REVIEW

GLYCEMIC VARIABILITY IN DIABETIC PATIENTS ON CHRONIC HEMODIALYSIS: IMPORTANCE AND MONITORING METHODS

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ABSTRACT

Diabetes mellitus (DM) is associated with increased risk of chronic kidney disease (CKD). Several factors may increase the risk of hypoglycemia in diabetic patients with end-stage renal disease (ESRD). Increased glycemic variability in diabetic patients on chronic hemodialysis augments death risk; consequently, glucose monitoring may improve the prognostic of these patients. Carefully selected continuous glycemic monitoring devices may allow better monitoring, which is expected to translate into better treatment tailoring, from which diabetic patients on chronic hemodialysis may consistently benefit in terms of outcome, improved quality of life, and lower death risk.

KEYWORDS: *hemodialysis, diabetes, glucose variation*

INTRODUCTION

DM and arterial hypertension are the main determinants of CKD. In the last decades, the ever-higher prevalence of DM and arterial hypertension has resulted in a considerable increase in the number of patients with CKD [1]. The high death risk associated with CKD explains the importance of the meticulous care of these patients [2]. The mortality is even greater in patients with ESRD on renal replacement treatment (RRT), which includes patients on chronic hemodialysis, in which the higher prevalence of cardiovascular disease engenders increased risk of cardiovascular mortality [2,3].

Irrespective of being the cause or a mere comorbidity, DM accelerates the progression of CKD and increase cardiovascular death risk [4]. CKD is a well-known complication of DM, associated with both type 1 and type 2 DM [5]. Significant renal impairment in a diabetic patient induces higher risk of hypoglycemia. Moreover, in CKD patients with DM the therapeutic armamentarium is limited and even the few allowed oral antidiabetics require dosage adjustment to renal impairment. Dose should also be adapted in patients receiving exogenous insulin – generally insulin dose needs to be decreased as CKD progresses in order to prevent hypoglycemic episodes [6,7]. In most patients on chronic hemodialysis glycemic control is achieved by exogenous insulin and in only a minority the treatment includes another type of antidiabetic, usually agents with low or negligible hypoglycemia risk [7]. The present short review aims to describe the most recent management trends for diabetic patients that receive chronic hemodialysis. It focuses on both describing the impact diabetes has on the dialysis patients, but also on the importance of continuously monitoring their glucose levels.

MATERIALS AND METHOD

In order to select literature for this review, a search on PubMed was made using diabetes, hemodialysis and chronic as keywords. The search excluded articles published before 2010. Only one article published in 2000 was, however, cited due to its' quality of data and due to the fact that it fitted the aims of this research perfectly. 286 articles were found, but only 18 were considered relevant enough to be included (both systematic reviews and original articles). To make this selection the PICO (Population, Intervention, Comparison, and Outcomes) criteria were used. After the analysis of the data, the results were structured in two parts: Chronic kidney disease and glucose metabolism alterations in diabetic patients and monitoring glycemic imbalance in patients with CKD and the usefulness of devices for continuous glucose monitoring in patients on chronic hemodialysis.

RESULTS AND DISCUSSION

Chronic kidney disease and glucose metabolism alterations in in diabetic patients

Patients with CKD are at an increased risk of hypoglycemia as a consequence of the glucose metabolism alterations characteristic for diabetic patients with CKD. Factors favoring hypoglycemia in these patients include reduced kidney gluconeogenesis, impaired renal insulin clearance, and diminished kidney, liver, and muscle insulin removal due to uremia, impaired counterregulatory hormones' production, glucose lowering treatment, and poor food intake. Moreover, in patients with advanced stage CKD on hemodialysis, the employment of high glucose dialysis fluid may precipitate hypoglycemia [8]. Hypoglycemia may also occur in patients with low blood glucose level at the start of hemodialysis compounded by insufficient food intake (or none at all) during hemodialysis [8,9].

Regarding the influence of hemodialysis on the glycemic status in diabetic patients on chronic hemodialysis several issues deserve mentioning as being specific to hemodialysis as an RRT technique. Hemodialysis relies on two distinctive physico-chemical processes, diffusion and convection, that both influence insulin clearance. Moreover, it should be stressed out that the material the dialyzer membrane is made of is important in modulating insulin clearance: insulin clearance during hemodialysis is decreased by the employment of polyester-polymer alloy dialyzers but increased when polysulfone dialyzers are used.

