

Diabetes Mellitus type 2: Management and follow up in Primary Health Care Center, Review Article

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Abstract

Diabetes mellitus is a worldwide epidemic, affecting around half a billion patients and these numbers are expected to grow within the next few years and decades, Placing a huge burden on the health system worldwide, this is because the chronic hyperglycemic state is associated with multiple long-term complications including micro and macrovascular complications in addition patients may develop acute complications such as Diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state, and hypoglycemia, which all may lead to fatal consequences. Our objective was to look into the literature concerning diabetes management and follow-up in particular type 2 PubMed database was used for articles selection, papers were obtained and reviewed. Management of diabetic patients should be individualized but the main principles of care are to achieve adequate glycemic control, through lifestyle modifications, pharmacological and surgical management, in addition to early identification and modification of cardiovascular risk factors that could contribute to developing atherosclerotic diseases one of the main causes of mortality, in addition to establishing scheduled follow-up appointments to screen for complication through physical examination, history taking and laboratory test.

Keywords: Diabetes mellitus, DM, Management, Follow up, Primary health care

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases that causes affected individuals to have hyperglycemia, this happens due to either a defect in insulin secretion, insulin action, or both [1]. diabetes has become a worldwide epidemic, with astronomical numbers of estimated cases, where type 2 diabetes is responsible for up to 425 million patients, and a death toll of 4 million in 2017 [2], while type 1 diabetes accounts for approximate 9 million affected individuals [3]. And these numbers are only expected to increase by 25% in 2030 and 51% in 2045 [4]. Placing a huge burden on the health system worldwide, especially that Chronic hyperglycemic state can have devastating effects on the human body and are associated with long-term damage and dysfunction, in particular retinopathies, nephropathies, neuropathies, and vascular complications [5], in addition, patients may develop acute complications such as Diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state, and hypoglycemia, which all may lead to fatal consequences [6]. In this review, we will go discuss the management and follow-up for diabetic patients in particularly type 2 diabetes.

MATERIALS AND METHODS

PubMed database was used for articles selection, and the following keys used in the mesh ((diabetes) OR (diabetic)

AND (management)) OR (follow-up)). In regards to the inclusion criteria, the articles were selected based on the inclusion of one of the following topics; diabetes, management, and follow-up. Exclusion criteria were all other articles that did not have one of these topics as their primary endpoint.

Review

Management approach to patients with diabetes has multiple aspects and should be tailored based on individual needs and patients-factors [7], but we will try to summarize and present the general recommendations based on the latest evidence. We can classify the management into 3 broad categories which are glycemic control, prevention of complications, and

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management of short- and long-term complications, we will focus in our discussion on the former two.

Glycemic Control

The cornerstone of management in diabetic patients is proper glycemic control, as data from numerous research have found that the incidence of diabetic complications is directly related to poor glycemic control [8]. Latest recommendations advocate for using glycated hemoglobin (A1C) for glycemic assessment as it is considered a reliable measure of chronic hyperglycemia and a good predictor for long-term diabetes complications [9]. The target goal of glycated hemoglobin level should be individualized, balancing the health benefit on one hand and adverse effects such as hypoglycemic attacks and additional expenses on the other hand. But in general, most young patients without any established complications the recommended goal is <7 percent (53 mmol/mol) [10], to achieve such levels patients should aim and maintain daily Fasting glucose between 80 - 130 mg/dL and postprandial glucose below 180 mg/dL [11], but older patients with limited life expectancy, comorbid conditions or who already have developed complication a less strict control up to 8 percent (64 mmol/mol) or higher is desirable [10].

In newly diagnosed type 2 diabetic patients, blood glucose levels can be managed by a variety of lifestyle changes and non-pharmacological measures including a healthy and balanced diet, physical exercise, weight reduction, and bariatric surgery. In addition to patient education and consultation about self-management and care [12]. If glucose control was inadequate, non-compliance of patients or an initially high A1C pharmacological therapy can be deployed as we will discuss in the next section of the paper.

As for type 1 diabetic patients intensive insulin therapy should be commenced as early as possible in all patients as it has been proven to lower the risk of both micro and macrovascular complication [13, 14], some experts may recommend tighter control of A1C level below 6.5% but there are no long term data to support that, especially that the tighter the control the more chances of side effect which may include financial burden, weight gain and more dreadfully recurrent hypoglycemic attacks that could prove to be fatal [15], both traditional method of insulin administration using multiple daily insulin (MDI) injections and new developed continuous subcutaneous delivery of a rapid-acting insulin preparation via a pump (CSII) achieve similar outcomes and choice is mainly based on personal preferences of patients [16].

