Review of experimental attempts of islet allotransplantation in rodents: Parameters involved and viability of the procedure

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Abstract

The purpose of the present study was to organize the parameters involved in experimental allotransplantation in rodents to elaborate the most suitable model to supply the scarcity of islet donors. We used the PubMed database to systematically search for published articles containing the keywords "rodent islet transplantation" to review. We included studies that involved allotransplantation experiments with rodents’ islets, and we reviewed the reference lists from the eligible publications that were retrieved. We excluded articles related to isotransplantation, autotransplantation and xenotransplantation, i.e., transplantation in other species. A total of 25 studies related to allotransplantation were selected for systematic review based on their relevance and updated data. Allotransplantation in rodents is promising and continues to develop. Survival rates of allografts have increased with the discovery of new immunosuppressive drugs and the use of different graft sites. These successes suggest that islet transplantation is a promising method to overcome the scarcity of islet donors and advance the treatment options for type 1 diabetes.

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Key words: Islet transplantation; Allograft; Immunosuppression; Type 1 diabetes; Islet grafts; Diabetes mellitus; Islet; Hyperglycemia

Core tip: This is an important systematic review for readers to analyze the different existing methodologies of islet allotransplantation. This article reviews all aspects of donors and recipients, the types and dosages of immunosuppressive therapy, graft survival time and evolution of the recipient’s blood glucose. Therefore, the present article permits reproduction and improvement of the experiments involving islet allotransplantation in rodents to develop alternative therapies for type 1 diabetes.

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INTRODUCTION

It is estimated that 4% of the world population is affected by diabetes mellitus, of which 10% have type 1 diabetes[1]. Furthermore, the incidence of diabetes cases in Europe has increased, especially in children and teenagers, in whom the incidence of type 1 diabetes increased by 4% last year. One trend is the occurrence of type 1 diabetes mellitus at younger ages, between 10 and 14 years. Today, the disease is already at 0-5 years[2]. According to the IBGE-CENSUS-2010, there are currently 12054827
diabetics patients in Brazil[3]. Thus, approximately 1.2 million diabetics in Brazil may benefit from research aimed at improving treatment of type 1 diabetes.

Currently, insulin is the primary treatment method for diabetes. However, approximately 5%-10% of patients have severe and unexpected fluctuations in their blood glucose levels, resulting in multiple episodes of hypoglycemia, which has serious clinical consequences. In such cases, pancreas transplantation is an alternative treatment option that is already in clinical use. Another alternative option is islet transplantation, which is a less invasive therapeutic method but is still in development[3]. Regarding the effectiveness of treatment, some results showed 80% insulin independence within the first year in postoperative patients treated with islet transplantation[6]; however, the survival rate of islets remains low.

The scarcity of islets is a significant obstacle hindering the widespread use of islet allograft therapy. According to the Network of Organ Procurement and Transplantation, in 2011, only 1562 pancreases were recovered from 8000 donor organs available in the United States. Furthermore, many donated pancreases are not suitable for islet extraction or do not fit the selection criteria. It is also common for islets to be handled incorrectly. For these reasons, only a small number of islet transplantsations can be carried out[5].

Some restrictions were found in the technical development of islet transplantation: the number of donor pancreases available for islet transplantation, below that required for healing the millions of people with type 1 diabetes; technical difficulties and the cost of islet isolation; poor durability of insulin independence; and autoimmune rejection after transplantation, which must still be overcome. It is therefore essential to develop an unlimited source of cells capable of secreting insulin in response to glucose and that can be transplanted with little or no need for systemic immunosuppression[6,7].

The purpose of the present study is to review experimental allotransplantation procedures that have been attempted in rodents to analyze the parameters involved and the viability of the procedure.

**SEARCH PROCESS**

**Search process**

The study was performed using the PubMed database to search for published articles containing the keywords “rodent islet transplantation”. However, to filter the results, we searched PubMed records for the period January 2000-December 2013 using the following search terms for islet allotransplantation in rodents: "{rodent islet transplantation AND ["2000"(Date-Completion): "3000"(Date-Completion) AND (allotransplantation) NOT porcine] NOT tilapia] NOT nonhuman primate”.

This ensured that articles discussing transplantation in porcine, tilapia and nonhuman primates (more common species used for transplantation) were excluded from the review to focus on those articles related to allotransplantation in rodents. Following the PubMed search, we reviewed the references from the publications retrieved and obtained the entire text of publications that could potentially be included in the systematic review. Unpublished studies and letters were ignored. Studies that did not have a full text available in English were purchased for review.

