A real-world experience of a prescribing policy for SGLT2-inhibitors in HFrEF in a Malaysian public tertiary cardiac centre

Vee Sim Yong, MPharm[1,2], Chia How Yen, MD[1,2], Sahrin Saharudin, MD[1,2], Sze Ling Tan, MClinPharm[3], Nor Fadhilah Kaukiah, BSc (Biology)[1,2], Houng Bang Liew, MB BCh BAO[1,4]

[1]Clinical Research Centre, Hospital Queen Elizabeth II, Sabah, Malaysia, [2]Institute for Clinical Research, National Institute of Health (NIH), Malaysia, [3]Pharmacy Department, Hospital Queen Elizabeth II, Malaysia, [4]Cardiology Department, Hospital Queen Elizabeth II, Malaysia

SUMMARY

A prescribing policy for SGLT2-inhibitors was implemented in a local public tertiary cardiology centre in Sabah to improve access for heart failure (HF) patients. The study evaluated 169 HF patients with reduced ejection fraction (HFrEF) who met the policy criteria. After starting SGLT2-inhibitors, a significant proportion of patients experienced decreased NTproBNP levels, indicating a positive response. HF hospitalisation rates within 1 year were lower compared to the previous year. No adverse events were reported, suggesting that the treatment is safe. Findings demonstrates the benefits of implementing prescribing policies to enhance treatment accessibility and generate valuable real-world data at the local healthcare level.

KEYWORDS:
HFrEF, prescribing policy, empagliflozin, SGLT2-inhibitors, real-world

INTRODUCTION

Heart failure (HF) is a chronic and progressive condition that typically represents the end stage of various cardiovascular disorders, with high risk of readmissions and mortality.[1] In Malaysia, hospital admissions due to HF constitute approximately 6 to 10% of all the acute medical admissions.[2] Sodium-glucose cotransporter 2 inhibitors (SGLT2 inhibitors), an antihyperglycemic agent, has emerged as the fourth pillar of Guideline Directed Medical Therapy (GDMT) together with renin-angiotensin system (RAS) inhibitors, beta blockers and mineralocorticoid receptor antagonists (MRA) to reduce the HF burden of readmissions and mortality. However, given that Malaysia's healthcare system is mostly government-funded, introducing new therapy often requires careful planning to maintain a balance.

Malaysia is a part of Southeast-Asia, known for its cultural diversity. Of the estimated population of 33 million, the state of Sabah has the third highest population (10.4%) in Malaysia. The public tertiary cardiac centre in Sabah caters to the state's population, translating to approximately 3.5 million people.

However, access to SGLT2-inhibitors is limited in the public healthcare setting, where resources need to be carefully planned and fully maximised. Careful selection of patients who may reap greater benefit can improve access to this medication. We evaluated the outcome of HF patients prescribed with GDMT and SGLT2-inhibitors in a local public tertiary cardiac centre in Sabah, Malaysia, through the introduction of the centre's prescribing policy for SGLT2-inhibitors in HFrEF. Patient eligibility was determined based on the centre's prescribing policy, which include patients with HFrEF (LVEF ≤40%), optimised on GDMT, either NYHA II and above despite on GDMT, or NTproBNP levels > 600 pg/ml. Patients with eGFR<30 mL/min/1.732, known hypersensitivity to SGLT2-inihibitors, and known history of ketoacidosis were excluded.

In this observational study of patient enrolment from September 2020 to June 2022, 169 HFrEF patients with available records for review were initiated with SGLT2-inhibitors. Their baseline characteristics were analysed (Table I). Mean age was 53.8 year (SD13.02), with 83.43% males. Majority of ethnicity profiles were Sabah-natives (56.8%), Chinese and Malay. Patients were primarily initiated with SGLT2-inhibitor as outpatients (68.05%). Data available from 58 patients in this group showed an average eGFR of 61.358 ml/min/1.73m^2.

There were 33.14% (n = 56) patients with DeNovo HF, while 66.86% (n = 113) had a history of HF for 6 months and above. Common HFrEF aetiologies observed were ischemic cardiomyopathy, and non-ischemic dilated cardiomyopathy. More than 80% had co-morbidities, mainly hypertension, diabetes mellitus, coronary artery disease, dyslipidaemia and atrial fibrillation.

