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Aamir Jalal Al-Mosawi*

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The use of Oral Anti-Diabetic Medications in Diabetes Mellitus type 1: An Educational Article and Expert Opinion

Aamir Jalal Al-Mosawi*

Advisor doctor and expert trainer The National Training and Development Center and Baghdad Medical City

***Corresponding Author:** Aamir Jalal Al-Mosawi, Advisor doctor and expert trainer The National Training and Development Center and Baghdad Medical City

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Abstract

Diabetes mellitus type 1 is lifelong condition resulting from failure of production of insulin because of the loss of pancreatic islet beta-cells because of autoimmune damage. Patients with this type of diabetes need lifelong treatment with insulin to remain alive. Poor diabetic control which predisposes to a variety of complications is not uncommon in patients treated with insulin alone. Therefore, the use of medications that can possibly enhance the therapeutic effect of insulin and reduce the risk of diabetic complications has been considered.

Oral anti-diabetics including acarbose, an inhibitor of intestinal α-glucosidase, metformin, a biguanide, sulfonylureas including glipizide, and sitagliptin, an inhibitor of dipeptidyl peptidase 4 (DPP-4) are primarily used for the treatment of non-insulin dependent diabetes (Type 2).

The aim of this paper is to provide an overview of the use of oral anti-diabetics in the treatment of insulin dependent diabetes (Type 1).

Expert opinion: The current evidence-based expert opinion recommends the judicious use of oral anti-diabetics especially acarbose and metformin in the treatment of unsatisfactorily controlled insulin dependent diabetes type 1. These medications can help in improving diabetic control through reducing glucose levels after meals, and can contribute to lowering the levels of glycosylated hemoglobin (HbA1c). The use of these oral anti-diabetics can also help in reducing insulin requirement.

Key words: diabetes mellitus type 1; oral anti-diabetics; expert opinion

Introduction

Acarbose is first of the inhibitors of intestinal alpha-glucosidase to be introduced as an oral anti-diabetic medication.

In 1983, McCulloch and colleagues reported a double-blind crossover study which included 14 patients with insulin-dependent diabetes who received acarbose, alpha-glucosidase inhibitor for six weeks with the aim preventing nocturnal hypoglycemia.

Six patients received acarbose 200 mg, and mid-evening hypoglycemia in association with severe abdominal colic and flatulence. Eight patients received acarbose 100 mg before the evening meal, and experienced considerable reduction in nocturnal hypoglycemic attacks and midevening hypoglycemia [1].

In 1991, Marena et al reported a placebo-controlled study which included fourteen patients with insulin-dependent diabetes type 1 (insulin-dependent) who had normal weight and poorly controlled hyperglycemia. The patients received either 100 mg acarbose or placebo three times daily for six weeks.

Thereafter, the usual insulin treatment was replaced with an artificial B-cell insulin delivery that was programmed for euglycemia. Acarbose or placebo was continued before meals.

The study showed that acarbose reduced mean blood glucose levels (P=0.002) and HbA1c levels (P below 0.001). Marena et al suggested that acarbose can contribute to a better control of hyperglycemia diabetes type 1 and also help in decreasing insulin requirement [2].

In 1993, Escobar-Jiménez et al reported a multi-center placebo-controlled study which included 137 patients with diabetes type 1 (Insulin-dependent). During the first part of the study (3 months), patients received either acarbose 50 mg three times daily or placebo for one month, and thereafter, they received either acarbose 100 mg three times daily or placebo for two months.

After 1 month of wash out with placebo, the patients received the inverse medication for 3 more months (Second part of the study). The most important side effects were meteorism and flatulence. The use of acarbose was associated with reduction of glycemia after meals (P=0.007), and glycosylated hemoglobin HbA1 (P= 0.0005) [3].

In 1997, Hollander and colleagues reported a multi-center placebo-controlled study which included patients with diabetes type 1 (Insulin-dependent) who treated with either acarbose 50 to 300 mg 3 times daily or placebo for 36 weeks. The use of acarbose reduced mean glucose levels 60 minutes after a test meal 59 mg/dl, and also reduced mean HbA1c levels 0.48%. Acarbose was found to be safe, and the most important side effects included flatulence, abdominal pain, and diarrhea [4].

In 1998, Sels and colleagues reported a multi-center placebo-controlled study which included 62 adults (35 males and 27 females) with diabetes type 1, aged 18-64 years (Mean age: 38 years). Patients received either acarbose 75-300 mg (Mean: 200 mg daily) or placebo. Treatment with acarbose for 8 and 16 reduced glycosylated hemoglobin (HbA1c) levels ($P < 0.001$). Discontinuation of acarbose was associated with an increase of HbA1c levels. Common unwanted effects included flatulence which occurred in 43% of the patients, diarrhea which occurred in 27% of the patients, and abdominal pain which occurred in 11% of the patients.