Eligible studies were selected for analysis based on the following inclusion criteria: (1) studies must be related to allotransplantation; (2) the species studied must be rodent species; and (3) articles must be relevant and the information up to date.

The review was written in English, and the relevant information, such as donor/recipient, immunosuppression, allotransplantation site, graft survival time, glucose variations and diabetes induction method, was organized into tables.

**DATA ABSTRACTION**

The authors abstracted the characteristics of the study, such as the source(s) for experimental (e.g., medical records and clinical databases) and relevant data, into the tables-donor/recipient; immunosuppression; allotransplantation site; graft survival time; glucose variations; and diabetes induction method.

**SEARCH RESULTS**

A total of 2650 articles from 2000 to 2013 were found. Only 25 articles were related to allotransplantation. These articles were selected based on their relevance and updated information (Tables 1-6; Figure 1A and B).

**DISCUSSION**

Islet transplantation has the potential to provide an adequate supply of insulin to the transplanted patient and provide a solution to the problem of islet donor shortage[8].

The first successful islet transplantation for the surgical treatment of diabetes occurred in 1990 by Shapiro et al[3]. Insulin independence was achieved in a patient with type 1 diabetes at one month post-transplant. However, many technical difficulties were found that needed to be overcome to continue the development of this technique and reproduce this experiment. In the decade between 1991 and 2000, 450 islet transplantation attempts were made in type 1 diabetic patients, with a success rate of only 8%. Fifty percent of successful cases were reported when patients had become diabetic because they were undergoing a pancreatectomy.

Then, in 1999-2000, Shapiro et al[3] successfully achieved insulin independence in 7 diabetic patients by performing experiments based on the modified Edmonton protocol[9-12].

Islet transplantation has increasingly been shown to reduce morbidity 20-fold compared to pancreas transplant because it is surgically less invasive[9].

In the present study, we reviewed studies consisting of rodents similar in age and weight undergoing allograft transplantation. Strains of mice aged 6-12 wk and weighing 200 g to 350 g were used. According to these studies
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Figure 1  Quantitative and comparative analysis of the different donor strains (A) and recipient strains (B).

Table 1  Description of the experimental studies on allografts (A) and recipient strains (B).

| Ref. | Donor/recipient | Immunosuppression | Allotransplantation site | Graft survival time |
|------|-----------------|------------------|-------------------------|--------------------|
| Fotiadis et al.[9] | Lewis→Wistar | Mycophenolate mofetil (MMF) and Cyclosporine A (CsA) | Spleen | N/A |
| Merani et al.[10] | Lewis→Wistar | AEB-071 (Protein kinase C inhibitor) + CsA, CTLA4-Ig, MMF | Kidney capsule | 100 d |
| Nishimura et al.[11] | C57BL/6→Balb/c | Tacrolimus | Kidney capsule | N/A |
| Makhlouf et al.[12] | C57BL/6/Balb/c | Blockade of CD28:B7 and anti-CD40L; CTLA-4 | Kidney capsule | 1 wk |
| Salazar-Bañuelos et al.[13] | Wistar→Sprague Dawley | No immunosuppression | Medullary channel | 21 d |
| Wee et al.[14] | Lewis→Fisher | CsA + Tautomycetin (synergists) | Liver (portal vein) | Control group - 5.2 ± 0.5 d TMC - 5.1 ± 0.9 d TMC (0.03 mg/kg) + CsA (5 mg/kg) - > 41 d TMC (0.1 mg/kg) + CsA (5 mg/kg) - 103.8 ± 56.8 d |
| Plesner et al.[15] | Balb/c→EBA | No immunosuppression | Kidney capsule | 60 d |
| Watanabe et al.[16] | Balb/c→C57BL/6 | Tacrolimus and DHMEQ (NF-κB inhibitor) | Kidney capsule | 100 d |
| Gyselmann et al.[17] | Balb/c→C57BL/6 | No immunosuppression | Kidney capsule | 9.2 ± 4.9 d (Autoimmune diabetes) 15 ± 3 d (Not chemically diabetic autoimmune) |
| Xekouki et al.[18] | Wistar→Lewis | CsA and MMF | Spleen (parenchyma) | 8 d (CsA) 10.92 d (MMF) 11 d (MMF 2) |
| Baker et al.[19] | A/J→C57BL/6 | Monoclonal antibody antiBIP-10 | Kidney capsule | 19.7 ± 2.3 d (C57BL/6) 20.2 ± 2.7 d (CXCR3−/−C57BL/6) |
| Li et al.[20] | FVB→Balb/c | No immunosuppression | Kidney capsule | N/A |
| Vieiro et al.[21] | C57BL/6→C3H | Trinitiated thymidine (preoperative) and CsA | Subcutaneous | N/A |
| Neuzillet et al.[22] | C3H→Balb/c | No immunosuppression | Kidney capsule | 13.8-27.5 d | > 100 d |
| Melzi et al.[23] | C57BL/6→Balb/c | Rapamycin+FK506+anti-IL-2Ra chain mAbs and rapamycin+IL-10 | Kidney capsule | |
| Fiorina et al.[24] | Balb/c→C57BL/6 | No immunosuppression | Kidney capsule | 14 d LTJ-R-Ig; 27 d CTLA4-Ig; 55 d LTJ-R-Ig+CTLA4-Ig; 11 d LTJ mAb anti mouse |
| Fan et al.[25] | C57BL/6→Balb/c | LTR-R-Ig, CTLA4-Ig or LTR mAb anti mouse | Kidney capsule | |
Wee et al.\textsuperscript{[4]} studied the effects of tautomycetin and concluded that it does not affect the viability of the islets and spleen, but it is capable of inhibiting the proliferation of T cells. When tautomycetin was combined with subtherapeutic doses of CsA, it led to increased survival of islets. A dose of CsA of 15 mg/kg prolonged the survival of islets the longest. Thus, the mixture of tautomycetin with CsA or other calcineurin inhibitors increased islet survival.

