COMMENTARY ARTICLE

Post-transplantation diabetes mellitus (Ptdm) after renal transplant: A brief review

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Post-Transplantation Diabetes Mellitus (PTDM) refers to diabetes that occurs in previously non-diabetic persons after solid-organ transplantation. PTDM is a multifactorial, complex metabolic disorder associated with impaired long-term graft function, reduced recipient survival, and increased risks of cardiovascular disease and infectious complications.

Key Words: *Post-transplantation diabetes mellitus; Renal metabolic disorder; Cardiovascular disease; Hyperglycemia*

DESCRIPTION

Although (PTDM) was first reported in 1964, throughout the time, PTDM has undergone through changes in nomenclature including steroid diabetes, Post-Transplantation Diabetes Mellitus (PTDM), New Onset Diabetes Mellitus (NODM), Transplant-Associated Hyperglycemia (TAH), and New Onset Diabetes After Transplantation (NODAT) [1]. Due to lack of unanimously adopted definition of PTDM used over the years, there is heterogenous reporting of data regarding the epidemiology of PTDM in Renal Transplant Recipients (RTRs), however it is approximated to affect almost one-third of the renal transplant recipients with no history of DM[2,3]. In 2014, the International Expert Panel consisting of transplant nephrologists, diabetologists, and clinical scientists recommended changing the terminology NODAT back to PTDM, excluding transient post-transplantation hyperglycemia. The terminology NODAT could be misleading because it apparently excludes patients with pre-transplant DM, which may be often undiagnosed [4,5].

Although PTDM and pre-transplant diabetes -typically type 2DM-are different entities in terms of the mechanisms implicated in their pathogenesis, the criteria applied for diagnosis are similar with the American Diabetes Association (ADA) recommendations for diagnosis of DM in the general population, with the pre-requisite that at least 6 weeks have passed form transplantation [6]. Treatment strategies of PTDM include initially lifestyle changes, which are followed by pharmacological therapy if the glycaemic targets are not achieved [7]. However, itis worth mentioning that there is a dearth of high-quality evidence for the currently available antidiabetic agents in the management of hyperglycaemia in PTDM, both in terms of efficiency, safety and outcomes as well. Moreover, it is always imperative to individualize the therapy to the special requirements of this patient population, considering the associated multiple comorbidities, the immunosuppressive regimen and drug-to-drug interactions as well as potential allograft dysfunction[8].

The new era of anti-diabetic agents like the newer generation basal insulins and the modern non-insulin anti-diabetic agents including Dipeptidyl-Peptidase 4 Inhibitors (DPP-4 inhibitors), glucagon-like peptide-1 receptor agonists (GLP-1receptor agonists) and sodium-glucosecotransporter-2 inhibitors (SGLT2 inhibitors) have been studied with promising results in patients with Diabetic Kidney Disease (DKD)[9]. A recent real-word study reported insulin degludec to be effective and safe in long standing diabetes patients undergoing renal transplant. Insulin degludec was well tolerated and was effective in lowering FPG, PPPG and HbA1C in early post-transplant OPD settings [10]. Amongst the non-insulin agents, DPP-4 inhibitors are promising therapeutic option in CKD patients and especially those at high risk for hypoglycaemia [11-13]. All DPP-4 inhibitors can be used safely in patients with advanced CKD with proper dose adjustments, except for linagliptin which can be used without any dose modification as it undergoes elimination *via* the enterohepatic circulation [14,15]. Very recently, the long-term efficacy and safety of linagliptin has been demonstrated in NODAT in an outpatient-based 1-year follow-up study with significant improvement in glycemic control, renal parameters (serum creatinine, EGFR) with minimal hypoglycemia, mainly attributed to the concomitant usage of insulin and sulphonylureas [16]. GLP-1 receptor agonists have recently gained interest because of their potential for therapy of type 2 diabetes and obesity as well as associated cardiorenal protection[17-19], however long term studies are required in this specific patient population. As for SGLT-2 inhibitors, the latest clinical evidences of their usage in patients with type 2 DM demonstrated unequivocal results with regards to cardio protection as well as diminished risk of new onset albuminuria and progression of CKD, free of their hypoglycaemic effect [20-22]. Despite the fact that clinical data in regards to the usage of DPP-4 inhibitors and especially SGLT2 inhibitors and GLP-1 receptor agonists are restricted in RTRs, information from the accessible clinical studies clearly hints that they are by and large safe and have insignificant interactions with the immunosuppressive agents. Considering the good safety profile of DPP-4 inhibitors in patients with CKD and particularly the emerging clinical benefits identified with SGLT2 inhibitors and GLP-1 receptor agonists, it makes sense to use them more in this specific population.

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