Hypoglycemic Medications for Type 2 Diabetes

With a plethora of developed hypoglycemic drugs that are available, making the optimal choice of medication based on each patient's unique characteristic and needs is a difficult task, we will briefly discuss the main pharmacological options to help guide physicians for making the right choice.

Metformin

The recommended initial choice of monotherapy in newly diagnosed type 2 asymptomatic patients, is due to its comparable glycemic control to other medications, weight reducing properties, and reduction of cardiovascular risks [17-19], in addition to being more affordable and with a relatively safer side effect profile, such as fewer hypoglycemic attacks [20]. the full extent of its mechanism of action is still not fully understood but the main effect is inhibiting the gluconeogenesis in the liver, other effects include insulin sensitization and gut alteration but are yet to be fully studied. The most common side effect is GI upset and vitamin B12 deficiency while the most serious is lactate acidosis especially in predisposed patients who suffer from a hepatic impairment, heart failure, and chronic kidney disease (CKD), therefore metformin is contraindicated to be prescribed in patients with eGFR less than 30 mL/min or severe hepatic or cardiac impairment, dosing starts with 500 mg once per day taken in the evening, which could be increased with gradual titration till reaching the maximum dose of 2grams/day [21]. In case of intolerance or inadequate control within 3 months despite reaching maximum dose a second line of therapy could be added.

Sulfonylurea

sulfonylureas are a group of drugs that exert their action on pancreatic β -cells causing a rise in insulin plasma concentrations, in addition to a reduction in insulin hepatic clearance, these drugs are cheap, generally safe, and could be used as monotherapy as a combination, put patient should be educated on possible side effect especially the hypoglycemic attacks and weight gain, therefore they are usually avoided in the elderly who are at high risk of complications if hypoglycemia does occur, additionally they are associated with increased cardiovascular complication and worst prognosis in patients who develop the cardiac event [22].

GLP-1 RA (receptor agonist)

Are a group of analogues similar to the naturally produced GLP-1 hormone, which acts on β Cells leading to increase in insulin production in responses to high glucose levels, additionally it causes a reduction in glucagon release, slowing of gastric emptying, decrease in appetite and mild weight reduction, a key difference between these analogues and the natural hormone is that former is more resistant to degradation by DPP-4 enzymes and thus they exert a more potent action, GLP-1 RA medications are expensive and usually indicated as an add-on therapy in individuals with a co-morbid atherosclerotic disease where there have been found to decrease mortality from CVS complications or with history of recurrent hypoglycemia, but they are not recommended to be used in patients with eGFR <30 mL/min or with history of pancreatitis as they may cause flare-ups, their most prevalent side effects are gastrointestinal complains, a good point to keep in mind that studies have demonstrated no additional benefit was observed when

combined GPP-4 inhibitors and thus such regimen should be avoided [23, 24].

DPP-4 inhibitor

The mechanism of action in these drugs is similar to GLP-1 RA mentioned above, with the difference being in site action where they act on the DPP-4 enzyme inhibiting its breakdown of GLP-1 hormone, and that they produce a milder degree of effect if compared to GLP-1 RA, in addition to being inferior regarding mortality reduction, frequent side effects include respiratory tract infection, skin and musculoskeletal symptoms but don't seem to increase the incidence of pancreatitis. As a result of what's mentioned earlier their use is mainly in patients who develop intolerance or adverse effects to GLP-1 RA [25-27].

Thiazolidinedione

Thiazolidinedione directly decreases insulin resistance, which subsequently causes a decrease in insulin requirement, alteration in adipose tissue distribution, decrease in plasma LDL and free fatty acid concentration, increases in HDL, and decrease in cardiovascular risk factors, henceforth are a good candidate inpatient at risk of cardiovascular events, similar to sulfonylureas they can lead to weight gain, but more commonly edema and fluid overload which could have a catastrophic effect on a patient with heart failure and therefore is generally contraindicated in such patients, other rare side effects include bladder cancer and hepatitis [28].

SGLT2 inhibitor

They act on proximal tubules of the kidney inhibiting glucose transporters and enhancing excretion, due to such mechanism hypoglycemia is a rare complication, also they promote modest weight loss and decline blood pressure, they are a favorable option in patients with heart failure, atherosclerotic disease, and chronic kidney disease with some experts calling it the drug of choice for cardiorenal protection, adverse effects include genitourinary infections, increased risk of fractures, foot amputations, DKA and AKI and henceforth should be avoided in patient with history developing such complications [29, 30].