Merani et al.\textsuperscript{[4]} demonstrated that inhibition of PKC by using the new drug AEB -071 slowed the rejection of islet allografts in rodents. Furthermore, addition of CsA therapy with 5 mg/kg AEB prevented graft rejection in 80% of the rats transplanted by immunosuppressive action of the complement system and had no toxic effects. Watanabe et al.\textsuperscript{[4]} conducted studies with DHMEQ, an inhibitor of NF-\(\kappa\)B, and concluded that the proinflammatory responses activated by HMGB1 were reduced. Moreover, the immunosuppression allows allograft acceptance even in cases where only a few islets were transplanted.

Xekouki et al.\textsuperscript{[4]} analyzed the effects of CsA and MMF. Their results suggest a beneficial effect of MMF in maintaining the architecture of the islets without prominent side effects in other organs, such as the kidneys or liver.

Baker et al.\textsuperscript{[3]} studied CXCR3 gene deletion and \(\alpha\)IP-10 antibody therapy and concluded that they modulate posttransplant lymphocytic infiltration into the graft and contribute to prolonging allograft survival.

Fan et al.\textsuperscript{[5]} concluded that the simultaneous blockade of LIGHT and CD28 prolongs graft survival because of a synergistic effect; the presence of T-regulatory cell activity develops donor-specific immunological tolerance. Moreover, prevention of allograft rejection and induction of donor-specific tolerance in lymphocyte-sufficient recipients can be achieved by local cotransplantation of the islets.
allografts with regulatory T cells.

Jung et al.[20] concluded that the combination of RosA and MR1 in a murine allogeneic islet transplantation model prolonged graft survival compared to the MR1-alone treatment group.

Pålhamn et al.[27] evaluated the immunosuppressive limitations of AR-C117977, an immunosuppressant drug that maintains long-term graft survival and induces operational tolerance, and concluded that AR-C117977 combined with CsA resulted in significant prolongation of graft survival compared with AR-C117977 or CsA therapy alone. Furthermore, CsA therapy alone did not prevent acute rejection.

Wang et al.[28] studied local expression of B7-H4 and concluded that it prolongs islet allograft survival in vivo.

Studies investigating immunosuppressant drugs and their toxic effects on islets in vivo are still in development. The most utilized immunosuppressants were CsA, MMF and CTLA4 Ig, as shown in Table 4. The concomitant use of glucocorticoids was associated with high rejection rates and is not recommended. Their immunosuppressive and toxic effects have not been rigorously tested, and studies are still underway.

