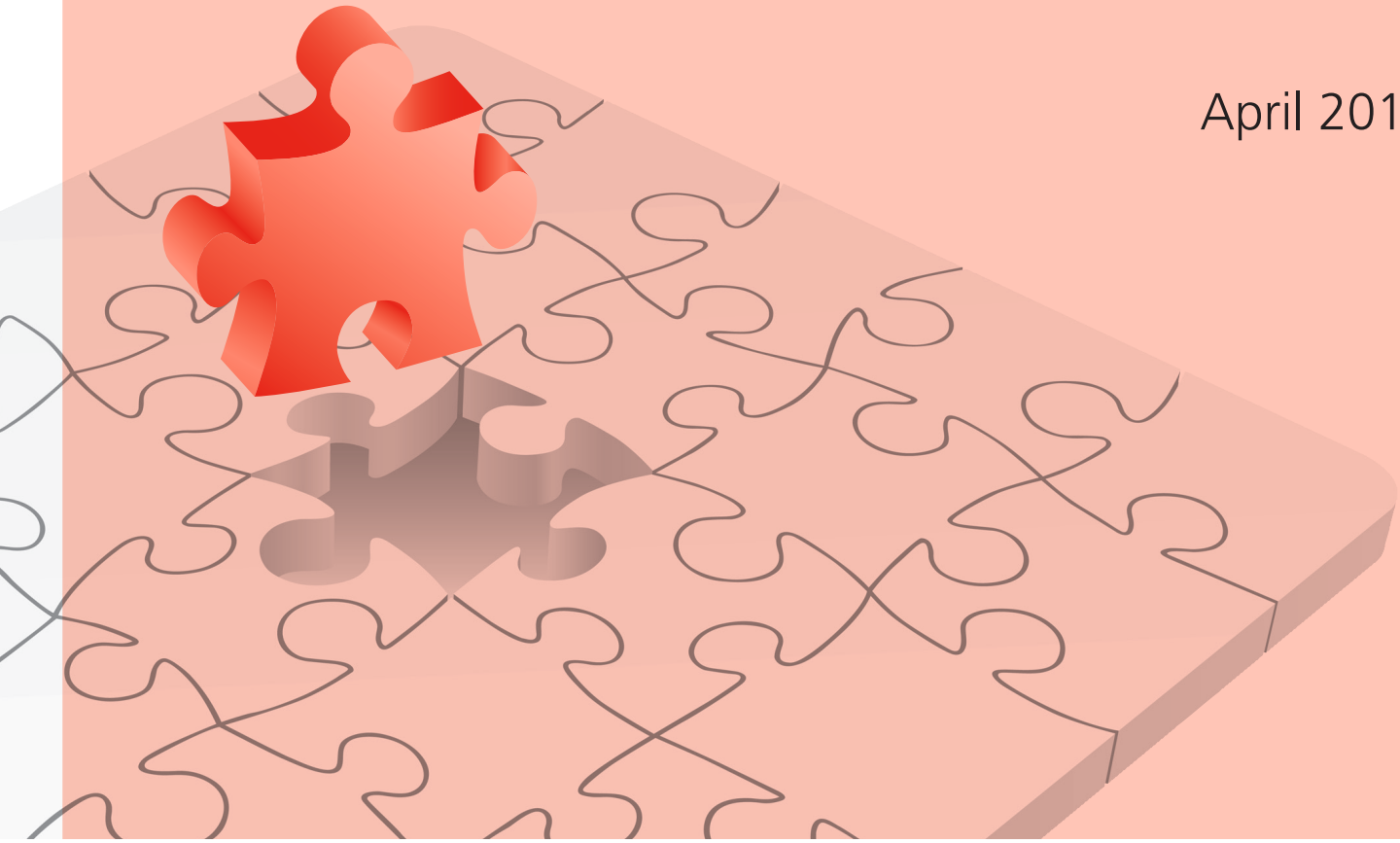
JBDS-IP Joint British Diabetes Societies for inpatient care

Management of adults with diabetes on the haemodialysis unit

April 2016



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With special thanks to Christine Jones for her administrative work and help with these guidelines and with JBDS-IP

Contents

Why we need this guideline

Diabetic nephropathy remains the principal cause of end-stage renal failure (ESRF) in the UK,[1] as elsewhere in the developed world,[2] and the well-described projected global increase in the prevalence of diabetes implies an increasing burden of this disease. People with diabetes on regular hospital haemodialysis are a vulnerable group at high risk of adverse cardiovascular outcomes, the leading cause of mortality on this population.[3]

Accordingly, people with diabetes and ESRF require improved delivery of care, in particular to overcome organisational difficulties. These national guidelines, the first in this area, are intended to support the practice of all healthcare professionals who care for this vulnerable group of patients, based on the best available evidence or on expert opinion where there is no clear evidence to inform practice. We aim to provide clear advice to clinicians caring for people with diabetes on maintenance haemodialysis and to encourage and improve education for clinicians and patients to promote patient empowerment and self-management.

A greatly abbreviated version of the guideline is presented here, to provide an overview of the scope of the documents. Recommendations are given at the head of each section; see below for grades of evidence. The full guideline is available online[4]: consult this before designing a therapeutic intervention.