Insulin Therapy in Type 2 Diabetes

Insulin therapy is recommended to be initiated if A1C level at presentation was $>9\%$ or glycemic control was inadequate despite using optimal treatment [31], it could be used as monotherapy or in conjunction to the previously used oral hypoglycemic medications, but if patient is on Sulfonylureas or Thiazolidine then a change of regimen is warranted to any of the following drugs Metformin, GLP-1 RA, DPP-4 inhibitors, and SGLT2, this occurs mainly due to increased risk of adverse effects chiefly hypoglycemia [32], a good dose to start therapy with is 0.1-0.2 units/per kg/per day of basal or long acting insulin injected early in morning or prior to bedtime insulin dose which is known as augmentation dose, this dose could be titrated gradually by 2 to 4 units/per

week till reaching the desired glycemic control, guided by frequent measures of fasting blood glucose levels [33], if patients don't achieve optimal control despite reaching 0.5 unit/kg then switching to a replacement dose administered through multiple daily injections (MDI) or an insulin pump are both viable options [31], but detailed insulin regimen and options are beyond the scope of this article and won't be discussed here, a crucial points for achieving good outcomes of therapy is patient education, as they should receive a thorough and extensive education on how to monitor their glucose levels, adjusting the dose based on consumed food or physical exercise, healthy and harmful eating habits and what possible side effects they may experience such as weight gain and hypoglycemia, in addition if family members are available they could be involved and taught for example on how to help in cases of hypoglycemic attack [34].

Surgical Management

Numerous researches have demonstrated positive outcomes in an obese patient with type 2 diabetes undergoing bariatric surgical procedures, these effects range from improved glycemic control to the cessation of insulin therapy and full remission for a while, some studies have even shown that surgeries had better glycemic control compared to medical therapy [35]. But not all patients will have such astonishing results and the key point for good outcomes is choosing appropriate candidates for surgery such as a patient with BMI >35 kg/m² [36].

Cardiovascular Risk Reduction

Diabetic patients are more prone to developing atherosclerotic cardiovascular complications which are considered one of the main causes of mortality in this population, therefore a major aspect of treatment is identifying and managing other risk factors of developing CVD, these include smoking cessation and weight reduction, another risk factor to alter is hypertension to maintain blood pressure $<140/90$, but if a patient has an established ASCVD or 10-year ASCVD risk $\geq 15\%$ then a more stringent goal of $<130/80$ is more desirable, if patients have hypertension and associated proteinuria then the prescription of either ACEI or ARBs is recommended, in addition to correction of any dyslipidemia using statins or other lipid-lowering medications, finally patients who have established ASCVD should start using aspirin therapy at a dose of 75–162 mg/day, on the other hand, the use of aspirin as a mean of primary prevention is still debatable and further research need to be conducted [37, 38].

Follow up

As we have discussed through this paper diabetic patients are at risk of developing a wide array of possible complications, therefore the implementation of routine follow-ups and evaluations is necessary for continuous assessment of glycemic control, and early identification and management of any arising complication.

Clinic Visits

A diabetic patient should have at least 2 – 4 appointments per year with their primary care physician, during which the doctor should perform a thorough physical examination with blood pressure measurement and foot examination, additionally, a full history must be taken from patients looking for any symptoms suggesting complications, also physician should counsel their patient regarding weight loss, and smoking cessation, lastly patients need to undergo a dilated eye examination annually performed by an ophthalmologist, but if retinopathy was detected then the frequency of examination should be increased to guide therapy [38].

Laboratory Test

Glycemic control of patient needs to be assessed using A1C level at 6 months intervals assuming good control, but suboptimal glucose level will warrant testing at 3 months increments till adequate control is achieved, moreover lipid profile should be taken as part of initial evaluation and repeated every 5 years if the result were within the desired range, however, if a patient were found to have dyslipidemia then a follow-up test after 1-3 months post-initiation of management is needed and future tests to be done once per year, finally patients are recommended to assess their urinary albumin once yearly if unfortunately urinary albumin was found to be >30 mg/g increasing frequency of testing is needed [38].

CONCLUSION

Management of diabetic patients should be individualized taking into consideration each patient's unique characteristics and needs, but the main principles of care are to achieve and maintain adequate glycemic control through the use of lifestyle modifications, pharmacological and surgical management, in addition to early identification and modification of cardiovascular risk factor such as smoking, hypertension, dyslipidemia and obesity which all could contribute to developing atherosclerotic diseases one of the main causes of mortality, also providing proper patient education and support to aid him in his therapeutic journey, finally to encourage patient to have routinely scheduled follow-up appointments to screen for complication through physical examination, history taking and laboratory test.