In relation to the different locations for transplantation studied according to the table, the kidney capsule was the most frequently used site for transplantation. Second was the portal vein in the liver[19], who used the portal vein (liver) as the site of allograft transplantation and sacrificed the mice at 100 d postoperative. Melzi et al.[29], Watanabe et al.[30] and Merani et al.[31] obtained a survival rate of 100 d, where the site of engraftment

Table 3  Comparative analysis of the different types of rodents used and their basic characteristics-Age and Weight

| Ref. | Donor/recipient | Age | Weight |
|------|----------------|-----|--------|
| Fotiadis et al.[32] | Lewis→ Wistar | N/A | 220 g;300 g |
| Merani et al.[33] | Lewis→ Wistar | N/A | 200 g (male)/150 g (female) |
| Nishimura et al.[34] | C57BL/6 → Balb/c | 9-12 wk /8-12 wk | N/A |
| Makhlouf et al.[35] | C57BL/6→ Balb/c | 6-8 wk (male)/ N/A | N/A |
| Salazar-Bañuelos et al.[36] | Wistar→ Sprague Dawley | N/A | 260-326 g |
| Wee et al.[37] | Lewis→ Fisher | 10-12 wk | N/A |
| Pleset et al.[38] | Balb/c→ EBA | 10-14 wk /N/A | N/A |
| Watanabe et al.[39] | Balb/c→ C57BL/6 | 10-14 wk /male | N/A |
| Gysenens et al.[40] | Balb/c→ C57BL/6 | (8-21 d) → (> 180 d) | N/A |
| Xekouki et al.[41] | Wistar→Lewis | N/A/male | 220-300 g |
| Baker et al.[42] | A/J→ C57BL/6j | 8-12 d/male | N/A |
| Li et al.[43] | FVB→ Balb/c | 8-12 wk | N/A |
| Vieiro et al.[44] | C57BL/6→ C3H | N/A | N/A |
| Neuzillet et al.[45] | C3H → Balb/c | N/A | N/A |
| Melzi et al.[46] | C57BL/6→ Balb/c | 9 wk (female)→ 9 wk (female) | 20-22 g |
| Fiorina et al.[47] | Balb/c→ C57BL/6 | N/A | N/A |
| Fan et al.[48] | C57Bl/6 → Balb/c | N/A - adults (female) | N/A |
| Jung et al.[49] | Balb/c→ C57Bl/6 | 12 wk (male)→ 12 wk (male) | 25-30 g |
| Pålhamn et al.[50] | Balb/c→ C57Bl/6 | N/A - (female) | N/A |
| Wang et al.[51] | Balb/c→ C57Bl/6 | 8-10 wk (female)→ 8-10 wk | N/A |
| Chen et al.[52] | Sprague Dawley→ Lewis | N/A (male) | 250-350 g → 196 ± 15 g |
| Giraud et al.[53] | C57BL/6 → Balb/c | N/A | N/A |
| Qi et al.[54] | Wistar→ Lewis | 9-10 wk (male) | 250-300 g |
| Potiron et al.[55] | Wistar→ Lewis | N/A (male) | 200-300 g |
| Jahr et al.[56] | Lewis→ Wistar | N/A (male)→ N/A (male) | 310-330 g→ 215-245 g |

Table 4  Analysis of the immunosuppressant drugs used at international islet transplantation research centers

| Immunosuppressant | Number of centers using the immunosuppressant (based on data from the literature) |
|-------------------|----------------------------------------------------------------------------------|
| CsA   | 6                                                                                   |
| MMF   | 3                                                                                  |
| CTLA4 Ig | 4                                                                              |
| CD40 Ig | 2                                                                                  |
| NF-KB Inhibitor (DHMEQ) | 1                                                                                           |
| Anti-CD154 mAb (MR1) | 2                                                                                           |
| Trinitated thymidine | 1                                                                                           |
| Tacrolimus | 1                                                                                           |
| Blockade of CD28:B7 | 1                                                                                           |
| Tacoptyminecin | 1                                                                                           |
| Protein Kinase C Inhibitor (AEB-071) | 1                                                                                           |
| Monoclonal antibody anti-BIP-10 | 1                                                                                           |
| Rapamycin+Fk506+anti-IL-2 | 2                                                                                           |
| 2Ran chain mAbs, n=31 and rapamycin+HL-10; n=29 | 1                                                                                           |
| LTP R-Ig | 1                                                                                           |
| LTR mAb | 1                                                                                  |
| ROS-A | 1                                                                                  |
| AR-C117977 | 1                                                                                           |
| B7-H4 and Ad LacZ | 1                                                                                           |
| Anti-CD154 mAb | 1                                                                                           |
| No immunosuppression | 9                                                                                           |
### Table 5 Quantitative analysis of immunosuppressant drugs use

