Impact of Sodium Glucose Cotransporter-2 inhibitors (SGLT2is) on Health-Related Quality of Life (HRQoL) outcomes in adult patients with Type 2 Diabetes Mellitus (T2DM)

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic condition that is associated with an increased risk of cardiovascular disease and kidney damage. Sodium-glucose co-transporter 2 inhibitors (SGLT2is) are a new family of diabetes medications that block glucose absorption from the proximal tubule of the kidney, resulting in glycosuria. Canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin are the four SGLT2is that are now commercially marketed in various countries.

In the therapeutic treatment of T2DM, SGLT2is are routinely used. Recent research has found that SGLT2is not only reduces blood glucose but also protects the heart and kidney, potentially reducing cardiovascular events, delaying the course of renal failure and significant weight loss, considerably improving patients' quality of life, and lowering medical expenditures for families and society.

OBJECTIVES

The objective of this systematic literature review (SLR) was to evaluate the impact of SGLT2is on HRQoL in patients with T2DM.

METHODS

- Electronic searches on EMBASE and Medline were performed to capture HRQoL evidence in patients receiving SGLT2is published between 2012–2022.
- The protocol was registered on PROSPERO (ID: CRD42022323618).
- Studies reporting HRQoL and treatment satisfaction outcomes using EuroQol-5 Dimension (EQ-5D), short-form 36 or 12 (SF-36/12), Impact of Weight on Quality of life (IWQoL), diabetes therapy-related quality of life (DTR-QoL) and other tools in adults with T2DM, insulin-resistant and non-insulin dependent diabetes receiving SGLT2is were included.

RESULTS

- A total of 46 citations qualified for inclusion in this SLR.
- These included 21 RCTs, (1-21) representing the highest level of evidence in clinical research. *(Fig 1)*

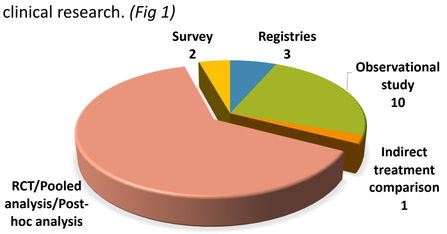

Fig 1: Design of included studies

- Tools used included EQ-5D, EQ-5D visual analogue scale (VAS), SF-36 or SF-12, DTR-QoL, Current Health Satisfaction Questionnaire (CHES-Q), Diabetes Treatment Satisfaction Questionnaire (DTSQ), and IWQoL. *(Fig 2)*
- The most used tool was IWQoL-lite used in 10 publications, (5,16,17,21-27) followed by EQ-5D (2-4,16,18,19,28 29) and CHES-Q in nine. (22,23,26,30-34)

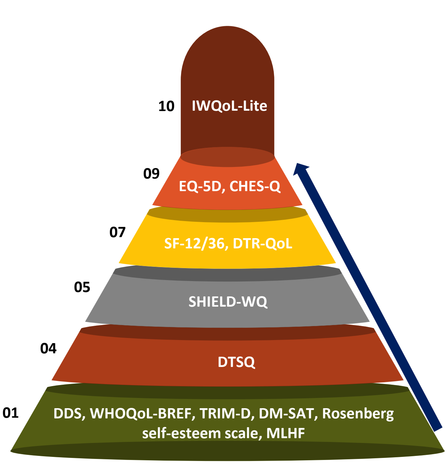

Fig 2: Total Number of publications Employing Assessment Tools

Abbreviations: DDS, Diabetes distress scale; DM-SAT, Diabetes Medications Satisfaction; MLHF; Minnesota Living with Heart Failure Questionnaire; SHIELD-WQ, Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes Weight Questionnaire-9 ; TRIM-D, Treatment Related Impact Measure - Diabetes; WHOQoL-BREF; World Health Organization Quality Of Life Brief Version.

- The most common comparators were placebo, metformin, sulfonylureas, sitagliptin, glimepiride, and insulin.
- Some studies also compared different medication dosages and combinations.
- A total of 16 publications reported data from North America, (2,6, 7,9,10,17,21,23,24,30,32-37) six from Europe, (20,35,36,37,38,28) one each from Asia (22) and Latin America (31) and 13 reported multinational data. (3-5,8,12,15,16,18,25-27,29,42)

Improved HRQoL

- **EQ-5D VAS and index scores showed improvement from baseline, though intergroup differences were not statistically significant.**

RESULTS (cntd)

- Eight of nine publications reported improvements in EQ-5D scores with SGLT2is ± metformin/saxagliptin, with EQ-5D VAS scores increasing from 67.3–74.6 at baseline to 75.3–78.2 at week 24 (p=0.0001). (2-4,15,16,19,28,39) A real-world study comparing sequential order of treatment with three drug classes, i.e., SGLT2i added to glucagon-like peptide-1 (GLP-1) receptor agonists, GLP-1 added to SGLT2is, and GLP-1ras + SGLT2is showed significant improvements in EQ-5D scores from baseline, with mean differences of 5.1, 8.9, and 3.8 points, respectively (p<0.0001). (39)
- SGLT2is were associated with improvements in all SF-36 mental and physical component summary scores at 6, 12, 24, and 36 months. (17,20,23,24,27,41,42)
- In seven studies reporting DTR-QoL, DTR-QoL scores improved in all the studies and were accompanied by reductions in body weight. SGLT2is had a **more** favourable impact on DTR-QoL compared with the comparators. (1,11,13,14,19,43,44)
- All the studies (n=10) reporting data for **canagliflozin and dapagliflozin showed improvements in IWQoL scores at week 24, 26 or 52 as compared to baseline and to comparators including sitagliptin/glimepiride/placebo ± metformin.** Weight loss was associated with improved treatment satisfaction. (5,16,17,21-27)
- **HRQoL was directly proportional to weight loss**, meaning that higher weight loss was associated with better HRQoL and treatment satisfaction with SGLT2is. (45)
- SGLT2is have been shown to have a positive impact on HRQoL outcomes, with **improvements in physical health, self-esteem, emotional health, and overall QoL**. (46)
- The combination of metformin with an SGLT2i was also associated with improvements in HRQoL outcomes. Canagliflozin consistently showed greater positive impacts on HRQoL and work-related QoL compared to other treatments.

No change in HRQoL

- All the parameters improved at follow-up from baseline but the intergroup differences were statistically non-significant.
- There were no significant differences in EQ-5D index scores between patients treated with dapagliflozin plus metformin plus sulfonylurea and placebo at week 24, (4) week 52, (16) and over 102 weeks in EQ-5D index scores. (18)
- Patients with T2DM treated with empagliflozin did not show a significant improvement in DTSQ scale score with regard to perceived hyperglycaemia and perceived hypoglycaemia at all visits from week 28 onward up to the final assessment. (12)

LIMITATIONS & GAPS

- Sample sizes in these studies varied widely from 18 (10) to 9,210, limiting interpretation of the results. (35)
- Most studies didn't consider diabetes duration or complication severity, potentially impacting quality of life assessment.

CONCLUSIONS

- Treatment with SGLT2is enhances diabetes patients' quality of life, particularly in terms of their sense of self and physical health, as it allowed them to have flexible eating habits. This lifestyle shift results in an increase in physical wellness and self-esteem.
- It is important to use both generic and diabetes-specific HRQoL questionnaires to better assess the HRQoL in diabetic patients.
- The choice of glucose-lowering agent can impact treatment goals, and therapies that offer weight loss and avoidance of symptomatic hypoglycaemia can have a positive impact on HRQoL.

Conflict of interest – None declared

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