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REFERENCES

1. Skyler JS, Bakris GL, Bonifacio E, Darsow T, Eckel RH, Groop L, et al. Differentiation of Diabetes by Pathophysiology, Natural History, and Prognosis. *Diabetes*. 2017;66(2):241-55. doi:10.2337/db16-0806
2. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global Diabetes Prevention Interventions: A Systematic Review and Network Meta-analysis of the Real-World Impact on Incidence, Weight, and Glucose. *Diabetes Care*. 2018;41(7):1526-34. doi:10.2337/dc17-2222
3. Green A, Hede SM, Patterson CC, Wild SH, Imperatore G, Roglic G, et al. Type 1 diabetes in 2017: global estimates of incident and prevalent cases in children and adults. *Diabetologia*. 2021. doi:10.2139/ssrn.3751311
4. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. *Diabetes Res Clin Pract*. 2019;157:107843. doi:10.1016/j.diabres.2019.107843
5. Forbes JM, Cooper ME. Mechanisms of diabetic complications. *Physiol Rev*. 2013;93(1):137-88. doi:10.1152/physrev.00045.2011
6. Fayfman M, Pasquel FJ, Umpierrez GE. Management of Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. *Med Clin North Am*. 2017;101(3):587-606. doi:10.1016/j.mcna.2016.12.011
7. Pfeiffer AF, Klein HH. The treatment of type 2 diabetes. *Dtsch Arztebl Int*. 2014;111(5):69-81.
8. Rodríguez-Gutiérrez R, Montori VM. Glycemic Control for Patients With Type 2 Diabetes Mellitus: Our Evolving Faith in the Face of Evidence. *Circ Cardiovasc Qual Outcomes*. 2016;9(5):504-12. doi:10.1161/CIRCOUTCOMES.116.002901
9. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights*. 2016;11:95-104. doi:10.4137%2FBMIS38440
10. Kirkman MS, Briscoe VJ, Clark N, Florez H, Haas LB, Halter JB, et al. Diabetes in older adults. *Diabetes Care*. 2012;35(12):2650-64. doi:10.2337/dc12-1801
11. Wei N, Zheng H, Nathan DM. Empirically establishing blood glucose targets to achieve HbA1c goals. *Diabetes Care*. 2014;37(4):1048-51. doi:10.2337/dc13-2173
12. Raveendran AV, Chacko EC, Pappachan JM. Non-pharmacological Treatment Options in the Management of Diabetes Mellitus. *Eur Endocrinol*. 2018;14(2):31-9. doi:10.17925/EE.2018.14.2.31
13. Reichard P, Nilsson BY, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. *N Engl J Med*. 1993;329(5):304-9. doi:10.1056/NEJM199307293290502
14. Nathan DM, Bayless M, Cleary P, Genuth S, Gubitosi-Klug R, Lachin JM, et al. Diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: advances and contributions. *Diabetes*. 2013;62(12):3976-86. doi:10.2337/db13-1093
15. Brown RJ, Wijewickrama RC, Harlan DM, Rother KI. Uncoupling intensive insulin therapy from weight gain and hypoglycemia in type 1 diabetes. *Diabetes Technol Ther*. 2011;13(4):457-60. doi:10.1089/dia.2010.0159
16. Pala L, Dicembrini I, Mannucci E. Continuous subcutaneous insulin infusion vs modern multiple injection regimens in type 1 diabetes: an updated meta-analysis of randomized clinical trials. *Acta Diabetol*. 2019;56(9):973-80. doi:10.1007/s00592-019-01326-5
17. Maruthur NM, Tseng E, Hutfless S, Wilson LM, Suarez-Cuervo C, Berger Z, et al. Diabetes Medications as Monotherapy or Metformin-Based Combination Therapy for Type 2 Diabetes: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2016;164(11):740-51. doi:10.7326/M15-2650
18. Yerevanian A, Soukas AA. Metformin: Mechanisms in Human Obesity and Weight Loss. *Curr Obes Rep*. 2019;8(2):156-64. doi:10.1007/s13679-019-00335-3
19. Zhang K, Yang W, Dai H, Deng Z. Cardiovascular risk following metformin treatment in patients with type 2 diabetes mellitus: Results from meta-analysis. *Diabetes Res Clin Pract*. 2020;160:108001. doi:10.1016/j.diabres.2020.108001
20. van Dalem J, Brouwers MC, Stehouwer CD, Krings A, Leufkens HG, Driessen JH, et al. Risk of hypoglycaemia in users of sulphonylureas compared with metformin in relation to renal function and sulphonylurea metabolite group: population based cohort study. *BMJ*. 2016;354:i3625. doi:10.1136/bmj.i3625