| Ref.            | Immunosuppression                  | Dose                          | Administration frequency |
|-----------------|------------------------------------|-------------------------------|--------------------------|
| Fotiadis et al. | MMF and CsA                         | 12 mg/kg and 23 mg/kg (MMF) 5 mg/kg (CsA) | -                        |
| Merani et al.   | AEB-071 (Protein Kinase C Inhibitory) + CsA, CTLA4-Ig, MMF | 30 mg/kg (AEB-071) 2.5 mg/kg and 5 mg/kg (CsA) 0.25 mg (CTLA4-Ig Intraperitoneal) 10 mg/kg (MMF) | 2 times a day, oral (AEB-071) 2 times a day, oral (CsA) 0, 2, 4 and 6 PO, Intraperitoneal (CTLA4-Ig) Once a day, oral (MMF) |
| Nishimura et al. | Tacrolimus                          | 0.5 mg/kg                     | Infused subcutaneously - Daily - for 14 d |
| Makhoul et al.  | Blockade of CD28:B7 and anti-CD40 L; CTLA-4 | 280 µg                        | Intraperitoneal - 0, 2, 4 and 6 PO |
| Wee et al.      | CsA+Tautomycin (Synergist)          | 5 mg/g and 15 mg/kg (CsA)     | Once a day for 7 d        |
| Watanabe et al. | Tacrolimus and DHMEQ                | 1.5 mg/kg (Tacrolimus)        | Once a day 0 to 3 PO and 2 times a day 0 to 14 PO (DHMEQ); Once a day 0 to 3 PO (DHMEQ)+0 to 14 PO (Tacrolimus) |
| Xekouki et al.  | CsA and MMF1                        | 5 mg/kg (CsA)                 | Oral - Daily - 12 consecutive days |
| Baker et al.    | Monoclonal antibody antiBIP-10      | 300 µg intraperitoneal         | Daily - 14 d¹             |
| Vieira et al.   | Trinitated thymidine (preoperative) and CsA  | 20 mg/kg (CsA)               | N/A                      |
| Melzi et al.    | Rapamycin + FK506 + anti-IL-2Ra chain mAbs and rapamycin+IL-10 | 1 mg/kg (Rapamycin) 0.05 µg/kg (IL-10) 0.5 µg/kg (FK506) 1 mg/kg (mAbs) | Intraperitoneal: Once a day - 30 PO (Rapamycin) 2 times a day - 30 d (IL-10) Once a day - 30 d (FK506) 0.4 PO (mAbs) |
| Fan et al.      | LTβ1 R-Ig, CTLA4-Ig or LTR mAb anti mouse | 200 µg                       | Intrapertitoneal- days - 1, 3, 5, 7 and 9 |
| Jung et al.     | CD154 mAb (MR1) anti mouse + ROS-A | 250 µg (CD154 mAb (MR1) anti mouse) 200 mg/kg of Ros A | Intrapertitoneal injection 0, 2, 4, 6 and 8 PO (CD154 mAb (MR1) anti mouse) 8 consecutive days (ROS-A) |
| Pählman et al.  | AR-C117977 or CsA                   | 0.2 ml - 3, 10, 30, or 100 mg/kg (AR-C117977) | Subcutaneous - once a day 0 to 9 PO (AR-C117977) |
| Wang et al.     | B7-H4                               | 0.5 ml - 20 mg/kg (CsA)       | Once a day 0-9 PO or 0-39 PO (CsA) |
| Potiron et al.  | CTLA4 Ig or CD40 Ig                 | 5 107 IP of AdCTLA4 IM and/or 5 107 IM or 2 109 IV of AdCD40lg IM administration: 10 µL per point (3 points) IV administration: 150 µL with 0.9% sodium chloride | IM administration - anterior tibialis muscle; N¹ administration - venile vein |
| Jähr et al.     | Anti-rat antilymphocyte serum       | Intrapertitoneal administration 0.5 ml. 1 d after islet transplantation | -                        |

¹First dose administered 4 h preoperatively. N/A: Not available; MMF: Mycophenolate mofetil; CsA: Cyclosporine A.

### Table 6 Analysis of induction and treatment of diabetic process with islet transplantation

| Ref.            | Number of transplanted islets | Diabetes induction method                                                   | Hyperglycemia induction (preoperative) | Normalization of hyperglycemia (postoperative) | Graft rejection | Criteria for primary graft dysfunction (PGD) |
|-----------------|-------------------------------|-----------------------------------------------------------------------------|----------------------------------------|------------------------------------------------|----------------|--------------------------------------------|
| Fotiadis et al. | 1812 ± 145                    | Streptozotocin (60 mg/kg) + PBS-Solution (Phosphate Buffer Solution) - 10 mg/mL (pH 4.5); | 7 d                                    | 3 d                                            | 12 d (MMF)     | 3 d (CsA)                                  |
| Merani et al.   | 1500                          | Streptozotocin (75 mg/kg) intraperitoneal                                    | 5 d                                    | 3 d                                            | 22 d           | Glucose above 200 mg/dL; after 2nd PO 2 consecutive times |
| Nishimura et al. | 2-10/dorsal skinfold chamber | -                                                                          | -                                      | -                                             | N/A            | -                                          |
| Makhoul et al.  | 350 (Balb/c)                  | Streptozotocin and spontaneously (225 mg/kg in peritoneal cavity)           | 2 wk                                   | 3 d                                            | 10 d (Balb/c)  | 5 d (NOD) and 7 d complete rejection (NOD) N/A¹ |
| Salazar-       | 840 (of Wistar)               | -                                                                          | -                                      | -                                             | 200 mg/dL; - 2 to 3 consecutive days              |

¹First dose administered 4 h preoperatively. N/A: Not available; MMF: Mycophenolate mofetil; CsA: Cyclosporine A.
| Authors          | Dose | Streptozotocin Concentration | Route | Duration | Response |
|------------------|------|----------------------------|-------|----------|----------|
| Wee et al[14]    | 4000 | (35 mg/kg)                 |       | N/A      | N/A      |
| Plesner et al[15] | 550  | (375 mg/dL)                |       | 1 d      | 60 d     |
| Watanabe et al[16] | 600 or 300 | (180 mg/kg)           |       | 5-7 d    | N/A      |
| Gyselmanns et al[17] | 300 | (90 mg/kg)                 |       | 24 h     | N/A      |
| Xekouki et al[18] | 2000 | (60 mg/kg) diluted in phospated solution 10 mg/mL |       | 1 wk     | 7 d (MMF) |
| Baker et al[19]  | 300  | (220 mg/kg)                |       | N/A      | 7 d      |
| Li et al[20]     | 400 (200/Kidney capsule) | (220 mg/kg)             |       | N/A      | 3-7 d    |
| Vieiro et al[21] | 200  | (270 mg/kg)                |       | N/A      | 3 h      |
| Neuzillet et al[22] | 550 |                           |       | 4 h      | N/A      |
| Melzi et al[23]  | 400  | (175 a 200 mg/kg intravenous) |       | 1-2 wk   | 29 d     |
| Fiorina et al[24] | NA  | (200 mg/kg)                |       | N/A      | 14 d     |
| Fan et al[25]    | 500  | (200 mg/kg)                |       | N/A      | 27 d     |
| Jung et al[26]   | 300 IEQ | (180 mg/kg)              |       | 1 d      | N/A      |
| Pålhnman et al[27] | 500-600 | Alloxan Intravenous     |       | N/A      | CsA - 16 d |
| Wang et al[28]   | 400  | (200 mg/kg)                |       | 3-4 d    | 30 mg    |
| Chen et al[29]   | 3000 IEQ | Dissolved in saline (50 mg/kg) |       | 1 wk     | N/A      |

N/A: Not available
was the kidney capsule.

It is important to note that there was no standard level of hyperglycemia that the mice must present to be recipients of islet transplantation. A range of blood glucose levels from 180 mg/dL to 500 mg/dL was observed, as shown in Table 7.

The articles have many independent variables that influence the study results, such as species of rodent, immunosuppressant drugs and dosages, criteria for diabetes and allograft site. Thus, more research is needed to develop the ideal allograft model of islet transplantation.

CONCLUSION

Based on the analyzed studies, we can infer that islet allotransplantation in rodents is promising and continues to develop. The survival rates of allografts have increased with the discovery of new immunosuppressive drugs and the use of different graft sites. These advancements have the potential to overcome the scarcity of islet donors and improve the treatment of type 1 diabetes.

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