The appraisal of insulin clearance during hemodialysis should be coupled with an estimation of pancreatic beta-cells status, which is intimately linked to the residual insulin

secretion, in order to properly predict the need for exogenous insulin or other antidiabetic medication in diabetic patients on chronic hemodialysis. In patients with significant residual insulin secretion due to pancreatic beta-cells preservation, decreased insulin clearance is associated with higher hypoglycemia risk. By contrast, in patients with low residual insulin secretion, blood glucose level is increased after hemodialysis, even more so if polysulfone dialyzers are employed, which are characterized by increased insulin clearance [8].

Most studies confirm that intensive glycemic control from the early stages of disease, is instrumental in preventing chronic complications, including microvascular ones in patients with DM [8]. On the contrary, in diabetic patients with CKD, intensive glycemic control not only fails to improve prognosis, but may even result in substantially increased death risk [8,10]. By the same token, the cardiovascular benefit of intensive glycemic control is abolished in diabetic patients with advanced stage CKD and high hypoglycemia risk [8, 11].

The changes in glucose metabolism typical for diabetic patients with CKD augment the risk of hypoglycemia, which may reduce both the quality of life and the survival. Starting RRT by hemodialysis increases even more this risk. It should be pointed out that in patients with severe hypoglycemia episodes in the predialysis period, the death risk considerably increases after starting hemodialysis [8].

In order to achieve optimal management of the diabetic patient, glycemic control assessment should include the estimation of glycemic variability, which proved to be not only more useful than glycated hemoglobin (HbA1c) monitoring in clinical practice, but also an important factor in estimating risk of both hypoglycemic episodes and cardiovascular complications in diabetic patients [12]. In diabetic patients with ESRD on RRT by hemodialysis, an increased glycemic variability is associated with higher death risk justifying the need to evaluate glycemic variability in these patients [13].

Monitoring glycemic imbalance in patients with CKD and the usefulness of devices for continuous glucose monitoring in patients on chronic hemodialysis

For glucose monitoring, the guidelines recommend periodical assessment of HbA1c and glucose self-monitoring or continuous glucose monitoring by means of special devices [14].

In certain patients, particular aspects should be considered when choosing among the various methods of glucose monitoring. In diabetic patients on chronic hemodialysis the usefulness of measuring the HbA1c is limited as these patients frequently have anemia and reduced red blood cell lifespan and the administration of the specific treatment with erythropoietin promotes erythropoiesis leading to the release in the bloodstream of young red blood cells full of hemoglobin not yet exposed to the glycation process [15, 16]. Therefore, in diabetic patients with advanced stage CKD the employment of parameters less influenced by these hematological alterations was advocated. One of these markers is glycated albumin, which reflects average blood glucose levels over the previous 3 weeks [15]. In diabetic patients on chronic hemodialysis glycated albumin is a prognostic factor of all-cause death risk [8, 17]. Glycated albumin is less useful in patients with low plasma albumin levels due to high catabolic status with secondary malnutrition, increased urine loss due to nephrotic syndrome or increased loss of other causes [8, 15].

Another method of glucose monitoring available for diabetic patients with CKD is glucose self-monitoring. Glucose levels measured by home self-monitoring are more useful for tailoring the treatment and provide important information on the patient's glycemic control. The accuracy of these monitoring methods increases with the number of measurements. Glucose self-monitoring is recommended both before and after meal, before exercise, in the evening before going to bed, and every time the patient feels low glucose symptoms [18]. However, it should be stressed out that this glucose monitoring method may miss asymptomatic spells of hypoglycemia, hence the recommendation of assessing, at least in some cases, the need for continuous glucose monitoring by means of special devices. As the diabetic patients with ESRD are at an increased risk of hypoglycemic episodes, they are one of the categories of patients in which continuous glucose monitoring is recommended [8,15].

As the glucose monitoring devices measure glucose level in the interstitial fluid, they reflect more reliably the patient's metabolic status compared to the glucose profile derived from glucose self-monitoring results. Blood glucose sensors owned either by the patient or the treating clinic and are used for periodically assessing the patients or for research purposes. In either case, the monitored parameters are the time span glucose level is in the target range, time span blood glucose is below the target range, time span blood glucose is above the target range [15,18].

CONCLUSION

To conclude, based on the data selected for this short review, continuous glucose monitoring is strongly recommended in patients with CKD. This recommendation awaits confirmation by further studies.

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