21. Flory J, Lipska K. Metformin in 2019. *JAMA*. 2019;321(19):1926-7. doi:10.1001/jama.2019.3805
22. Sola D, Rossi L, Schianca GP, Maffioli P, Bigliocca M, Mella R, et al. Sulfonylureas and their use in clinical practice. *Arch Med Sci*. 2015;11(4):840-8. doi:10.5114/aoms.2015.53304
23. Tran KL, Park YI, Pandya S, Muliyl NJ, Jensen BD, Huynh K, et al. Overview of Glucagon-Like Peptide-1 Receptor Agonists for the Treatment of Patients with Type 2 Diabetes. *Am Health Drug Benefits*. 2017;10(4):178-88.
24. Nauck MA, Kahle M, Baranov O, Deacon CF, Holst JJ. Addition of a dipeptidyl peptidase-4 inhibitor, sitagliptin, to ongoing therapy with the glucagon-like peptide-1 receptor agonist liraglutide: A randomized controlled trial in patients with type 2 diabetes. *Diabetes Obes Metab*. 2017;19(2):200-7. doi:10.1111/dom.12802
25. Zheng SL, Roddick AJ, Aghar-Jaffar R, Shun-Shin MJ, Francis D, Oliver N, et al. Association Between Use of Sodium-Glucose Cotransporter 2 Inhibitors, Glucagon-like Peptide 1 Agonists, and Dipeptidyl Peptidase 4 Inhibitors With All-Cause Mortality in Patients With Type 2 Diabetes: A Systematic Review and Meta-analysis. *JAMA*. 2018;319(15):1580-91. doi:10.1001/jama.2018.3024
26. Brunton S. GLP-1 receptor agonists vs. DPP-4 inhibitors for type 2 diabetes: is one approach more successful or preferable than the other? *Int J Clin Pract*. 2014;68(5):557-67. doi:10.1111/ijcp.12361
27. Richard KR, Shelburne JS, Kirk JK. Tolerability of dipeptidyl peptidase-4 inhibitors: a review. *Clin Ther*. 2011;33(11):1609-29. doi:10.1016/j.clinthera.2011.09.028
28. Lebovitz HE. Thiazolidinediones: the Forgotten Diabetes Medications. *Curr Diab Rep*. 2019;19(12):151. doi:10.1007/s11892-019-1270-y
29. Singh M, Kumar A. Risks Associated with SGLT2 Inhibitors: An Overview. *Curr Drug Saf*. 2018;13(2):84-91. doi:10.2174/1574886313666180226103408
30. Saisho Y. SGLT2 Inhibitors: the Star in the Treatment of Type 2 Diabetes? *Diseases*. 2020;8(2). doi:10.3390/diseases8020014
31. Petznick A. Insulin management of type 2 diabetes mellitus. *Am Fam Physician*. 2011;84(2):183-90.
32. Davies MJ, D'Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, et al. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2018;41(12):2669-701. doi:10.2337/dci18-0033
33. Howard-Thompson A, Khan M, Jones M, George CM. Type 2 Diabetes Mellitus: Outpatient Insulin Management. *Am Fam Physician*. 2018;97(1):29-37.
34. Gagliardino JJ, Aschner P, Baik SH, Chan J, Chantelot JM, Ilkova H, et al. Patients' education, and its impact on care outcomes, resource consumption and working conditions: data from the International Diabetes Management Practices Study (IDMPS). *Diabetes Metab*. 2012;38(2):128-34. doi:10.1016/j.diabet.2011.09.002
35. Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Leccesi L, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med*. 2012;366(17):1577-85. doi:10.1056/NEJMoa1200111
36. Ilyas S, Al-Refai R, Maharjan R, Diaz Bustamante L, Ghattas KN, Khan S. Bariatric Surgery and Type 2 Diabetes Mellitus: Assessing Factors Leading to Remission. A Systematic Review. *Cureus*. 2020;12(8):e9973. doi:10.7759/cureus.9973
37. Capodanno D, Angiolillo DJ. Aspirin for Primary Cardiovascular Risk Prevention and Beyond in Diabetes Mellitus. *Circulation*. 2016;134(20):1579-94. doi:10.1161/CIRCULATIONAHA.116.023164
38. American Diabetes A. Standards of Medical Care in Diabetes-2021 Abridged for Primary Care Providers. *Clin Diabetes*. 2021;39(1):14-43. doi:10.2337/cd21-as01