ABCD debate at the annual ABCD virtual meeting 18 December 2020

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Motion: This house believes that cardiologists should initiate SGLT-2 inhibitors in patients admitted under cardiology care

Speakers ***For the motion:*** Dr Stephen Wheatcroft, Consultant Cardiologist and Professor of Cardiometabolic Medicine, University of Leeds, West Yorkshire

Against the motion: Professor John Wilding. Department of Cardiovascular and Metabolic Medicine, Institute of Life Course and Medical Sciences, Clinical Sciences Centre, Aintree University Hospital, Liverpool

Introduction

ABCD debates have been a regular feature of the ABCD annual meetings and delegate feedback have previously shown the debate to be a very popular part of the programme. It has always fulfilled the aims and objectives to provide high quality CME to delegates through a light-hearted debate on a suitable topic which is an important component of day-to-day clinical practice.

Format

The format is generally to allow both speakers to present their argument (both for and against) based on evidence, current guidance and pragmatism, to make their case for the audience. The debate generally starts with an introduction from the Chairperson to describe the aims and objectives of the debate and outline the process, which starts with delegates voting for and against the motion, at the outset. This is followed by presentation from an expert, speaking for the motion. Apart from fact checking about the presentation, questions are not allowed at this stage. This is then followed by the speaker against the motion. Audience participation is encouraged during the Q&A session including any astute observations or comments from the floor. Both speakers are then given time to summarise their evidence and recommendation to the participants, followed by another vote to see if the motion is carried or defeated.

Context of the current debate

There has been a plethora of recent trials looking at the cardiovascular outcome trial data for the class of drugs known as sodium-glucose co-transporter 2 (SGLT2) inhibitors.[1–8] Although these started as drugs to manage hyperglycaemia in type 2 diabetes, they have shown improvements in cardiovascular and renal outcomes. Dapagliflozin, one of the SGLT2 inhibitors, is now licensed for heart failure and renal failure with or without diabetes.[9] Given that one of the major aims of treatment of type 2 diabetes is cardiovascular protection, this class of drugs has become a very potent tool in the management of type 2 diabetes. The recent evidence of their benefit in reducing mortality in patients with heart failure means that cardiologists are able to prescribe these drugs. These drugs are associated with a small but serious risk of diabetic ketoacidosis (DKA).[10] The Association of British Clinical Diabetologists (ABCD) has made considerable efforts to ensure these drugs are used by non-diabetologists safely and effectively.[11,12]

Table 1 Salient and evidenced-based reminders about the relationship of diabetes with cardiovascular disease (Professor S Wheatfield)

1	Type 2 diabetes in essence is a cardiovascular disease. Cardiovascular events are a leading cause of mortality in people with diabetes
2	Type 2 diabetes is associated with poorer outcome after an acute myocardial infarction than in people without diabetes and this has not significantly improved over recent years
3	Diabetes is associated with poor outcomes after admission to hospital with acute heart failure
4	People with type 2 diabetes are most likely to see a cardiologist. • The EuroAspire study showed that 27.2% of subjects with coronary artery disease had diabetes • 34% of people admitted to hospital with heart failure in England and Wales had type 2 diabetes
5	We therefore need new therapies and tools to change this particular narrative

Table 2 Benefits of SGLT2 inhibitors in people with type 2 diabetes (summarised by both speakers)

1	This novel class of drugs works on the kidneys and has multiple mechanisms of action, with consequent metabolic and haemodynamic effects on the heart, kidneys, adipose tissue and liver
2	Multiple trials have shown that SGLT2 inhibitors reduce major adverse cardiovascular events and heart failure in people with type 2 diabetes with established cardiovascular disease
3	Reduction in heart failure hospitalisation is also seen in people with diabetes and risk factors for cardiovascular disease and in people with heart failure whether or not they have diabetes
4	The reduction in risk of cardiovascular disease is comparable to early landmark trials with simvastatin (4S Study) and ramipril (HOPE trial)
5	The risk of serious side effects with these agents has been low in published trials
6	The incidence of diabetic ketoacidosis and hypotension is low and it may therefore be safe to start these drugs in the acute setting in those patients who are haemodynamically stable, but there are currently few data to support this

Table 3 How can we maximise the benefit of SGLT2 inhibitors in patients with type 2 diabetes?

1	The hospital setting provides a window of opportunity to start this class of drugs under specialist care
2	The attitudes of UK cardiologists to prescribing these drugs is changing, with more of them aware of the benefits of SGLT2 inhibitors and therefore willing to start these drugs on cardiology wards
3	Cardiologists need to become more aware of the recent published evidence about the benefit of SGLT2 inhibitors in people with and without diabetes
4	Cardiologists should be informed and educated about the safe and appropriate use of this class of drugs
5	The American College of Cardiology in their recent guidance has suggested that these agents should be considered for use in: • Patients with type 2 diabetes and ASCVD • At the time of diagnosis of ASCVD in a patient with type 2 diabetes on a drug regimen that does not currently include a GLP1-RA or SGLT2 inhibitor with proven cardiovascular benefit • At the time of diagnosis of type 2 diabetes in patients with clinical ASCVD • At hospital discharge after admission for an ASCVD- or diabetes-related clinical event

ASCVD, atherosclerotic cardiovascular disease; GLP1-RA, glucagon-like peptide-1 receptor agonist.