Baseline drug utilisation prior to initiation were also analysed. Majority were optimised on three GDMT drugs (85.8%). Overall, 95.27% patients were on RAS inhibitors (75.15% on ACEi, 10.65% on ARB and 8.88% on ARNi). Beta-blockers were prescribed for 97.6%, while 91.7% were prescribed for MRA.

NTproBNP levels were categorised to < 1000 pg/ml, 1000 to 3000 pg/ml and >3000 pg/ml. From 161 available readings, 62.11% had baseline NTproBNP levels >3000 pg/ml. Within 1 year following SGLT2-inhibitor initiation, 45.9% of these patients showed decreased NTproBNP levels, 10.56% had

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Corresponding Author: Vee Sim Yong
Email: veesim84@gmail.com

Table I: Characteristics of the patients at baseline

Baseline demographics	Total no (%)
Gender	
Male	141(83.43)
Female	28(16.57)
Age (Mean)	53.8(SD 13.02)
Race	
Sabah-native	96(56.8)
Malay	22(13.02)
Chinese	35(20.71)
Others	16(9.47)
NYHA functional class	
I	74(43.79)
II	71(42.01)
III	9(5.33)
IV	15(8.88)
Cause of heart failure	
Ischemic	59(34.9)
Nonischemic	40(23.67)
Valvular heart disease	5(2.96)
Others	18(10.6)
Under investigation	52(30.77)
Co-morbidities	
Hypertension	89(52.5)
Diabetes mellitus	60(35.6)
Coronary artery disease	60(35.6)
Dyslipidemia	44(26.04)
Atrial fibrillation	33(19.53)
Others	18(10.65)
None	31(18.34)
NTproBNP levels (n = 161)	
<1000 pg/ml	14(8.7)
1000 to 3000 pg/ml	47(29.19)
>3000 pg/ml	100(62.1)
Heart failure medication	
RAS inhibitors	16(95.27)
Beta-blocker	165(97.6)
MRA	155(91.7)
Diuretics	104(61.54)

increased levels, while 43.48% lacked a repeat NTproBNP reading. The decrease in NTproBNP seen is consistent with findings from studies showing 5-13% reduction in HFrEF treatment with empagliflozin.[3] [However, a significant number of patients did not have subsequent readings while a minor subset of patients recorded elevated NTproBNP levels following SGLT2-I initiation, but this was not further explored. There were a total 107 patients with 1 year follow-up after SGLT2-inhibitor initiation, and 62 patients who did not attend the 1 year visit. In these 107 patients, 43% reported HFH within a year prior to initiating SGLT2-inhibitors. After SGLT2-inihibitors initiation, HFH within 1 year was reported in 15.9% of these patients. In this group of 107 patients, there were five deaths reported within the year. One was attributed to advanced HF, while the cause of death of the remaining four patients was undocumented.

There were no adverse events reported, suggesting drug safety although this may be under reported in cases where patients sought treatment elsewhere and failed to report the events during their clinic visits.

This communication was intended to describe the implementation strategy of providing empagliflozin to HFrEF patients, through a localised prescribing policy, matching closely to the study population seen in randomised-control trials such as the EMPEROR-REDUCED trial, where participants were above 18 years of age, with NYHA II, III or IV, with LVEF ≤40%, high levels of NTproBNP and receiving all appropriate treatments as available and tolerated.[4] Our findings demonstrate that the use of SGLT2 inhibitors echoes the similar benefits seen in randomised-controlled trials to reduce HF hospitalisation and death within 1 year.

The introduction of new therapies in any healthcare system comes with additional costs for healthcare providers or patients. Affordability, particularly in heavily subsidised public healthcare systems, can pose a barrier to accessing these new therapies, but it can be addressed through further economic evaluations. While treatment guidelines may provide strong evidence for implementing new treatments, barriers continue to exist in real-world practice. Although it may not always be feasible to fully translate new evidence into real-world practice, our findings support the benefits of initiating SGLT2-inhibitors in reducing HF hospitalisations and mortality and highlight the need for careful patient selection through prescribing policies to improve the access to new treatments in real-world practice, eventually benefitting a wider group of patients. Widespread implementation of this prescribing policy can also generate robust real-world,

diverse, Asian data and help inform healthcare policy at the local level.

CONFLICT OF INTEREST

The authors have no financial disclosure or conflicts of interest concerning materials in this article. This study has been approved by the Malaysia's Medical Research and Ethics Committee (NMRR-21-789-59532(IIR)).

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