

# Nutritional management of diabetes mellitus in adult kidney transplant recipients

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## GUIDELINES

No recommendations possible based on Level I or II evidence.

## SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- Pre-transplant weight and pre-transplant weight gain increase the risk of the development of diabetes therefore weight management strategies should be a priority for patients awaiting a kidney transplant. (Level III evidence)
- There are no Level III or IV studies examining the safety and efficacy of dietary interventions for the prevention and management of diabetes in adult kidney transplant recipients. The following suggestions for clinical care are based on advice given for prevention and management of diabetes in the general population.
- In addition to this, Dietary advice to all adult kidney transplant recipients should reflect the current recommendations for reducing the risk of and managing type 2 diabetes in the general population.
- To reduce the risk of diabetes mellitus, the following dietary guidelines, which are in line with guidelines for the general population,<sup>1</sup> should be the following:
  - consume a diet with <30% total energy as fat and <10% energy as total saturated fat, and
  - consume a variety of carbohydrate-containing foods which are rich in dietary fibre and of low glycaemic index (cereals, vegetables, legumes and fruits).
- In line with guidelines for the management of type 2 diabetes in the general population:<sup>1</sup>
  - the focus of diet therapy in the management of new-onset diabetes mellitus after organ transplantation (NODAT) should be the prevention of macrovascular disease, by controlling blood pressure and managing dyslipidaemia, and
  - overweight and obese individuals should be encouraged to lose weight; weight loss improves lipid levels in individuals with diabetes and there is Level I evidence in non-transplant populations that weight is most readily lost during active, supervised treatment.

## BACKGROUND

New-onset diabetes mellitus after organ transplantation (NODAT) has emerged as an increasingly important determinant of outcome and survival in transplant recipients. Its reported prevalence among renal transplant recipients varies widely because of the use of inconsistent definitions of diabetes. However, an International Consensus Expert Panel<sup>2</sup> convened in 2003 agreed that the definition of NODAT should be in accordance with the American Diabetes Association (ADA)'s criteria for the diagnosis of diabetes mellitus,<sup>3</sup> which specifies:

1 symptoms of diabetes mellitus plus casual plasma glucose  $\geq 200$  mg/dL. Casual is defined as any time of day. Classic symptoms include polyuria, polydipsia and unexplained weight loss, **OR**

2 fasting plasma glucose  $\geq 126$  mg/dL ( $\geq 7.0$  mmol/L). Fasting is defined as no caloric intake for at least 8 h, **OR**

3 an oral glucose tolerance test value  $\geq 200$  mg/dL (2 h after ingestion of 75 g anhydrous glucose dissolved in water).

The prevalence of NODAT has been reported at around 20% at 1 year<sup>4</sup> and best available data suggest that the disorder is a life-long problem for the majority of those diagnosed, not a temporary aberration driven by high-dose steroid exposure in the early post-transplant phase.<sup>5</sup>

NODAT is caused by the combination of insulin resistance and deficient insulin production.<sup>3</sup> Non-modifiable risk factors for the development of NODAT include: age, ethnicity, family history of type 2 diabetes and HCV infection. Key modifiable risk factors the choice of immunosuppressive regimen, particularly steroid exposure and use of tacrolimus, and obesity.<sup>6–10</sup>

Diabetes mellitus has a major impact on graft and patient outcomes. It places patients at increased risk of the key causes of premature graft failure – death with function and chronic allograft dysfunction.<sup>4</sup> Several studies have documented that diabetes mellitus is an independent predictor of

major cardiovascular events after transplantation<sup>11,12</sup> and is also a likely contributor to chronic allograft dysfunction.<sup>13</sup>

In the non-transplant population, there is a strong body of evidence for the safety and efficacy of dietary measures for managing type 2 diabetes.<sup>14</sup>

This review set out to explore and collate the evidence for the efficacy of nutrition interventions in the prevention and management of diabetes in adult kidney transplant recipients, based on the best evidence up to and including September 2006.

