67	5.59±1.40
HbA1c(%)	12.20±3.50	7.33±1.42	11.49±1.46	6.80±0.60
Fasting C -peptide(nmol/L)	0.62±0.25	0.60±0.50	0.71±0.30	1.01±0.23*
AUCC	4.56±2.50	4.76±1.42	5.93±2.54	9.59±2.98**
Anti-GAD (units/mL)	495.91 (495.12-496.66)	271.94 (270.26-273.64)	1832.01 (1831.45-1832.57)	38.92 (38.23-39.61)***
Insulin dose (U/kg/day)	0.66±0.30	0.52±0.34	0.61±0.27	0.15±0.15**

Note: Comparison at the same points (baseline and follow-up, respectively) between insulin therapy group and AHCST group. Data are shown as mean±SD or geometric mean (95%CI). *P<0.05, **P<0.01, ***P<0.001

Figure 1. Proliferation of PBMC in groups were detected by CCK8. The vertical axis represents relative OD, divided by absorbance of normal one.

Fig 1

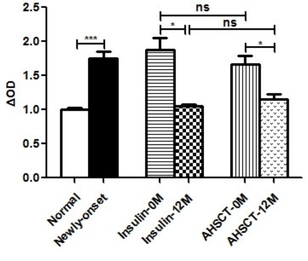

Figure 2. Comparison in proportion of Treg(A), Th1(B) and Th17(C) cells inter groups. * P<0.05, ** P<0.01, *** P<0.001; ns=no significance.

Fig.2A

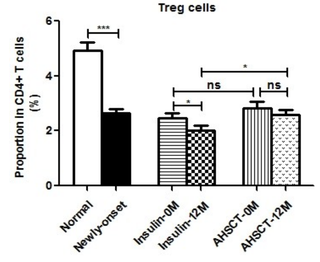

Fig.2B

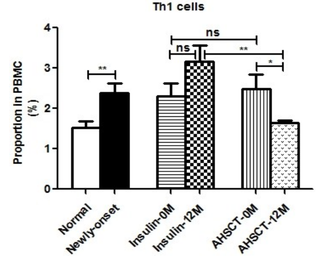

Fig.2C