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508.BONE MARROW FAILURE: ACQUIRED

In Vivo Effects of Porcine and Rabbit Antithymocyte Globulin in Patients with Severe Aplastic Anemia

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Background: Severeaplastic anemia (SAA) is a bone marrow failure disorder mediated by T lymphocytes, resulting in severe deficiency of hematopoietic stem cells. Horse antithymocyte globulin (H-ATG) plus cyclosporin was the first-line therapy for SAA patients in the absence of an HLA-matched sibling [1]. The inhibitory effect of Rabbit-ATG (R-ATG) on lymphocytes is more deeply than that of H-ATG, and the recovery of CD4 T cells is slower, resulting in poor efficacy in SAA patients [2]. Porcine ATG (P-ATG) and R-ATG are two available immunosuppressive choices in China mainland, the first-line formulation of ATG remains unknown.

Methods: From November 2020 through September 2022, we performed a prospective, multi-center, non-randomized trial comparing two ATG formulations. 15 patients received R-ATG therapy and 45 patients treated with P-ATG were collected by prospective registration (ChiCTR2200055696) in the Chinese Eastern Collaboration Group of Anemia (CECGA). The pharmacokinetics, dynamic changes of peripheral blood cells were evaluated. Hematologic responses were also evaluated at 3, 6 months after treatment.

Results: In both P-ATG-treated and R-ATG-treated patients, ATG reached highest concentration 5 days after treatment (1268.4 ± 381.1 ug/ml and 641.2 ± 448.5 ug/ml for P-ATG and R-ATG, respectively), and gradually decreased. At week 2, week 3 and 1 month from the peak values when be assessed, the P-ATG concentration decreased by 70.3%, 81.7%, and 85.4%, while the R-ATG concentration decreased by 68.9%, 88.5%, and 92.2%, respectively. R-ATG showed more powerful effects in depleting peripheral blood lymphocytes than P-ATG, while P-ATG displayed rapid recovery of T cells ($CD3^+$ T cells, $CD4^+$ T cells and $CD8^+$ T cells) (P-ATG vs R-ATG, $CD3^+$ T cells: 30.18 ± 6.04% vs 0.49 ± 0.37%, p=0.0036; 60.58 ± 8.02% vs 7.16 ± 7.16%, p=0.0016; 77.83 ± 3.17% vs 59.67 ± 7.93%, p= 0.015 for day 3, week 1 and week 3, respectively; $CD4^+$ T cells: 9.13 ± 2.20% vs 0.03 ± 0.02%, p=0.013, 24.49 ± 4.21% vs 1.75 ± 1.75%, p=0.0076; 38.49 ± 3.02% vs 17.62 ± 3.79%, p=0.0007 for day 3, week 1 and week 3, respectively; $CD8^+$ T cells: 16.77 ± 4.15 vs 0.10 ± 0.067, p=0.015; 27.55 ± 3.56% vs 4.94 ± 4.94%, p=0.0036; 33.80 ± 2.19% vs 35.67 ± 6.20, p=0.72 for day 3, week 1 and week 3, respectively). There were lower number of neutrophils in patients treated with R-ATG than those treated with P-ATG during the first week after immunosuppressive therapy (P-ATG vs R-ATG, Day 3: 3.46 ± 0.49 vs 1.29 ± 0.56, p=0.02; Day 5: 3.73 ± 0.56 vs 1.12 ± 0.55, p=0.02). The overall response rates were comparable between P-ATG and R-ATG at third month and sixth month (60% vs 40%, p=0.24; 60% vs 60%, p=1). Early infection rates (within 1 month) showed no significant differences in two formulations (P-ATG vs R-ATG, 33.33% vs 46.67%, p=0.76). There were five deaths in patients treated with P-ATG and three deaths in R-ATG-treated patients (P-ATG vs R-ATG, 11.1% vs 20.0%, p=0.40).

Conclusion: P-ATG and R-ATG showed different pharmacokinetics and effects on neutrophils, lymphocyte subsets, which may lead to diverse immunosuppression. These two kinds of globulins showed comparable overall response rate after treatment.

Reference

1. Scheinberg P, Nunez O, Weinstein B, et al. Horse versus rabbit antithymocyte globulin in acquired aplastic anemia. *N Engl J Med*. 2011;365(5):430-438.
2. Feng X, Scheinberg P, Biancotto A, et al. In vivo effects of horse and rabbit antithymocyte globulin in patients with severe aplastic anemia. *Haematologica*. 2014;99(9):1433-1440.

Disclosures No relevant conflicts of interest to declare.

Figure 1

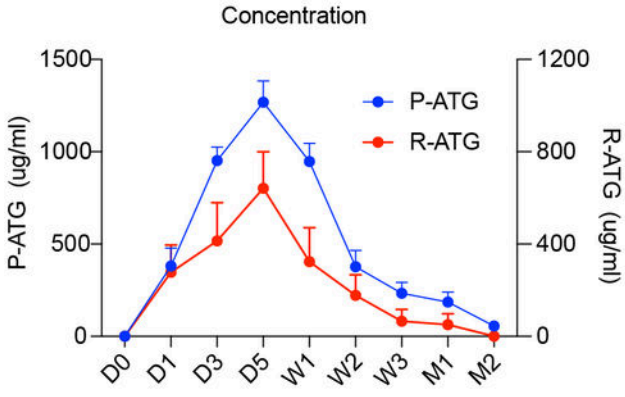

Figure 1 Pharmacokinetics of P-ATG and R-ATG. Concentrations of P-ATG (n=13) and R-ATG (n=10) detected by ELISA.

Figure 2

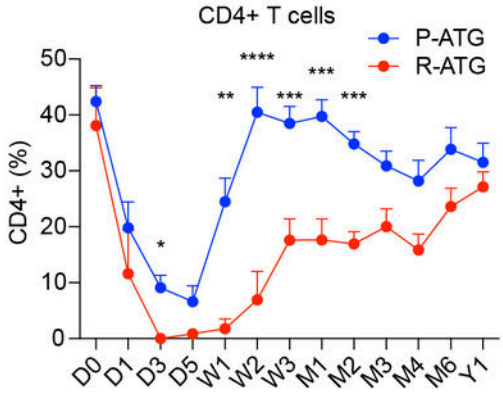

Figure 2 Dynamic changes of CD4+ T cells in patients treated with P-ATG and R-ATG. Bars represent mean ± SEM, *P < 0.05; **P < 0.01; ***P < 0.001; ****P<0.0001.

Figure 1

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