3e Symposium Experimenteel Onderzoek Heelkundige Specialismen

Leiden, 8 oktober 1990

SEOHS '90 Secretariat
Department of Surgery
University Hospital Leiden
P.O. Box 9600
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The Netherlands

Part one

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Please indicate preferred session:
- ■ Experimental Animal Models
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SUCCESSFUL CANINE PANCREATIC ISLET TRANSPLANTATION USING VIASPAN™

Technically, pancreatic islet transplantation as a therapeutical approach to human diabetes has become more realistic. The lack of efficient means of purifying islets from contaminating exocrine tissue however, remains a major impediment to safe islet transplantation. Recently we demonstrated that the use of UW organ preservation solution (Viaspan™, Du Pont) for the isolation of canine islets consistently results in >90% purified islets. In order to test the viability of Viaspan-isolated islets, we introduced this new approach to islet isolation in our current study of metabolic control after autotransplantation of canine islets. Five normal dogs underwent total pancreatectomy. Islets were isolated from the excised pancreas by collagenase digestion at 38 °C and, after addition of ice-cold isolation medium - either the Viaspan solution (n=3) or $RPMI_{1640}$ tissue culture medium (n=2) - by discarding ducts and large blood vessels, and gentle syringing (14G) with expulsion over a 400 µm filter. Next islets were purified by density gradient centrifugation, and autotransplanted into the spleen of the dog by retrograde venous infusion. Graft function was assessed up to 3 mo by determining the glucose and insulin response to an intravenous glucose injection (IVGTT) and a meal. The islet dose at transplantation ranged from 3500-13000 islets (Ø> 75 µm)/kg b.w. One animal became overtly hyperglycemic within 7 days after receiving 3500 Viaspan-isolated islets/kg b.w., although well-preserved islets could be demonstrated by immunostaining for insulin. The other grafts (>6000 islets/kg b.w.) were successful (normal fasting glucose) but demonstrated, compared to preoperative values, a 50% reduced glucose tolerance and insulin response at IVGTT. Postprandially moderate hyperglycemia (~10 mM) and in contrast to IVGTT, a normal insulin response was observed. In dogs "one-to-one" transplantation was successful in recipients of >6000 isolated islets/kg b.w.. The difference in the effect of islet transplantation on the insulin response to intravenous glucose and a meal, may be related to the postprandial activation of the entero-insular axis. The use of Viaspan solution for isolation of viable highly purified islets, should promote safe islet transplantation.

Deadline for receipt of abstracts: JULY 1st, 1990

Part two

Instructions

1. Enter name of author(s), institution and abstract title in the appropriate space.
2. Your entire abstract, INCLUDING TITLE (in capitals), but NOT NAME of author or institution, must be typed in Part One of the Abstract Submission Form.
3. Abstracts must be factual and include the specific objective of the study, a brief statement of methods, a summary of results and conclusions.
4. Submit the original copy of the abstract typed (preferably electric with elite type) on the Abstract Submission Form with 5 (Xerox) copies. Do not use eraser.
5. All typing must be single spaced. The title of the abstract (in capital letters) should start at the very top of the left hand corner. The text of the abstract must be a single paragraph, starting with a three space indentation. Leave no top or left hand margin within the space allotted to the abstract.
6. In case the contribution should not be presented by the first author, please UNDERLINE THE NAME of the presenting co-author.

Important
- Your abstract will appear in the abstract book exactly as typed.
- Further forms may be obtained from the Symposium Secretariat if required.
Abstracts cannot be considered if received after July 1st. 1990

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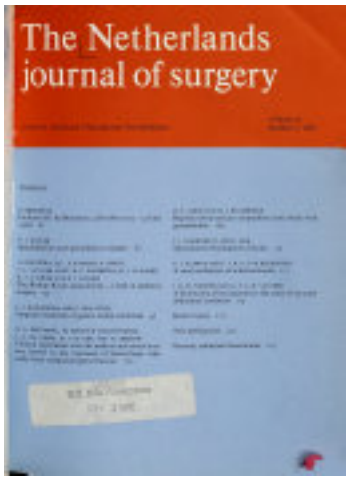
Title of abstract: Successful canine pancreatic islet transplantation using ViaSpan™

Author(s): M.P.M. van der Burg, O.R. Guicherit, R.J. Ploeg, J.P. Scherft, J.A. Bruijn, M Frölich, F.A. Prins, H.G. Gooszen

Institution(s): Surgery, Surgical Research, Cell Biology, Pathology and Endocrinology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In liver transplantation, there is a need for markers which can predict the viability of a preserved liver graft prior to implantation. 5'-Nucleotidase (5'-NT) activity in the bile canalicular membranes is a sensitive parameter of ischemic liver cell damage. We assessed the localization of bile canalicular 5'-NT activity as an indicator of preservation induced injury in cold stored canine livers. Four canine livers were cold stored in UW-solution for 24 hours and were transplanted orthotopically. The 5'-NT activity was determined in biopsies taken after cold flush of the liver, at the end of the preservation time and one hour after reflow in the recipient dog. All dogs survived with serum aspartate transaminase (AST), values having returned to near-normal by p.o. day 3. They were sacrificed on p.o. day 6. The results are shown in the Table (p. 176).