Evidence grades for recommendations:

1A Strong recommendation. High quality evidence

1B Strong recommendation. Moderate quality evidence

1C Strong recommendation. Low quality evidence

1D Strong recommendation Very low quality evidence

2A Weak recommendation. High quality evidence

2B Weak recommendation. Moderate quality evidence

2C Weak recommendation. Low quality evidence

2D Weak recommendation. Very low quality evidence

Section 1: Organisation of care

Recommendations

1.1. All people with diabetes undergoing maintenance haemodialysis should have a documented annual review of their diabetes which includes foot and eye screening through the GP diabetes register. The responsibility for undertaking this rests with the diabetes service caring for the patient. In order to ensure that this is effectively undertaken:

a) The assessment should be coordinated in a manner that recognises that the patient is dialysing three times per week

b) The information pertaining to the review should be available to all healthcare staff involved in the care of the patient

c) There should be a named link worker on the dialysis unit for each patient who can ensure that the assessments have been undertaken and have been acted upon *(Grade 1B)*

1.2. All people with diabetes undergoing maintenance haemodialysis should have regular access to a named Diabetes Specialist Nurse (DSN) responsible for providing support in relation to on-going care of diabetes and its complications. Where commissioned, the DSN would be able to work within the diabetes/renal outpatient clinic and provide regular rounds on the dialysis unit, offering patient education and clinical advice where necessary.

A link nurse on the renal unit will be expected to coordinate regular foot checks, blood glucose monitoring training and injection technique. This could be a healthcare assistant or a registered nurse following appropriate training and competency assessment. The link nurse would be expected to escalate foot problems to the DSN for specialist foot assessment and on- going referral to the specialist foot team. *(Grade 1D)*

1.3. A process to coordinate the management of acute metabolic, eye, cardiovascular and/or foot emergencies should be established with effective communication between the dialysis unit, the specialist diabetes team and primary care. *(Grade 1C)*

1.4 All diabetes patients on maintenance haemodialysis programmes with acute and/or chronic glycaemic instability should have specialist diabetes input. *(Grade 1C)*

The management of these patients is complex, with a strong requirement for effective multidisciplinary care, but guidance on glycaemic targets or management algorithms has been lacking. Ideally, all patients undergoing maintenance haemodialysis should be reviewed in combined renal diabetes clinics, but attendance rates are often low and such clinics are not well established. The low participation rates are probably related to the fact that many of these patients are elderly and socially deprived, with lives dominated by their dialysis schedule. Indeed, important aspects of care may be overlooked, with renal, diabetes and primary care physicians assuming that these needs are being met elsewhere.[5] Diabetes specialist nurses (DSN) should play a vital role in coordinating care and signposting patients for urgent care for eye, foot or acute metabolic complications. They can support, educate and empower such patients and staff; their review of individuals on dialysis units alongside haemodialysis staff would ensure that all individuals have ongoing diabetes support and timely intervention.

References for Section 1

1. UK Renal Registry. 2014 – The Seventeenth Annual Report. Available at https://www.renalreg.org/reports/2014-seventeenth-annual-report/ (accessed Feb 2016).
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4. Joint British Diabetes Societies and Renal Association. Management of adults with diabetes on the haemodialysis unit. Full version available on ABCD, Diabetes UK and DISN UK Group websites.
5. Atherton G. Renal replacement and diabetes care: the role of a specialist nurse. J Diabetes Nursing 2004;8:70-72.

Section 2: Assessment of glycaemic control

Recommendations

2.1. All units treating patients with diabetes on maintenance haemodialysis should ensure that they are aware of the method used to measure glycated haemoglobin (HbA1c) within their local laboratory and this should ideally be using an HPLC based assay to prevent the overestimation of HbA1c due to carbamylation of haemoglobin. *(Grade 1A)*

2.2. Units managing patients with diabetes on maintenance haemodialysis should be aware of the factors that are likely to render HbA1c less reliable including:

- Under dialysis or poor diet resulting in persistent metabolic acidosis;
- Recent transfusions;
- Haemaglobinopathy;
- Rapid rise of Hb in the preceding 2 months in response to erythropoietin. *(Grade 1A)*

2.3. Clinicians managing patients with diabetes on maintenance haemodialysis should be aware that it is more likely that the HbA1c will underestimate average blood glucose particularly in patients with good to moderate glycaemic control. *(Grade 1B)*

2.4. Glycated albumin may offer the opportunity to assess glycaemic control over a shorter time period (15 to 20 days) and with greater accuracy in patients with diabetes on MHDx. This assay is not widely available and has not yet been fully validated such that the use of this assay in assessing glycaemic control in these circumstances should be undertaken as part of a clinical research programme. *(Grade 2C)*

2.5. The use of self monitoring of blood glucose (SMBG) remains a cornerstone of the assessment of glycaemic control in patients with diabetes on maintenance haemodialysis who are being treated with agents that increase the risk of hypoglycaemia. *(Grade 1A)*

2.6. The reliability of SMBG should be augmented by ensuring the provision of appropriate equipment, testing strips and training of the operator. *(Grade 1B)*

2.7. Continuous glucose monitoring (CGM) may provide valuable information on the glycaemic control of patients with diabetes on maintenance haemodialysis, however, its use is limited by technical issues relating to device calibration, which must be taken into account for accurate interpretation of data. *(Grade 1C)*

2.8. When using CGM, it is advised to commence the CGM on a non-dialysis day to minimise calibration problems caused by rapid changes in blood glucose due to the dialysis process. *(Grade 1C)*

Biomarkers

HbA1c measurement is the main biomarker for assessing glycaemic control in chronic kidney disease (CKD) patients with diabetes.[1] However, the accuracy of the HbA1c values in late CKD stages may be open to question,[2,3] and the relationship between HbA1c and average glycaemia has not been confirmed in patients receiving dialysis. Haemoglobinopathies may also render HPLC-based measurement of HbA1c unreliable.[4] Racial and ethnic differences in the relationship between HbA1c and blood glucose may also occur.[5] Anaemia may also distort the relationship between HbA1c and blood glucose.

