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Evidences on SGLT2 inhibitors and NOACs and their relevance to the Bhutanese health system

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Sodium-glucose co-transporter 2 (SGLT2) inhibitors have not only antihyperglycemic effects but also reduce the risk of hospitalization for heart failure and reducing worsening of renal functions or death from kidney failure. The EMPEROR-Reduced trial in 2020 showed lower rate of hospitalizations for heart failure (HR = 0.75, 95% CI 0.65 - 0.86, p <0.001) and slower annual rate of decline in estimated glomerular filtration rate (–55 vs –2.28 mL/min/1.73m2 per year, p<0.001) in patients heart failure with reduced ejection fraction[1]. While the DAPA-HF trial in 2019 reported lower risk of worsening heart failure or death from cardiovascular causes[2], the DAPA-CKD trial in 2020 showed that dapagliflozin reduced the risk of worsening kidney function or death from kidney failure (HR = 0.5695% CI 0.45 - 0.68; p<0.0001), hospitalization for heart failure or cardiovascular death (HR = 0.71, 95% CI 0.55–0.92; p=0.0089) in patients with chronic kidney disease with and without type 2 diabetes[3].

Non-vitamin K antagonists such as direct thrombin inhibitors dabigatran, factor Xa inhibitors axpixban, rivaroxaban are now the first line of recommendations for many conditions requiring anticoagulation such as atrial fibrillation and venous thromboembolism[4]. Warfarin has a narrow therapeutic index and is known for frequent and life-threatening complications while International Normalized Ratio monitoring not available in all hospitals in Bhutan. Apart from the sociodemographic and compliance factors, there are well-characterized genetic polymorphism CYP2C9 and VKORC1 genes that influence the rate of warfarin metabolism. Such patients have poor quality of anticoagulation and suboptimal International Normalized Ratios and Time in Therapeutic Range. Warfarin however is indicated for specific conditions such as mechanical heart valves, antiphospholipid syndromes and anticoagulation with comorbid chronic kidney disease. Novel oral anticoagulants on the other hand have lesser rates of complications and require lesser monitoring.

How can such evidences help patients and the health system in Bhutan? Bhutan has a three-tiered health system that guides resource allocation such as the availability of medicines, testing facilities and placement of doctors. Warfarin is available only at the National and Regional Referral Hospitals through the Essential Medicines List 2016[5]. With improved socioeconomic conditions and easier access to transport, many patients bypass the referral system and access health care in tertiary hospitals for diagnosis of conditions and follow up treatment in local hospitals. Doctors are now available in primary level hospitals leading to early diagnosis of medical conditions and prescription of wider ranges of medicines. SGLT2 inhibitors and novel oral anticoagulants may be made available for prescription through the Essential Medicines List at the primary care levels so that patients in rural areas have better disease outcomes in a context where there is relatively lesser resources available for therapeutic monitoring. Newer developments in medical science offers opportunities for improving patient care and treatment outcomes within the context of the Bhutanese health system.

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