Sels and colleagues recommended using acarbose up 100 mg three times daily to improve the control diabetes type 1 [5].

In 1999, Riccardi et al from Italy reported a multi-center placebo-controlled study which included 121 patients with unsatisfactorily controlled diabetes mellitus type 1. Patients received acarbose or placebo plus diet high- or low in fiber for 24 weeks. Acarbose was given I am dose of 50 mg three times daily during the first 2 weeks, and 100 mg three times daily during the following weeks.

Compared with placebo, acarbose reduced plasma glucose levels measured two hours after meals ($P < 0.02$). The glucose lowering effect of acarbose was not related to carbohydrate and/or fiber intake. Mild gastrointestinal unwanted effects were reported in 75% of patients who received acarbose, and in 39% of patients who received placebo [6].

In 2000, Juntti-Berggren from Sweden reported a placebo-controlled study which showed that acarbose in a dose of 100 mg can considerably decrease mean insulin requirement in patients with diabetes type 1 over a three-hour period after meals without affecting gastric emptying [7].

In 2012, Yan-rong Ma and colleagues from China reported a study which showed that the addition of acarbose 50 mg to insulin in patients with diabetes type 1 can markedly lessen fluctuations in glucose level and reduce insulin dosage [8].

In 1985, Gin et al reported a placebo-controlled study which included 10 patients with diabetes mellitus type I diabetic who had normal weight. The patients received either metformin 850 mg two times a day or placebo for one week. Metformin improved insulin action by improving glucose uptake 18% (P less than 0.01). The beneficial effects of metformin were attributed to increasing insulin binding to insulin receptors [9].

In 1985, Leblanc et al from France reported a placebo-controlled study which included ten obese patients with poorly controlled insulin requiring diabetes in spite of treatment with large doses of lente insulin given once daily. The showed that the use of metformin 2550 mg daily improved insulin resistance and reduced insulin requirement [10].

In 2001, Lacigová et al reported a placebo-controlled study which included nineteen patients with poorly controlled diabetes type 1 who had insulin resistance. Three months treatment with metformin 850 mg twice daily resulted in an improvement in glycemic control in association with a decrease in insulin requirements ($P < 0.05$) and a decrease in body weight ($P < 0.001$) [11].

In 2002, Ricardo Gómez from the United States and his research group emphasized that metformin can decrease blood glucose by decreasing glucose output from the liver and improving resistance to insulin sensitivity without increasing insulin level.

They conducted a study which included ten adolescents and young adults (4 males, 6 females) with diabetes mellitus type 1. The patients were treated initially with metformin 250 mg twice daily, and the dose was increased to a maximum of 2500 mg daily to achieve an acceptable blood glucose level. Seven of the ten patients experienced a mean reduction in glycosylated hemoglobin (HbA1c) of 11% from before metformin treatment [12].

Also in 2002, Laurent Meyer and his research group from France reported a placebo-controlled study which included 62 patients (37 males and 25 females) who had diabetes mellitus type 1. Metformin treatment 850 mg twice daily was associated with a lower insulin requirement compared with an increased insulin requirements in patients who received placebo ($P = 0.0043$).

Metformin treatment was also associated with marked lowering of total cholesterol ($P = 0.04$) and LDL cholesterol ($P = 0.05$).

Three patients stopped metformin because of the occurrence of abdominal pain and diarrhea.

Milder gastrointestinal unwanted effects also occurred in eight patients who received metformin and two patients who received placebo ($P = 0.069$).

Laurent Meyer and his research group considered metformin to be safe, and has a beneficial insulin-sparing effect in diabetes type 1[13].

In 2003, Jill Hamilton from Canada and her research group reported a 3-month placebo-controlled study which included 27 adolescents with diabetes type 1 with high insulin daily requirement more than 1 unit/ kg (plus/minus 1), and high glycosylated hemoglobin (HbA1c >8%). Treatment with metformin decreased insulin requirement and also reduced HbA1c 0.6% more than in the placebo group ($P < 0.05$). Treatment with metformin considerably improved fasting blood glucose levels ($P < 0.05$). Mild hypoglycemia was reported more frequently in patients treated with metformin than in patients who received placebo ($P = 0.03$) [14].

Also in 2003, Stefan Särnblad from Sweden and his colleagues reported a 3-month placebo-controlled study which included 26 adolescents with diabetes type 1 (8 males and 18 females) with high insulin daily requirement more than 1.2 unit/ kg (plus/minus 0.3), and high glycosylated hemoglobin levels (HbA1c about 9.5%). The patients received either metformin or placebo. Metformin treatment considerably reduced glycosylated hemoglobin from 9.6 to 8.7% ($P<0.05$). Patients who received placebo didn't experience a change in glycosylated hemoglobin levels. Metformin associated improvement in metabolic control was attributed to augmenting glucose uptake by insulin [15].

