Compromised Anti-microbial Function of Mesenchymal Stem Cells in Diabetic Patients

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Disclosure

The authors declare no conflict of interests related to this presentation.
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Mesenchymal Stem Cells in Diabetic Infection

- Diabetic foot infection, including skin infection and osteomyelitis, is a severe complication of late-stage diabetes.
- Mesenchymal stem cells (MSCs) facilitate bacterial clearance. In bacterial infection, MSCs, via paracrine mediators, regulate the host cell metabolism and inflammatory response. Particularly, MSCs augment the antibacterial function of neutrophils.
It is generally believed that hyperglycemia in diabetes is toxic to MSCs/progenitors and detrimental to their regenerative function.

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**Hypothesis**: the antibacterial function of MSCs is compromised in diabetes.
Mesenchymal Stem Cells in Diabetes

Study Design:

1. **Patient information:** Bone marrow donors included diabetic (n = 6; age 51-78 years; 4 female and 2 male) and non-diabetic patients (n = 4; age 14-67 years; 2 female and 2 male), with IRB approval.

2. **Isolation of mesenchymal stem cells (MSCs):** Bone marrow concentrate collected during foot and ankle surgery was centrifuged through a gradient medium for isolation of mononuclear cells, which were plated for the attachment and growth of MSCs.
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Study #1

Diabetic patients
n=6

Normal controls
n=4

LPS treatment → MSCs-dia

Conditioned medium

MSCs-c

LPS treatment

Conditioned medium

E. coli

Colony counting
1. There was no statistical difference in the number of E. coli colonies when regular medium produced by MSC-dia and MSC-c was added into the bacterial culture.

2. When MSC-dia and MSC-c were treated with LPS, and the conditioned medium was collected and added into bacterial cultures, the number of E. coli colonies in MSC-dia group was about 3 times of that in the MSC-c group (p < 0.05).
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Study #2

- Diabetic patients
  - n=6
  - LPS treatment
  - MSCs-dia
- Normal controls
  - n=4
  - LPS treatment
  - MSCs-c
- Cord blood
- Macrophages
- Heat inactivated E. coli
- Bacterial phagocytosis
Macrophages were counted in defined areas of the Petri dishes and designated as infected or uninfected, according to the presentation of bacterial bodies or not. While the infection rate of macrophages co-cultured with MSC-c was 85% (±5.5%), it was 70% (±6.6%) when macrophages were co-cultured with MSC-dia (p = 0.006).
Discussion:

- Experiments applying conditioned medium produced by MSCs into E. coli culture showed that MSCs produced paracrine factors to interfere the growth of E. coli. Although more bacterial colonies were formed when MSC-dia medium was applied but great variations make no difference between MSC-c and MSC-dia groups in term of inhibiting E. coli growth.
- After activation with LPS (a bacterial wall molecule), MSC-dia had reduced inhibition of bacterial growth, via paracrine factors, and regulation of macrophages for bacterial phagocytosis. The results suggest that the anti-bacterial function of MSCs in diabetic patients are influenced not only by hyperglycemia but also other health conditions, such as inflammation.
Conclusion: This study demonstrated that MSCs in diabetic patients are compromised in anti-bacterial infection. Regulating the function of MSCs could be a new strategy for managing diabetic infection.
References: