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UNIVERSIDADE ESTADUAL PAULISTA
FACULDADE DE MEDICINA VETERINÁRIA E ZOOTECNIA

O IMPACTO DAS VIAS INTRAPANCREÁTICA, INTRAVENOSA E INTRACAPSULAR RENAL NO TRANSPLANTE DE CÉLULAS-TRONCO MESENQUIMAIS – REGENERAÇÃO MORFOFUNCIONAL DO DIABETES TIPO 1 EXPERIMENTAL.

BIANCA MARIANI GONÇALVES

Botucatu – SP
Fevereiro, 2018

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Dissertação apresentada junto ao Programa de Pós-Graduação em Medicina Veterinária para obtenção do título de Mestre.

Orientador: Prof. Dr. Luiz Henrique de Araújo Machado
Co-orientador: Prof. Dra. Célia Regina Nogueira

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Palavras-chave: diabetes experimental; efeito parácrino; imunomodulação; reparação tissular; terapia celular.

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DEDICATÓRIA

Dedico este trabalho primeiramente a Deus, por ser essencial em minha vida. Dedico-o também aos meus pais, ao meu futuro marido e ao meu querido orientador; sem vocês nada disso seria possível.

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LISTA DE FIGURAS

GONÇALVES, B.M. O impacto das vias intrapancreática, intravenosa e intra-capsular renal no transplante de células-tronco mesenquimais – regeneração morfofuncional do diabetes tipo I experimental. Botucatu, 2018. 87p. Dissertação (Mestrado) - Faculdade de Medicina Veterinária e Zootecnia, Campus de Botucatu, Universidade Estadual Paulista "Júlio de Mesquita Filho".

RESUMO

O diabetes mellitus (DM) é uma das doenças que mais tem aumentado sua incidência na última década. As células-tronco mesenquimais derivadas de tecido adiposo (CTMs-TA) possuem características imunomoduladoras e reparadoras, sendo capazes de reverter efeitos sistêmicos da doença. Sendo assim, nosso trabalho teve como objetivo avaliar o impacto do transplante de CTMs-TA pelas vias intravenosa, intrapancreática e intra-capsular renal em ratos diabéticos e comparar a que melhor exerce efeito regenerador. Para o estudo, utilizamos 45 ratos, *wistar*, fêmeas, divididos em 5 grupos: GCS – controle sadio; GCD – controle diabético; GIV – diabético, via intravenosa; GIP – diabético, via intrapancreática; GIR – diabético, via cápsula renal. Para a indução, utilizamos uma única aplicação intraperitoneal (i.p) de Aloxana (120mg/kg), e após 3 dias, os animais foram submetidos ao transplante com as CTMs-TA ($2x10^6$cel/animal). Após 15 dias do transplante, os animais foram eutanasiados. O transplante de CTMs-TA pela cápsula renal foi capaz de reverter a hiperglicemia, além de restaurar o diâmetro das ilhotas e restabelecer a função das massa β-pancreática. Concluímos que a cápsula renal foi a que apresentou melhores resultados na regeneração morfofuncional do pâncreas diabético. As CTMs-TA utilizadas neste estudo foram capazes de exercer um importante efeito parácrino, podendo ser utilizadas como alternativa para a melhoria da qualidade de vida de indivíduos diabéticos.

Palavras-Chave: terapia celular, células β, reparação tissular, efeito parácrino.

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ABSTRACT

Diabetes mellitus is one of the diseases that has increased your incidence in the last decade. Adipose-Derived Mesenchymal Stem Cells (ATMSCs) have immunomodulatory and regenerate characteristics, thus are capable of reverse the damages of the disease. Therefore, our study aimed to evaluate the impact of ATMSCs transplantation by the intravenous, intrapancreatic and intra-capsular renal routes in diabetic rats and detect the best route to promote regenerative effects. We used 45 female wistar rats, divided into 5 groups: GCS – healthy control; GCD - diabetic control; GIV - diabetic, intravenous; GIP - diabetic, intrapancreatic route; GIR - diabetic, via renal capsule. For induction, we used a single intraperitoneal application (i.p) of Alloxan (120mg / kg) and after 3 days, the animals were transplanted with the ATMSCs ($2x10^6$/ animal). After 15 days of transplantation, the animals were euthanized. The transplantation of ATMSCs by the renal capsule were able to reverse hyperglycemia, besides restoring the islet diameter and restoring the function of β-pancreatic mass. We conclude that the renal capsule presented the best results in the morphofunctional regeneration of the diabetic pancreas. The stem cells used in this study were able to exert an important paracrine effect,and could be used as an alternative to improve the quality of life on diabetic patients.

Key Words: cellular therapy, β cellular, tissue repair, paracrine effects

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6. CONCLUSÕES GERAIS

- Concluímos que a via intra capsular renal foi eficaz em reverter o estado diabético de maneira significante em 33% dos animais além de ser eficaz em melhorar a condição clinica dos animais e assegurar uma taxa de sobrevivência de 100% até o final do estudo, sem a necessidade de insulinoterapia ou com doses menores em relação às doses inicialmente empregadas.
- O uso de MSc não diferenciadas foi eficaz em promover efeito imunomodulador quando utilizado pela cápsula renal, estando provavelmente associado ao estado da doença e ao método de obtenção das células que priorizou a manutenção de subtâncias bioativas cruciais para o processo anti-inflamatório.
- Tanto a cápsula renal, quanto o uso de células não diferenciadas parecem eficazes para uso em terapia gênica de pacientes diabéticos, visando contenção de fatores auto-imunes e regeneração morfofuncional do tecido lesionado.

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