## SEARCH STRATEGY

Relevant reviews and studies were obtained from the sources below and reference lists of nephrology textbooks, review articles and relevant trials were also used to locate studies. Searches were limited to human studies on *adult* transplant recipients and to studies published in English.

**Databases searched:** MeSH terms and text words for kidney transplantation were combined with MeSH terms and text words for both diabetes mellitus and dietary interventions. Medline – 1966 to week 1, September 2006; Embase – 1980 to week 1, September 2006; the Cochrane Renal Group Specialised Register of Randomised Controlled Trials.

**Date of searches:** 22 September 2006.

## WHAT IS THE EVIDENCE?

There are no published studies examining the safety and efficacy of dietary interventions for the prevention and management of diabetes in adult kidney transplant recipients. However, observational studies have shown a correlation between pre-transplant weight and pre-transplant weight gain and the risk of developing type 2 diabetes after transplant.<sup>7,15,16</sup>

Boudreaux *et al.*<sup>15</sup> retrospectively examined the incidence of post transplant diabetes in three groups of previously non-diabetic transplant patients. Two groups had been randomized to a stratified prospective trial comparing the use of different immunosuppressive regimes while the third consisted of a separate group of adult transplant recipients treated also with a different immunosuppressive regime. The purpose of the retrospective analysis was to determine the relative role of several factors in the pathogenesis of post transplant diabetes. The incidence of post transplant diabetes was significantly greater in patients older than 45 (34.2% *vs* 5.2%) and heavier than 70 kg (21.1% *vs* 5.1%); in recipients of cadaveric allografts (15.7% *vs* 4.6%); and in patients hospitalized for infections (22.4% *vs* 4.7%). (Level III)

The cross sectional population study by Cosio *et al.*<sup>16</sup> examined the incidence of post transplant diabetes in 2078 kidney transplant recipients. All patients were non-diabetic at the time of transplant and all received cyclosporine and prednisone but none received tacrolimus. A relative risk of 1.4 for post-transplant diabetes was documented for every 10 kg increase in body weight greater than 60 kg at the time of transplantation. (Level III)

Mathew *et al.*<sup>7</sup> conducted a prospective cohort study of 174 non-diabetic end stage kidney disease (ESKD) patients from pre transplant to a mean follow up period of 25.6 months post transplant. In this study the rate of increase in BMI during pre transplant haemodialysis was identified as a risk factor for development of post transplant diabetes. This was considered to be a surrogate marker for the severity of pre transplant malnutrition. The rate of weight gain after transplant was not associated with post transplant diabetes. It should be noted that the mean BMI of this Indian cohort pre transplant was  $18.3 \pm 2.4$  kg/m<sup>2</sup>. In this cohort malnutrition pre transplant was considered to be the risk factor for post transplant diabetes. (Level II)

## SUMMARY OF THE EVIDENCE

There are no published studies examining the safety and efficacy of dietary interventions for the prevention and management of diabetes in adult kidney transplant recipients. Observational studies have indicated a correlation between pre-transplant weight and pre-transplant weight gain and the risk of developing type 2 diabetes after transplant suggesting that weight management for patients awaiting kidney transplant should be a priority.

## WHAT DO THE OTHER GUIDELINES SAY?

**Kidney Disease Outcomes Quality Initiative:** No recommendation.

**UK Renal Association:** No recommendation.

**Canadian Society of Nephrology:** No recommendation.

**European Best Practice Guidelines:** Post-transplant diabetes mellitus should be treated as appropriate to achieve normoglycaemia.<sup>17</sup>

**International Guidelines:** No recommendation.

The suggestions for clinical care above are not in conflict with the European Best Practice Guidelines.

## IMPLEMENTATION AND AUDIT

No recommendations.

## SUGGESTIONS FOR FUTURE RESEARCH

Prospective, long-term controlled studies are required to examine the effectiveness of specific dietary modifications in the prevention and management of diabetes and impact of such modifications on the long-term health outcomes among kidney transplant recipients.

Studies examining the effectiveness of intensive *versus* standard dietary interventions on the management of diabetes – encompassing blood glucose, serum lipids and body weight – are also required.

## CONFLICT OF INTEREST

All of the authors have no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

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