HbA1c can be overestimated in the setting of increased blood urea nitrogen (due to production of carbamylated haemoglobin, read as HbA1c in electrical charge-based assays); uraemia (increased glycosylation rate), iron deficiency (common in haemodialysis). Factors that cause underestimation of HbA1c in ESRF include uraemia (shortened erythrocyte life); need for blood transfusions; and use of erythropoietin (higher proportion of younger red blood cells). Nevertheless, HbA1c remains of value in these patients and a correction factor has been proposed for use in dialysis patients (Table 1).[6] Fructosamine or glycated albumin levels are unaffected by the factors listed above, but the use of alternative biomarkers to HbA1c outside the research setting is insufficiently validated at this time and they may be unreliable if there is hypoalbuminaemia.

Table 1. Correction factor for HbA1c measurement in patients on dialysis[6]

Haematocrit	Treatment with erythropoietin	Adjustment for HbA1c
≥30%	–	HbA1c × 1.14
<30%	Low dosage	HbA1c × 1.19
<30%	High dosage	HbA1c × 1.38.

Self-monitoring of blood glucose and continuous glucose monitoring

SMBG is especially important in subjects receiving treatment(s) that may cause hypoglycaemia, those that suffer from regular hypoglycaemia, or those with hypoglycaemia unawareness. The reliability of SMBG varies with the meter in use (which should conform to ISO15197[7]), frequency/timing of measurements, the age and type of test strips (and environmental conditions in which they are used), the expertise of the person carrying out the test, and clinical factors including haemolysis, anticoagulation, hyperlipidaemia and metabolic acidosis. SMBG accuracy is instrument- and user-dependent: and therefore it is important to evaluate each patient's technique regularly and ideally validate the recorded results.

CGM is ideally suited for people with diabetes on maintenance haemodialysis, as it provides information on short-term glucose fluctuations associated with dialysis.[8] Calibration is an issue in these patients, however, as SMBG readings may be less reliable in people with ESRF, and may be changing rapidly around the time of dialysis. In addition, the time lag between capillary (SMBG) and interstitial glucose (CGM) is increased in ESRF, which reduces the ability of CGM to detect hypoglycaemia. Comparing CGM data between individuals is also difficult due to these uncertainties.

References for Section 2

1. National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. Am J Kidney Dis 2012;60:850-86.
2. Shima K, Chujo K, Yamada M, et al. Lower value of glycated haemoglobin relative to glycaemic control in diabetic patients with end-stage renal disease not on haemodialysis. Ann Clin Biochem 2012;49:68-74.
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5. Herman WH, Cohen RM. Racial and ethnic differences in the relationship between HbA1c and blood glucose: implications for the diagnosis of diabetes. J Clin Endocrinol Metab 2012;97:1067-72.
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8. Riveline JP, Teynie J, Belmouaz S, et al. Glycaemic control in type 2 diabetic patients on chronic haemodialysis: use of a continuous glucose monitoring system. Nephrol Dial Transplant 2009;24:2866-71.

Section 3: Glycaemic control and outcomes on maintenance haemodialysis

Recommendations

3.1. The target for HbA1c in patients with diabetes and on maintenance haemodialysis should be individualised but if the patient is on a hypoglycaemia inducing treatment should be aimed at between 58–68 mmol/mol (7.5–8.5%). *(Grade 1C)*

3.2. It is likely that HbA1c of >80 or 9.5% represents poor glycaemic control unless there is severe iron deficiency. *(Grade 2C)*

3.3. Reduction in treatment should be considered for patients with HbA1c <58 mmol/mol or 7.5% on potentially hypoglycaemia inducing agents. *(Grade 1C)*

While the long-term clinical benefits from maintaining effective glycaemic control in diabetes before ESRF is established are well known,[1,2] the benefits or improving chronic hyperglycaemia at the stage of HD are less clear and avoiding hypoglycaemia remains a priority to optimise outcomes. In the shorter term, attempting to intensively reduce HbA1c has little effect on outcomes and has the potential to increase mortality associated with severe hypoglycaemia, including in diabetes patients with CKD.[3–6] As there are no specific glycaemic guidelines for the ESRF population, this group of patients should be considered to be vulnerable to these outcomes. We therefore recommend individualised glycaemic goals for diabetes patients on maintenance haemodialysis, with less tight targets for those on treatments known to cause hypoglycaemia.

References for Section 3

1. Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359:1577-89.
2. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med 2005;353:2643-53.
3. Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008;358:2545-59.
4. VADT Investigators. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med 2009;360:129-39.
5. ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med 2008;358:2560-72.
6. ACCORD Study Group. Chronic kidney disease and intensive glycemic control increase cardiovascular risk in patients with type 2 diabetes. Kidney Int 2015;87:649-59.

Section 4: Antidiabetic therapies

Recommendations

4.1 Sulfonylureas are not licensed for use in patients on maintenance haemodialysis and should be avoided because of the increased incidence of hypoglycaemia in this setting. *(Grade 1B)*

4.2 Repaglinide can be considered in the haemodialysis patient. Dose reductions are to be expected and it should be noted that experience in this group is limited therefore increased monitoring is required. *(Grade 2C)*

4.3 Metformin is not licensed to be used in patients on maintenance haemodialysis and should be avoided because of the increased risk of lactic acidosis in this setting. *(Grade 1B)*

4.4 Acarbose is not licensed for patients on maintenance haemodialysis. *(Grade 2D)*

4.5 No dose adjustment is needed for pioglitazone for impaired renal function. Whilst pioglitazone is not licensed for use in patients with maintenance haemodialysis there has been some experience of this agent used in this context. *(Grade 1C)*

4.6 There is insufficient experience of the use of any of the current GLP-1 agents in patients on maintenance haemodialysis such that their use cannot be recommended. *(Grade 2D)*

4.7 Of the DPP4 inhibitors licensed in the UK, linagliptin, sitagliptin, vildagliptin and alogliptin can be used in patients on maintenance haemodialysis; however, dose reductions for sitagliptin, vildagliptin and alogliptin are required. *(Grade 1B)*

4.8 SGLT2 inhibitors may be used in patients with early stage chronic kidney disease (CKD; stages 1–2) with no dose adjustment, but as CKD progresses to moderate and severe disease (stages 3–5) they are to be avoided. *(Grade 1C)*

4.9 All people with diabetes on insulin should be dialysed against a dialysate containing glucose. *(Grade 1C)*

4.10 The aim of insulin therapy in diabetes patients on maintenance haemodialysis is to improve quality of life and avoid extremes of hypo- and hyperglycaemia. (Grade 1D)

4.11 Most patients on dialysis would benefit from reduction of insulin doses during and immediately following dialysis (i.e. on the dialysis day), although advice should be individualised ideally on the basis of CGM data. *(Grade 1C)*

4.12 Basal bolus regimes may be most flexible and best suited to the glycaemic variability seen in patients with diabetes on maintenance haemodialysis. (Grade D, expert opinion)

4.13 In patients who are less likely to be able to comply with the requirements of a basal bolus regime consideration should be given to once daily regimes with longer acting insulins. *(Grade 1D)*

4.14 CGM may allow clinicians to advise on variation of insulin regimen according to day of dialysis. *(Grade 1D)*

4.15 If patients have troublesome hypoglycaemia on NPH insulin, conversion to analogue insulins may be of benefit. *(Grade 1C)*

Overview

As renal function declines, peripheral insulin resistance increases, with declines in renal gluconeogenesis, hypoglycaemic counter-regulation, and the clearance of insulin (endogenous or injected) and other antihyperglycaemic agents. Some patients on maintenance haemodialysis can stop taking antidiabetic therapies transiently or permanently.[1] This summary will focus on the pharmacological groups used in the management of type 2 diabetes in haemodialysis patients. Algorithms for treatment of diabetes mellitus in haemodialysis patients should be individualised based on the safety profile and treatments available locally.

Non-insulin antidiabetic therapies for type 2 diabetes

Sulfonylureas (SU) do not have clear indications for use in severe CKD. Also, SU are generally highly protein bound and therefore unlikely to be dialysed, which can cause post-dialysis hypoglycaemia. Glibenclamide or glimepiride are contraindicated in CKD stages ≥3 (eGFR<60 mL/min) as active metabolites may accumulate. Gliclazide poses a lower risk for severe hypoglycaemia than glibenclamide and glimepiride, but should be used with caution when GFR is <40 mL/min. Accordingly, SU should be avoided in diabetes patients on maintenance haemodialysis due to their limited therapeutic indications and risk of hypoglycaemia. Repaglinide and nateglinide are highly protein bound and therefore unlikely to be removed in dialysis and should be used with caution in people on haemodialysis.

Metformin has no clinical value in the haemodialysis population due to risk of severe lactic acidosis secondary to drug accumulation.

Acarbose has not been studied in severe renal impairment. Accordingly, it is not recommended for use in dialysis.

Pioglitazone has a low risk of hypoglycaemia and its effects are not influenced by haemodialysis. It can be used in CKD down to a clearance of 4 mL/min, without dose adjustment; however, it is not licensed for use on haemodialysis. Thiazolidinedione-associated "heart failure" is largely caused by salt and water retention; the risk of this in patients on maintenance haemodialysis has not been studied, and thus we would not recommend pioglitazone in haemodialysis patients.

Clinical experience with **GLP-1 agonists** in patients with renal impairment is limited. Although daily liraglutide and weekly dulaglutide can be used where eGFR >50 mL/min, caution is recommended for use in patients with severe CKD. Lixisenatide and exenatide cannot be recommended for patients with severe CKD, including on haemodialysis.[2] Post-marketing reports of worsened renal function with GLP-1 agonists have appeared, especially in patients reporting gastrointestinal side-effects or dehydration. On balance, GLP-1 analogues cannot currently be recommended for patients on haemodialysis.

DPP4 inhibitors can be used in patients on haemodialysis. Within this class, only linagliptin is not eliminated via the kidney and does not need a dose reduction in this setting. Dose reductions for patients on haemodiaysis are required for other DPP4 inhibitors: labelled maintenance doses in this setting are sitagliptin (25 mg QD), vildagliptin (50 mg QD), alogliptin (6.25 mg QD). These reductions reflect generally a 50–75% reduction on the daily dose for people without CKD. Saxagliptin is not indicated for use in people with ESRF.

SGLT2 inhibitors (currently canagliflozin, dapagliflozin and empagliflozin) inhibit glucose re-absorption in functioning proximal renal tubules, thus providing an insulin independent antihyperglycaemic mechanism. Since their glucose-lowering action requires a working kidney they are contraindicated in haemodialysis patients.

Insulin in patients with end stage renal failure

Insulin requirements fall in line with reductions in eGFR. The process of haemodialysis has a number of effects on glycaemic control. These include removal of glucose (the dialysate should contain glucose for a patient with diabetes and ESRF), removal of glucoregulatory hormones (insulin, C-peptide, glucagon) and some antidiabetic drugs (insulin, some SU), and modulation of insulin action secondary to improved uraemia, acidosis, and phosphate metabolism. Therefore, glucose control on dialysis days may be very different to that on non-dialysis days, leading to unpredictable glucose levels, and glycaemic variability. While requirements for antihyperglycaemic therapy may be reduced in these patients to avoid hypoglycaemia (the so-called "burnt-out diabetes" phenomenon), most patients with diabetes on maintenance haemodialysis require some therapy for hyperglycaemia. Importantly, variation of oral hypoglycaemic or insulin therapy may be required on day of dialysis, when glucose levels will often be lower and glucose variability higher.

A basal-bolus regimen with regular SMBG may be the safest regimen, with analogue insulin considered in place of NPH where recurrent hypoglycaemia occurs. Alternatively, thrice-weekly long acting insulin at the end of dialysis in haemodialysis patients with diabetes may improve glycaemic control significantly (further research on this is needed with new ultra-long-acting insulins, such as degludec).[3,4] Biphasic insulin regimens may be more difficult to manage on haemodialysis due to the irregularity of diet, glucose levels and activity imposed by haemodialysis sessions; but patients stabilised on a biphasic insulin regimen may be reluctant to change; advice on 10–15% reduction in doses of insulin on dialysis days may be required to avoid hypoglycaemia. Some patients on biphasic insulin may need a bedtime carbohydrate snack (<20 g) to reduce the risk of nocturnal/early morning hypoglycaemia. The accompanying figure summarises principles of management of hyperglycaemia in insulin-treated patients in the setting of the hospital or satellite dialysis unit.

MANAGEMENT OF HYPERGLYCAEMIA IN HOSPITAL/SATELLITE DIALYSIS UNIT

- Patients should be encouraged to monitor and manage their own diabetes as far as possible
- **Patients should bring their own insulin/tablets with them to the Dialysis Unit**
- In patients on agents that could cause hypoglycaemia – blood glucose should be checked **pre dialysis** and **just before finishing dialysis**
- Blood glucose can fluctuate during dialysis **and most frequently drops in the last hour of dialysis**
- **Reduce total insulin dose by 10–15% during and immediately following dialysis**
- **Reduction in insulin dose (or oral hypoglycaemic agent) is required in those with HbA1c <58 mmol/mol(7.5%) to avoid hypo**

On rapid acting insulin:

Patients should **reduce their usual breakfast (if morning dialysis), lunchtime (if afternoon dialysis) or evening insulin (if evening dialysis) by 10–15%** at the start of each shift

On premixed/biphasic insulin:

Patients should r**educe dose by 10–15%** with breakfast (morning and afternoon dialysis) and with their evening meal (if starting evening dialysis)

On long acting insulin:

Patients should **reduce dose by 25%** in the morning or in the evening of dialysis

BLOOD GLUCOSE

Pre-dialysis BGM <7mmol/L:

- Give 20–30g carbohydrate prior to dialysis
- Recheck BG
- BGM just before finishing dialysis
- May need a carbohydrate snack before end of dialysis

Pre-dialysis BGM 7–15 mmol/L:

No action required

BGM 7–15 mmol/L just before finishing dialysis

No action required

BGM >15mmol/L just before finishing dialysis:

Ask patient to moinitor BGs and seek advice from GP or Diabetes Specialist Nurse if persistently high

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Section 5: Dietary management and nutrition

Recommendations

5.1 Each Haemodialysis unit should have access to appropriate dietary expertise able to provide a holistic approach to the patient with diabetes. *(Grade 1D)*

Dietary advice should be personalised and include information on both diabetes and renal aspects of the diet. *(Grade 1D)*

5.2 It is recommended that patients on haemodialysis achieve an energy intake of 30-40 kcal/kg ideal body weight (IBW). *(Grade 1D)*

If a patient is aiming to lose weight appropriate individualised advice should be provided on energy requirements. *(Grade 1D)*

5.3 It is recommended that patients on haemodialysis achieve a protein intake of >1.1 g/kg IBW. *(Grade 1C)*

5.4 Dietary advice should be given for both dialysis and non-dialysis days to minimise significant glycaemic and caloric excursions. *(Grade 1D)*

