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Letter to Editor

Pharmacology Section

Are the Newer Antidiabetic Agents Worth the Cost?

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Type 2 Diabetes Mellitus (T2DM) is a multisystem metabolic disease that requires lifelong medical management. While the burden of T2DM to society can be measured in dollars and rupees, the cost of T2DM to the patient may be immeasurable, reflecting the daily challenges of this chronic disease and uncertain quality of life. Citizens of the 21st century are experiencing a pandemic of T2DM which has motivated development of an armamentarium of new antidiabetic drugs. The new antidiabetic medicines, classified by mechanism of action, include: (i) the glucagon like polypeptide (GLP-1) analogues exenatide and liraglutide; (ii) the renal sodium glucose transport-2 (SGLT-2) inhibitors canagliflozin and dafagliflozin; (iii) the dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin; (iv) the amylin analogue pramlinitide; and (v) the insulin analogues: aspart, lispro, and glargine. The older, conventional antidiabetic medicines such as glibenclamide, glimepiride, metformin, pioglitazone, and the insulin preparations are, largely, much less expensive and therefore more affordable to the diabetic patient than the newer drugs. Furthermore, it is known that patient compliance with antidiabetic treatments, almost exclusively, depends on the direct cost to the patient [1]. This problem of compliance is magnified by the fact that antidiabetic treatments are lifelong and, hence, present the diabetic patient with substantial financial, behavioral and emotional challenges which must be overcome. Another challenge is that patients may not have health insurance, but even if they do, health insurance policies often do not cover drugs for outpatient use.

Zhang et al., analysed the benefits and harms of antihyperglycaemic treatment regimens considering clinical effectiveness, quality of life, and cost. They found that older agents like sulfonylureas were associated with greater benefit in terms of both life-years, quality adjusted life years, and less expensive compared with newer glucose lowering agents like, sitagliptin and exenatide. Monthly medication cost (USD) of metformin 81.75, sulfonylurea 54.85, whereas newer medications like GLP-1 agonist 325.97, DPP-4 inhibitor 232.84 [2].

Limited knowledge of the longterm safety of the newer antidiabetic agents is another important issue. For example, it has been reported that, a 51-year-old woman with longstanding T2DM developed liraglutide induced acute pancreatitis. Her symptoms resolved after withdrawal of this GLP-1 analogue [3]. GLP-1 agonists are contraindicated in patients with histories of pancreatitis, glomerular filtration rate < 30 mL/min, or gastroparesis. Another report demonstrates a significant risk of subclinical pancreatic inflammation, pancreatic cancer, and neuroendocrine tumours in users of exenatide [4]. The DPP-4 inhibitors are commonly associated with nasopharyngitis, headache, and respiratory infections, but pancreatitis, pancreatic cancer, elevation of hepatic enzyme activity; skin reactions and severe joint pain are also reported in users of DPP-4 inhibitors [5]. The SGLT-2 inhibitors are known to cause urinary and genital tract infections, dehydration, and hyperkalaemia. As per a recent report of a 60-year-old man with T2DM treated with glimepiride, metformin, insulin, and canagliflozin developed hypercalcaemia due to intestinal and urinary calcium absorption possibly due to inhibition of SGLT by the canagliflozin [6]. These are but a few examples of why more research is needed to support the safe use of these novel antidiabetic agents. Apart from the financial challenges faced by diabetic patients there is substantial uncertainty about the safety of the newer antidiabetic drugs—newer is not necessarily better.

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