Dog 1 and dog 3 had comparable 5'-NT scores (70%) after 24 h preservation with maximal AST values of 1669 U/l and 1584 U/l resp. Dag 2 had a lower 5'-NT score (61%) and a higher maximal AST (3388 U/l) after the same preservation time. Dog 4 had the best 5'-NT score after 24 h preservation (100%) and this dog came out with the lowest maximal AST value (715 U/l). A second finding was that one hour after reflow, the 5'-NT score was considerably decreased confirming that at reperfusion, an additional trauma to the graft is induced. These studies are continued with orthotopic transplants after 48 h and 72 h preservation times. Our ultimate objective is to define a cut-off point for 5'-NT activity, beyond which function of the liver graft is not life-supporting.

The determination of 5'-NT activity provides a simple test which may prove valuable to assess the viability of liver grafts. This method is further explored in relation with preservation and graft reperfusion studies.

Successful canine pancreatic islet transplantation using Viaspan™ – M. P. M. van der Burg, O. R. Guicherit, R. J. Ploeg, J. P. Scherft, J. A. Bruijn, M. Frölich, F. A. Prins and H. G. Gooszen (Department of Surgery, Laboratory of Experimental Surgery and Departments of Cell Biology, Pathology and Endocrinology, Academic Hospital, State University Leiden, Leiden)

Technically, pancreatic islet transplantation as a therapeutical approach to human diabetes has become more realistic. The lack of efficient means of purifying islets from contaminating exocrine tissue, however, remains a major impediment to safe islet transplantation. Recently, we demonstrated that the use of UW organ preservation solution (Viaspan™, Du Pont) for the isolation of canine islets consistently results in >90% purified islets. In order to test the viability of Viaspan-isolated islets, we introduced this new approach to islet isolation in our current study of metabolic control after autotransplantation of canine islets. Five normal dogs underwent total pancreatectomy. Islets were isolated from the excised pancreas by collagenase digestion at 38 C and, after addition of ice-cold isolation medium – either the Viaspan solution (n = 3) or RPMI 1640 tissue culture medium (n = 2) – by discarding ducts and large blood vessels, and gentle syringing (14G) with expulsion over a 400 µm filter. Next islets were purified by density gradient centrifugation, and autotransplanted into the spleen of the dog by retrograde venous infusion. Graft function was assessed up to 3 mo by determining the glucose and insulin response to an intravenous glucose injection (IVGTT) and a meal. The islet dose at transplantation ranged from 3500-13000 islets (diameter >75 µm)/kg b.w. One animal became overtly hyperglycemic within seven days after receiving 3500 Viaspan-isolated islets/kg b.w., although well-preserved islets could be demonstrated by immunostaining for insulin. The other grafts (>6000 islets/kg b.w.) were successful (normal fasting glucose) but demonstrated, compared to preoperative values, a 50% reduced glucose tolerance and insulin response at IVGTT. Postprandially moderate hyperglycemia (± 10 mM) and in contrast to IVGTT, a normal insulin response were observed. In dogs 'one-to-one' transplantation was successful in recipients of >6000 isolated islets/kg b.w. The difference in the effect of islet transplantation on the insulin response to intravenous glucose and a meal, may be related to the postprandial activation of the entero-insular axis. The use of Viaspan solution for isolation of viable highly purified islets, should promote safe islet transplantation.

Alginate-polylysine microencapsulation prevents allograft rejection in rat pancreatic islet transplantation – W. M. Fritschy, G. H. J. Wolters and R. van Schilfgaarde (Departments of Experimental Surgery and Surgery, Academic Hospital, State University Groningen, Groningen)

Microencapsulation is the envelopment of small pieces of tissue (e.g. isolated pancreatic islets) within a biocompatible and semipermeable membrane, as means of immuno-isolation in allogenic transplantation. In this study, we compared the effects of intraperitoneal transplantation of *a* unencapsulated isogenic islets (Albino Oxford→AO), *b* unencapsulated allogenic islets (Lewis→AO), and *c* alginate-polylysine microencapsulated allogenic islets (Lew→AO), on non-fasting blood glucose levels (BG) of streptozotocin diabetic rats (BG>20 mM). Each transplantation was performed with 8-12 µl islet tissue (2500-3000