DOI: https://doi.org/10.47391/JPMA.1192

SGLT2 inhibitors: A revolution in therapeutics of a major Non Communicable Disease

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Madam, Pakistan is encountering an ever-increasing burden of non-communicable diseases (NCDs) which is invariably a nightmare for our health care system and economy. According to the statistics of WHO NCD country profile 2018, NCDs, regrettably, causes 58% of deaths in Pakistan among which the leading reported aetiology is cardiovascular diseases (29%) [1]. Nearly 2000 Pakistanis lose their lives every day secondary to a rather preventable non-communicable disease [2]. This premature mortality burden is further worsened by its devastating economic consequences. A recent systemic review regarding the economic impact of NCDs among households in South-Asia has shown that out-of-pocket payments, catastrophic payments and impoverishments are considerably high in households with NCDs, especially cardiovascular diseases, adversely affect the people at all income levels [3]. A study published in the Lancet have foretold that, by 2025, the economic burden due to NCDs in Pakistan will climb up to $296 million [2]. Such cost-intensive and effort-intensive NCDs, particularly chronic heart disease, would warrant any standard optimized treatment improving the health outcomes at a reduced cost. In this regard Sodium glucose co-transporter 2 (SGLT2) inhibitors, a novel class of anti-glycemic drugs, have been tried since 2008 in heart failure patients to probe their effects beyond glycaemic control. McMurray et al[4] led a placebo-controlled phase 3 trial, termed

as DAPA-HF, in which Dapagliflozin, a SGLT2 inhibitor, 10 mg once daily was added to the standard regime of Heart failure patients with reduced ejection fraction (defined as an ejection fraction of less than 40%) independent of diabetes status. The trial enrolled 4744 patients who were randomly allocated to Dapagliflozin or placebo arm. After 18 months of median follow-up, surprisingly, the incidence of deteriorating heart failure and mortality secondary to cardiovascular diseases was considerably fewer in Dapagliflozin group (16.3%) in o placebo (21.2%). Additionally, Dapagliflozin users exhibited a striking improvement in morbidity related outcomes in terms of reducing heart failure hospitalization. [4] In tandem with this, recently, another trial (EMPEROR-reduced), of same design as DAPA-HF, was conducted including 3600 patients to test another SGLT2 inhibitor's efficacy. Empagliflozin (10 mg once daily). Patients enrolled in this trial have an ejection fraction much lower than those in DAPA-HF. After 16-month follow-up, the primary outcome of cardiovascular death or heart failure hospitalization, for Empagliflozin vs. placebo, was 19.4% vs. 24.7% respectively. Moreover, the all-cause mortality for Empagliflozin vs. placebo was 13.4% and 14.2% respectively [5]. These aforementioned findings have maintained that SGLT2 inhibition plays a remarkable therapeutic role in curtailing the risk of death and recurrent hospitalization. Conclusively, these two recent large-scale breakthrough trials have set a landmark in the management of a major non-communicable disease. From these trials, it can be inferred that SGLT2 inhibitors are evidence-based, state-of-the-art therapeutic options which have introduced to the world a new and promising possibility to address not only the adverse outcomes of such a major mortality-bringing NCD but also the huge economic impact, linked to its overall management, on people as well as health care authorities. It's high time, especially in low and middle- income countries, to promote the lucrative effects of this novel intervention among health-care professionals to better optimize the cardiac care and curb the exorbitant health care cost.

Disclaimer: None

Conflict of interest: None to disclose

Funding disclosure: None to disclose

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