5.5 The type of diabetes the patient has should be identified and the dietary aims agreed. *(Grade 1C)*

Total energy should come from 50-60% carbohydrate, <30% fat and at least 15% from protein. *(Grade 1D, expert opinion)*

5.6 Low-potassium fruit, vegetables and carbohydrates with low-moderate glycaemic index should be encouraged to allow patients to achieve the recommended '5-a-day' fruit and vegetable portions. *(Grade 1D)*

5.7 Foods containing phosphate additives should be targeted prior to advice on reducing low GI foods e.g. wholegrain products and foods with high biological protein. *(Grade 1D)*

5.8 A salt intake of <6 g/day is recommended. *(Grade 1C)*

5.9 Oily fish should be recommended with caution for patients with CKD on haemodialysis, mainly because of vitamin A and phosphate content. *(Grade 2D)*

5.10 It is recommended that patients on maintenance haemodialysis are prescribed a water-soluble vitamin supplement. *(Grade 2D)*

5.11 All patients should be screened for protein energy wasting (PEW) on each admission to hospital. If no screening procedures are in place at dialysis units, a referral pathway and/or referral criteria should be in place to identify those at risk for appropriate referral to the dietitian for nutrition support. *(Grade 1D)*

5.12 Initiation of nutrition support should be considered in those at risk of PEW; the indicators are the same in patients with and without diabetes. *(Grade 1C)*

5.13 Dietary counselling and oral nutrition support is the first-line treatment for patients who are unable to meet their nutritional needs orally.

Nasogastric, gastrostomy, or intradialytic parenteral nutrition feeding may be necessary if these interventions are insufficient. *(Grade 1D)*

5.14 The dietary advice and nutritional products prescribed should minimise any deleterious effects on blood sugar or lipid levels. Regular review of the nutritional intervention should be maintained to monitor this. *(Grade 1D)*

5.15 In patients on active treatment of diabetes with insulin:

- Where there is a pre-dialysis glucose of <7 mmol/L, 20–30 g of a low glycaemic index carbohydrate is recommended at the beginning of the haemodialysis session to prevent further decline of blood glucose level. *(Grade 1D)*
- Capillary glucose should be assessed pre- and post-dialysis. *(Grade 1D)*
- The unit should ensure a hypoglycaemia treatment is accessible to patient at all times, including during travelling to and from the dialysis unit. *(Grade 2D)*

5.16 In case of hypoglycaemia:

- Appropriate rapid-acting carbohydrate treatment should be provided to take into account fluid, potassium and phosphate restrictions. *(Grade 1D)*
- After treatment initiation, glucose level should be checked 15 minutes after the treatment is given. If not above 4 mmol/L, a repeat dose of the 15 g rapid glucose followed by 10–20 g complex or low glycaemic index carbohydrate is recommended. *(Grade 1C)*
- Patients and staff should be educated in regard to the appropriate treatment of mild to moderate hypoglycaemia and hypoglycaemia unawareness. *(Grade 1D)*

5.17 Patients with gastroparesis are encouraged to have a small meal size but frequent intake. A low-fat and low-fibre meal is recommended to manage gastroparesis. *(Grade 1C)*

5.18 Clinicians should ensure that patients on maintenance haemodialysis with diabetes are aware that they are more likely to be able to maintain intra-dialytic weight gain (IDWG) at <4.5% of dry weight or <2 kg if they optimise their HbA1c. *(Grade 1C)*

5.19 Overweight/obese patients who are being considered for a kidney transplant should be encouraged to lose weight. Dietary counselling should be a calorie restrictive diet, making sure that the protein requirements for the patient are met (≥1.1 g/kg IBW). *(Grade 1B)*

5.20 Dietary counselling should also ideally include behavioural change strategies and increased physical activity. *(Grade 1B)*

5.21 All patients with an elevated BMI who may not be considered for transplantation if unable to lose weight through diet, exercise and behavioural change should be considered for bariatric surgery or weight-reducing medication. *(Grade 1C)*

Overview

Patients with diabetes who commence maintenance haemodialysis may have received dietary advice from the diabetes and renal team, from dietitians or other health professionals, each with its own priority. This can lead to confusion and ultimately poor dietary adherence. Patients should identify achievable goals and changes to lifestyle behaviours, with good communication between specialities to help reduce confusion and provision of contradictory information. A clear care plan helps to achieve a holistic approach to patient care. It is therefore important that haemodialysis patients are routinely referred to a registered dietitian who is qualified to assess their overall diet and offer appropriate, individualised advice.[1]

The full guideline provides detailed advice on these aspects of nutritional support, and a highly abbreviated précis is provided here (see also Table 1).

Key dietary components

Energy intake should comprise 30–40 kcal/kg ideal body weight (50–60% from carbohydrate, <30% from fat and >15% from protein). An individualised plan is needed for those seeking to lose weight (but maintain BMI ≥23 kg/m^2).[2] The diabetes team can advise on balancing glycaemic control with increased nutrition support for patients who require an increased calorie load. Protein intake should be >1.1 g/kg ideal weight. Carbohydrate intake should be agreed within overall aims of diabetes management, separately for dialysis and non-dialysis days, with provision of education on insulin dose adjustment and carbohydrate management/counting, where applicable.

Individualised low potassium dietary advice is indicated if potassium is ≥6.0 mmol/L. Consumption of low-potassium carbohydrate options (e.g. pasta, rice, noodles, bread) may support greater intake of fruits and vegetables within a healthier diet overall. Insulin deficiency can promote hyperkalaemia.