In 2015, Cong Liu from China and his colleagues conducted a meta-analysis which included 8 published randomized controlled trials studies which showed that the use of metformin in diabetes type 1 decreased daily insulin requirement, and weight and improved lipids profile. The use of metformin did not increase risk of hypoglycemia and ketoacidosis. However, gastrointestinal symptoms occurred more with metformin than with placebo [16].

In 2011, Ellis et al from the United States reported a study which included 20 adults with diabetes type 1. Patients received sitagliptin 100 mg daily or placebo for 4 weeks, and then crossed over. The study showed that sitagliptin improved glycemic control. Compared with placebo, **s**itagliptin markedly lowered 2-hour postprandial blood glucose and 24-h glucose control despite reduction in total and prandial insulin dose.

The addition of sitagliptin markedly reduced insulin dose, and considerably lowered glycosylated hemoglobin (HbA1c) levels. The beneficial effects of sitagliptin were attributed to the lowering of the increased postprandial glucagon secretion by increasing glucose-dependent insulinotropic peptide and glucagon-like peptide 1 levels [17].

However, in 2013, Satish K Garg from the United States reported a placebo-controlled study which included 141 patients with diabetes type 1 who received either sitagliptin 100 mg daily or placebo for sixteen weeks. The study showed that sitagliptin had no significant beneficial effects on hyperglycemia, weight and insulin requirement [18].

In 1990, Leblanc et al reported a placebo-controlled study which included nine adults with diabetes mellitus type 1 (insulin dependent) who had normal BMI. Patients were randomized to receive either glipizide15 mg a day or placebo. The study showed that adding glipizide patients with diabetes mellitus type 1 to insulin treatment was not associated with improvement the glycemic control nor resulted in improvement insulin sensitivity [19].

In 1993, Selam et al a study which included 27 patients with recent development of diabetes type 1 who were treated with intensive subcutaneous injections for one month. The insulin was either discontinued or withdrawn and glipizide started. Three patients who had their insulin withdrawn (22%) experienced insulin-free remissions for 10.3 +/- 4.4 and 8.7 +/- 2.6 months, and seven patients who started glipizide (54%) experienced insulin-free remissions for 10.3 +/- 4.4 and 8.7 +/- 2.6 months.

The study suggested that treatment with insulin and glipizide was associated with more remissions than intensive treatment with insulin only. Selam et al thought that glipizide may have affected insulin sensitivity or possibly exerted an immunomodulatory effect [20].

The use of other oral anti-diabetic medications including sodium-glucose co-transporter (SGLT) inhibitors, liraglutide, glibenclamide, and empagliflozin in diabetes type 1 has also been reported [21].

Expert opinion

The current evidence-based expert opinion recommends the judicious use of oral anti-diabetics especially acarbose and metformin in the treatment of unsatisfactorily controlled insulin dependent diabetes type 1. These medications can help in improving diabetic control through reducing glucose levels after meals, and can contribute to lowering the levels of glycosylated hemoglobin (HbA1c). The use of these oral anti-diabetics can also help in reducing insulin requirement.

