Article published online: 2022-07-07

COMMENTARY

Metformin, the Remarkable and Unique Antidiabetic Agent

Abdulfattah Ali Lakhdar

Whipps Cross University Hospital, Barts Health NHS Trust, London, United Kingdom

Corresponding author: Dr. Abdulfattah Lakhdar Email: abdullakhdar@hotmail.com
Published: 01 August 2013
Ibnosina J Med BS 2013;5(4):240-242
Received: 16 December 2012
Accepted: 16 December 2012
This article is available from: http://www.ijmbs.org

Abstract
In the current issue of this *Journal*, Fiad and colleagues thoughtfully reviewed in detail the role of metformin in current clinical practice and highlighted the additional effects of metformin independent of the glycemic action of the drug. The review is comprehensive, up to date and is extensively supported by the literature. Metformin remains the first drug of choice in patients diagnosed with type 2 diabetes. Its vascular protection actions are particularly interesting though not yet fully understood. Its antineoplastic actions are very exciting. The authors clarify the issues of gastrointestinal side effects and renal limitations of its use and give practical ways of minimizing the potential loss of benefit to all treated patients.

Key words: Metformin, Diabetes, Vascular risk, Cancer, Pre-diabetes, Obesity

The current issue of this *journal* publishes a review by Fiad and colleagues on some interesting insights into Metformin therapy (1). The review is comprehensive, up to date and is extensively supported by the literature. The authors thoughtfully reviewed in detail the role of metformin in current clinical practice and highlighted the additional effects of metformin independent of the glycaemic action of the drug.

It is widely accepted now that Metformin is recommended as the drug of first choice in patients diagnosed with type 2 diabetes (both obese and non-obese) (2,3). In particular over the past 20 years, it has evolved as the absolute reference drug to treat this condition. Several potential survival benefits associated with the use of metformin highlighted in recent studies suggest benefits in respect to cardiovascular outcomes along diverse metabolic effects. It counters insulin resistance, lowers blood glucose (4), reduces insulin levels and improves lipid parameters (5) without promoting weight gain. Metformin is believed to

act at multiple sites, including the liver, muscle and gut, in both insulin-dependent and -independent manners (6). The impact of metformin on cardiovascular risk is unequivocal too. Reduced risk of diabetes-related death or myocardial infarction was seen in those receiving metformin when compared with either the intensive or conventional treatment arms in the UKPDS (UK Prospective Diabetes Study Group; 1998 (7) reported an unexpected reduction of 32% in all-cause mortality in the metformin treated patients. Data from numerous larger analyses are also available that supports a cardiovascular benefit with metformin (8,9). Metformin (500-750 mg/day) slowed the progression of carotid intima thickness in type 2 diabetes patients (10). Mechanisms underlying the beneficial effects of metformin on endothelial dysfunction and vascular protection remain partly speculative although long-term benefit from metformin can be due to its anti-glycating properties (11). Metformin use in patients with type 2 diabetes may reduce the risk of cancer and a plausible biological mechanism has been reported (12).

The use of metformin has been limited in patients with renal disease because of the perceived risk of lactic acidosis; however, it is likely that use of this drug would be beneficial in many patients with chronic kidney disease (13). Despite its array of benefits that comparatively outweigh alternative oral anti-glycaemic agents, the ability of clinicians to prescribe metformin is restricted. There are numerous contra-indications and cautions concerning the putative risks of metformin-related side effects that necessitate cessation of metformin. Notably the often stated, yet completely unsubstantiated, heightened risk for development of lactic acidosis in the context of renal insufficiency or a kidney transplant is particularly contentious. Evidence-based medicine begs the performance of well-designed trials to ascertain the safety and efficacy of metformin in these 'high-risk' populations where the benefits of metformin are likely to outweigh any minute risk such as advanced chronic kidney disease. Indeed, accumulated data open potential avenues for larger less prohibitive therapeutic utilisations of Metformin and this is discussed in detail in the accompanying review (1,14).

References

1. Fiad M, Hammadi FH, Al Nuaimi AA, Al Dhohuri JS. Emergening concepts in metformin therapy: Hyperglycmia and beyond. Ibnosina J Med BS 2013;5(4):227-239.
2. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al. Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2012;55:1577-96.
3. Global Guideline for Type 2 Diabetes: recommendations for standard, comprehensive, and minimal care. IDF Clinical Guidelines Task Force.Diabet Med. 2006;23:579-93.
4. Saenz A, Fernandez-Esteban I, Mataix A, Ausejo M, Roque M, Moher D. Metformin monotherapy for type 2 diabetes mellitus. Cochrane Database Syst Rev (3) 2005; CD00 2966.
5. De Fronzo RA, Goodman AM. Efficacy of metformin in patients with non-insulin-dependent diabetes mellitus. The Multicenter Metformin Study Group. N Engl J Med 1995; 333: 541-9.
6. Bailey CJ, Feher M. Diabetes Therapies: Treating Hyperglycaemia. MedEd UK Ltd, Halesowen 2009.
7. UKPDS Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998; 352:854–65.
8. Ekström N, Schiöler L, Svensson AM, Eeg-Olofsson K, Miao Jonasson J, Zethelius B, et al. Effectiveness and safety of metformin in 51 675 patients with type 2 diabetes and different levels of renal function: a cohort study from the Swedish National Diabetes Register. BMJ 2012;Open 2:e001076.
9. Roumie CL, Hung AM, Greevy RA Grijalva CG, Liu X, Murff HJ, Elasy TA, Griffin MR. Comparative effectiveness of sulfonylurea and metformin monotherapy on cardiovascular events in type 2 diabetes mellitus: a cohort study. Ann Intern Med 2012;157:601–10.
10. Matsumoto K, Gera Y, Abe Y, Tominaga T, Yeki Y, and Miyake S. Metformin attenuates progression of carotid arterial wall thickness in patients with type 2 diabetes. Diabetes Res Clin Pract 2004; 64:225-8.
11. Beisswinger P, Ruggiero-Lopez D. Metformin inhibition of glycation process. Diabetes Metab 2003; 29:6S95-6S103.
12. Evans J M, Donnelly L A, Emslie-Smith AM, Alessi D R, Morris AD. Metformin and reduced risk of cancer in diabetic patients. BMJ 2005; 330:1304.
13. Lipska KJ, Bailey CJ, Inzucchi SE.Use of metformin in the setting of mild-to-moderate renal insufficiency. Diabetes Care 2011;34(6):1431-7.

14. Wiernspencer N F. 50 years later: is metformin a vascular drug with antidiabetic properties? Br J Diabetes Vasc Dis 2007:7; 204-10.