Dietary advice should be provided to maintain serum phosphate at 1.1–1.7 mmol/L. Reduce foods containing phosphate additives before reducing low-glycaemic index foods, or those high in natural protein (e.g. eggs, nuts, dairy, seafood). Wholegrain products are high in phosphate, but this is unlikely to be absorbed due to their phytate content.

Salt should be limited to an intake of <6 g/day.

Provision of a water-soluble vitamin supplement is recommended, although there are no randomised trials to support this. Finally, advise caution regarding intake of oily fish, mainly because of its vitamin A and phosphate content.

Nutrition support

Prevention of protein energy wasting

PEW is a major cause of morbidity and mortality in haemodialysis patients, especially in diabetes. Ensuring adequate energy and protein intake and optimising dialysis prescription is recommended. All inpatients should be screened for PEW on admission and weekly thereafter. Screening tools in hospitals may not be specific enough to identify a dialysis patient at risk of PEW, particularly those using weight and BMI, as fluid changes can complicate their interpretation. Outpatients should be screened at their first clinic appointment and/or at initiation of dialysis and then 3–6 monthly. There should be procedures for referral to the renal dietitian if any member of the team identifies risk of PEW.

Delivering nutrition support

Nutrition support should be considered in haemodialysis patients with any of: BMI <20 kg/m^2; unintentional non-oedema weight loss >5–10% over 3–6 months; <85% ideal weight; subjective global assessment graded B/C or 1–5; intercurrent catabolic acute conditions preventing normal nutrition or adequate oral intake. All malnourished haemodialysis patients should receive dietary counselling, including on the use of oral nutritional supplements (ONS) and non-saturated fats where necessary.[3] Long-term nasogastric or gastrostomy feeding should be considered where ONS is insufficient. When intensive dietary counselling, ONS and enteral feeding have failed, intra-dialytic parenteral nutrition is recommended. Maintenance of serum glucose 6–10 mmol/L is recommended to avoid post-dialysis hypoglycaemia. Investigate and overcome causes of reduced oral intake.

Managing mild hypoglycaemia

Dialysis patients are at risk of hypoglycaemia, especially within 24 hours of dialysis (see Section 6 of the full guideline). Intake of 10–20 g of a low glycaemic index carbohydrate is recommended at the second hour of haemodialysis.

If the pre-haemodialysis blood glucose is <7 mmol/L, 20–30 g carbohydrate at the beginning of haemodialysis is recommended. For patients with hypoglycaemia symptoms, we recommend intake of 15–20 g carbohydrate (e.g. 1 medium slice of bread or 2 digestive biscuits). Patients should have access to a remedy for hypoglycaemia at all times, including during travelling to and from the dialysis unit. In patients given a large amount of food on dialysis there may be an increased incidence of hypotension during hours 3–4 due to increased intestinal blood flow.

Hypoglycaemia in hospital should be managed according to recommendations from the Joint British Diabetes Societies.[4] Many sources of rapid acting glucose recommended for treating hypoglycaemia can be inappropriate for maintenance haemodialysis patients due to their potassium, phosphorus or fluid content.

Managing gastroparesis

Small, frequent, low-fibre and low-fat meals with increased liquid nutrient intake (including liquid fat where increased caloric intake is needed) may be appropriate for patients with gastroparesis on haemodialysis (no alcohol or carbonated drinks). Foods of small particle size (or pureed) may also be helpful. It is advised to reduce the amount of insoluble fibre in the diet of patients with gastroparesis to prevent phytobezoar accumulation.[5] For patients with gastroparesis requiring enteral feeding, a post-pyloric enteral feeding such as jejunal feed (placed surgically or endoscopically) is appropriate.

Fluid management

Glycaemic control is important in fluid management of dialysis patients with diabetes as poor glycaemic control can lead to a vicious cycle of thirst and polydipsia and increase the risk of a higher IDWG (>4.5% of dry weight).

Managing obesity

The focus of nutritional care in patients on maintenance haemodialysis should be on total energy intake, rather than the source of energy in the diet, for optimal glycaemic control and weight reduction. However, there are virtually no standards, guidelines or studies with regards to obesity in patients with diabetes on haemodialysis.

Some studies suggest that obesity or weight variation are positively correlated with survival of patients on dialysis[6,7] However, some authors question the existence of this "obesity paradox". There is very limited evidence of the benefits of specific diets or bariatric surgery for weight loss in the CKD population, especially those on maintenance haemodialysis. Pharmacological treatment may be considered for people who have not reached their target weight loss on diet, activity and behavioural changes.[8] A lack of experience with GLP-1 agonists means they cannot presently be recommended in subjects with renal failure.

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Section 6: Complications of diabetes in haemodialysis patients

Recommendations

6.1 In managing patients with diabetes on maintenance haemodialysis, clinicians should be aware of the significantly increased risk of hypoglycaemia caused by:

- Poor or erratic nutritional intake;
- Reduced clearance of endogenous or exogenous insulin by the kidney and the liver;
- Decreased hepatic gluconeogenesis. *(Grade 1B)*

6.2 Patients with diabetes on maintenance haemodialysis should be adequately counselled on the increased risk of hypoglycaemia and that hypoglycaemia can occur with diminished classical symptoms. *(Grade 1B)*

6.3 Clinicians should counsel patients with diabetes and on maintenance haemodialysis about risk of hypoglycaemia on dialysis days, and consider reducing anti-hyperglycaemic therapy on dialysis days. *(Grade 1D)*
NB: SEE RECOMMENDATION 5.15: Patients on maintenance haemodialysis on active treatment of diabetes with insulin or oral hypoglycaemic agent(s), should have capillary glucose assessed pre- and post-dialysis.