References

1. McCulloch DK, Kurtz AB, Tattersall RB. (1983). A new approach to the treatment of nocturnal hypoglycemia using alpha-glucosidase inhibition. Diabetes Care, 6(5):483-487.
2. Marena S, Tagliaferro V, Cavallero G, Pagani A, Montegrosso G, Bianchi W, Zaccarini P, Pagano G. (1991). Double-blind crossover study of acarbose in type 1 diabetic patients. Diabet Med, 8(7):674-678.
3. Escobar-Jiménez F, de Leiva A, Piñón F, Soler J, Tebar J, Sancho MA, Herrera-Pombo JL, Pallardo LF, Vázquez JA, de la Calle H, et al. (1993). Eficacia clínica y tolerancia de la acarbosa en el tratamiento de pacientes diabéticos dependientes de la insulina (tipo I) [Clinical effectiveness and tolerance of acarbose in the treatment of insulin-dependent diabetic patients (type I)]. Med Clin (Barc), 100(13):488-491.
4. Hollander P, Pi-Sunyer X, Coniff RF. (1997). Acarbose in the treatment of type I diabetes. Diabetes Care, 20(3):248-253.
5. Sels JP, Verdonk HE, Wolffenbuttel BH. (1998). Effects of acarbose (Glucobay) in persons with type 1 diabetes: a multicentre study. Diabetes Res Clin Pract 1998 Aug; 41(2):139-145.
6. Riccardi G, Giacco R, Parillo M, Turco S, Rivellese AA, Ventura MR, Contadini S, Marra G, Monteduro M, Santeusanio F, Brunetti P, Librenti MC, Pontiroli AE, Vedani P, Pozza G, Bergamini L, Bianchi C. (1999). Efficacy and safety of acarbose in the treatment of Type 1 diabetes mellitus: a placebo-controlled, double-blind, multicentre study. Diabet Med, 16(3):228-232.
7. Juntti-Berggren L, Pigon J, Hellström P, Holst JJ, Efendic S. (2000). Influence of acarbose on post-prandial insulin requirements in patients with Type 1 diabetes. Diabetes Nutr Metab, 13(1):7-12.
8. Ma YR, Xu YC, Ge JP. (2012). [Improvement in blood glucose fluctuations of insulin-treated type 1 diabetic patients with additional use of acarbose and assessed by continuous blood glucose monitoring program]. Zhonghua Liu Xing Bing Xue Za Zhi, 33(8):854-856.
9. Gin H, Messerchmitt C, Brottier E, Aubertin J. (1985). Metformin improved insulin resistance in type I, insulin-dependent, diabetic patients. Metabolism, 34(10):923-925.
10. Leblanc H, Marre M, Billault B, Passa P. (1987). Intérêt de l'association infusion sous-cutanée d'insuline et metformine chez 10 diabétiques insulino-nécessitants obèses [Value of combined subcutaneous infusion of insulin and metformin in 10 insulin-dependent obese diabetics]. Diabete Metab, 13(6):613-617.
11. Lacigová S, Rusavý Z, Jankovec Z, Kyselová P. (2001). Metformin v léčbě diabetiků 1. typu: placebem kontrolovaná studie [Metformin in the treatment of type 1 diabetics: a placebo-controlled study]. Cas Lek Cesk, 24:140(10):302-306.
12. Gómez R, Mokhashi MH, Rao J, Vargas A, Compton T, McCarter R, Chalew SA. (2002). Metformin adjunctive therapy with insulin improves glycemic control in patients with type 1 diabetes mellitus: a pilot study. J Pediatr Endocrinol Metab 15(8):1147-1151.
13. Meyer L, Bohme P, Delbachian I, Lehert P, Cugnardey N, Drouin P, Guerci B. (2002). The benefits of metformin therapy during continuous subcutaneous insulin infusion treatment of type 1 diabetic patients. Diabetes Care, 25(12):2153-2158.
14. Hamilton J, Cummings E, Zdravkovic V, Finegood D, Daneman D. (2003). Metformin as an adjunct therapy in adolescents with type 1 diabetes and insulin resistance: a randomized controlled trial. Diabetes Care, 26(1):138-143.
15. Särnblad S, Kroon M, Aman J. (2003). Metformin as additional therapy in adolescents with poorly controlled type 1 diabetes: randomised placebo-controlled trial with aspects on insulin sensitivity. Eur J Endocrinol, 149(4):323-329.
16. Liu C, Wu D, Zheng X, Li P, Li L. (2015). Efficacy and safety of metformin for patients with type 1 diabetes mellitus: a meta-analysis. Diabetes Technol Ther 17(2):142-148.
17. Ellis SL, Moser EG, Snell-Bergeon JK, Rodionova AS, Hazenfield RM, Garg SK. (2011). Effect of sitagliptin on glucose control in adult patients with Type 1 diabetes: a pilot, double-blind, randomized, crossover trial. Diabet Med, 28(10):1176-1181.
18. Garg SK, Moser EG, Bode BW, Klaff LJ, Hiatt WR, Beatson C, Snell-Bergeon JK. (2013). Effect of sitagliptin on post-prandial glucagon and GLP-1 levels in patients with type 1 diabetes: investigator-initiated, double-blind, randomized, placebo-controlled trial. Endocr Pract, 19(1):19-28.
19. Leblanc H, Thote A, Chatellier G, Passa P. (1990). Effet du glipizide sur le contrôle glycémique et la sensibilité périphérique à l'insuline chez les diabétiques de type 1 [Effect of glipizide on glycemic control and peripheral insulin sensitivity in type 1 diabetics]. Diabete Metab, 16(2):93-97.

20. Selam JL, Woertz L, Lozano J, Robinson M, Chan E, Charles MA. (1993). The use of glipizide combined with intensive insulin treatment for the induction of remissions in new onset adult type I diabetes. Autoimmunity, 16(4):281-288.
21. Avgerinos I, Manolopoulos A, Michailidis T, Kitsios K, Liakos A, Karagiannis T, Dimitrakopoulos K, Matthews DR, Tsapas A, Bekiari E. (2021). Comparative efficacy and safety of glucose-lowering drugs as adjunctive therapy for adults with type 1 diabetes: A systematic review and network meta-analysis. Diabetes Obes Metab, 23(3): 822-831.


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