6.4 The heels of all patients with diabetes on haemodialysis should be protected with a suitable pressure relieving device during haemodialysis. *(Grade 2D)*

6.5. All patients with diabetes on dialysis should have their feet inspected at least weekly. *(Grade 2D)*

6.6 All patients with diabetes on dialysis should be considered high risk and should have regular review by the podiatry team. *(Grade 1C)*

6.7 Patients should have their feet screened three monthly using a locally agreed tool and by competent staff on the dialysis unit. *(Grade 1C)*

6.8 If the patient has an ulcer or there is any other concern the patient should be referred to the diabetic foot multidisciplinary team within one working day. *(Grade 1D)*

6.9 If the patient is on home dialysis it is the responsibility of the clinician in charge of their care (nephrologist or diabetologist) to ensure that the patient has an annual foot review and is attending review by the foot protection team. *(Grade 1D)*

6.10 Any patient presenting with a hot swollen foot should be referred to the diabetic foot team within 24 hours. *(Grade 1D)*

6.11 Patients with diabetes on MHDx approaching end of life or where a palliative care pathway has been agreed should be managed in accordance with Diabetes UK End of Life clinical care recommendations for patients with diabetes. Treatment and interventions should be focussed on symptoms. *(Grade 1D)*

Glycaemic variability and hypoglycaemia

Reduced insulin clearance in advanced CKD leads to lower insulin requirements and higher risk of hypoglycaemia if insulin or SU are not reduced. Uraemia-induced reduction in calorie intake may also reduce insulin requirement. Hypoglycaemia appears to occur twice as frequently amongst patients with CKD vs. normal renal function,[1] usually in the hours after dialysis in patients with ESRF. Hypoglycaemic unawareness is common in these patients.

Haemodialysed subjects usually have their lowest glucose readings after dialysis and a dialysate containing glucose should be used for all people with diabetes on insulin. Clinicians may need to identify subjects' individual glycaemic profile patterns and vary antidiabetic treatment accordingly.[2] Patients with diabetes with similar HbA1c may have significantly different daily plasma glucose profiles, within or between days. Long-term glycaemic variability increases hypoglycaemia risk and may promote vascular complications of diabetes.[3–7] However, there is limited evidence for addressing glycaemic variability as a strategy for improving cardiovascular outcomes. Further research is needed to define the role of CGM and optimal insulin administration in the dialysis setting (see above).

Diabetic foot disease in renal dialysis patients

ESRF and CKD[4–5] are independent risk factors for diabetic foot disease, neuropathy, peripheral arterial disease, delayed wound healing, amputation and post-amputation mortality. Dialysis/renal replacement therapy is strongly and independently associated with foot ulcers.[8–11] Neuropathy greatly increases the risk of pressure-related ulcers, and care must be taken to ensure adequate pressure relief on patients' heels in renal dialysis units when they are recumbent for prolonged periods.[12] Podiatry input on dialysis units reduces the frequency and severity of diabetic foot complications: regular podiatry assessment (at least 3-monthly) should be ensured, ideally on dialysis units as this frail, multi-morbid population may have difficulty accessing community podiatry services.

The Charcot foot (Charcot neuropathic osteoarthropathy) is associated with renal disease and very high morbidity. It is frequently misdiagnosed as infection, venous thrombosis, or gout, leading to potentially avoidable limb loss. A non-removable cast or walker is recommended for offloading an acute Charcot foot. However, patients on renal replacement therapy may tolerate this poorly due to changing peripheral oedema, and other methods of offloading (e.g. removable cast and wheelchair use) may be required.

End of life care in patients with diabetes on maintenance haemodialysis

A decision to withdraw from renal replacement therapy is recognised as a common cause of death. Clear guidance for the management of end of life care in these patients is essential in order to support teams (including palliative care) and carers during this difficult time.[13] Diabetes adds to the complexity of care planning for end of life and early liaison with the diabetes specialist team is recommended. Teams need to ensure that patients' wishes are paramount when planning end of life care and that effective communication with the patient, their relatives or carer and primary care physician is in place.

Diabetes medications, including insulin, may be reduced or stopped in some people with type 2 diabetes to avoid hypoglycaemia (but this can lead to diabetic ketoacidosis [DKA] and severe dehydration in people with type 1 diabetes). Glucose monitoring can be minimised to once/day (glycaemic target 6–15 mmol/L without diabetes symptoms), in those receiving insulin treatments and is only used to rule out hypoglycaemia, hyperosmolar hyperglycaemic state or DKA. The giving of fluids is entirely the choice of the patient or carer.

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Acknowledgements

A medical writer (Dr Mike Gwilt, GT Communications) provided editorial assistance (free of charge) in editing this guideline. Versions of this article will appear in Br J Diabetes and Diabet Med, reflecting funding of JBDS by the Association of British Clinical Diabetologists and Diabetes UK, respectively.