That context provided the organisers of the ABCD meeting with an excellent opportunity to set up this debate.

Speaking for the motion

Introducing and speaking for the motion, Professor Wheatcroft, who is an academic and interventional cardiologist at one of the biggest centres in the UK in Leeds, made his case by reminding us of the relationship between type 2 diabetes and cardiovascular disease and by reviewing the benefits of SGLT2 inhibitors (Tables 1 and 2). His reasons that cardiologists should prescribe these drugs in those patients admitted under cardiology are summarised in the Table 3. He reminded the delegates that cardiologists were best placed to prescribe this class of medication, and an inpatient cardiology setting was a perfect opportunity to address this. He asserted that, despite SLGT2 inhibitors being considered primarily as 'diabetes drugs', cardiologists had shown an ample interest and have learnt how to use them in patients with acute coronary syndrome and cardiac failure in cardiology wards. He was concerned that, if the initiation of SGLT2 inhibitors was left to GPs, it will increase primary care workload and, in a large proportion of patients, there will be an unnecessary delay in starting and a reduction in the clinical effectiveness which is seen within the first 6 months of starting this class of drugs. He shared the results of a recent national audit providing evidence to support his argument. Indeed, he was very optimistic that diabetologists and cardiologists could work together to ensure that these drugs are used wisely and in a timely manner for suitable patients.

He summarised his presentation with conclusions that cardiologists now have the right tools to improve outcomes with cardiovascular disease and type 2 diabetes and they are ideally placed for opportunistic initiation of these agents in the highest risk patients. He urged delegates to use guidance developed in collaboration with diabetes colleagues. He stressed that cardiologists, diabetologists, pharmacists and primary care need to work in collaboration for the benefit of patients with type 2 diabetes.

He acknowledged that education and training of patients was an important and significant concern but felt that the cardiology units had the set-up to achieve that, especially when it came to follow-up, particularly during cardiac rehabilitation which has become an established clinical practice in cardiology. In general, he made his point persuasively based on the available evidence and his own clinical practice of having joint clinics involving Cardiology and Diabetes services in Leeds. He acknowledged that this is not yet common practice elsewhere in the UK.

Speaking against the motion

Professor Wilding started his presentation by reviewing the data on the SGLT2 class of drugs in some detail before getting to the crux of the debate. His assertion was that, although he did not disagree with the previous speaker in terms of evidence and benefits of the SGLT2 inhibitors, none of the participants included in any of the trials were inpatients with acute coronary syndrome or heart failure. Evidence in this acute setting was therefore woefully lacking (Table 4). He was of the view that current ongoing trials on the safety of prescribing SGLT2 inhibitors in acute cardiac conditions such as after myocardial infarction or during hospitalisation for heart failure may provide the answer to this question (Table 5). He felt that during management of patients with acute coronary syndrome or cardiac failure, a high proportion of patients can be haemodynamically unstable and may have impaired cardiorenal function. In addition, several of their medications may change with either modification of previous medication or addition of several new drugs. Therefore, adding another agent which can potentially cause diuresis, hypotension and increase the risk of DKA will not be an evidence-based practice and in theory could cause more harm than good. Such a practice could potentially jeopardise the potential benefits from the increased uptake of these medications in the outpatient setting. He stressed that we should await further evidence before making hasty conclusions and changing our clinical practice – a view completely opposite to the speaker for the motion who suggested that we should not waste time and wait for the outcome of trials outlined in Table 5.

The debate

The Q&A session was lively and several clinical issues were raised by audience participation in relation to the use of these agents.

After the Q&A session, both speakers

Table 4 Some limitations of the published trials on SGLT2 inhibitors

1	Published trials to date did not include people with recent myocardial infarction or re-vascularisation
2	These trials also did not include people with acute/unstable heart failure
3	The risk of starting SGLT2 inhibitors in hospitalised patients is unclear and may be greater than seen in published trials
4	The current evidence only supports initiation of these drugs in stable patients in the outpatient setting

Table 5 Ongoing trials related to SGLT2 inhibitors which may have an impact on prescribing in future

1	EMPACT- MI
2	EMPULSE
3	DAPA-MI: Dapagliflozin effects on CV events in patients with acute heart attack
4	DICTATE-AHF: Efficacy and safety of Dapagliflozin in Acute Heart Failure
5	Ertugliflozin in Acute Heart Failure
6	EMPAG-HF: Effect of Empagliflozin on diuresis and renal function in patients with acute decompensated heart failure

Table 6 Vote count before and after the live debate

	Yes (for the motion)	No (against the motion)	Abstain
Before	51%	35%	14%
After	35%	65%	5%

Based on the above vote, the motion was therefore not supported. However, the Chairman acknowledged that this very lively and important debate provided an excellent CME for the delegates, and he closed the session expressing his sincere thanks to both the eminent speakers.

were graceful in acknowledging several excellent and practical issues raised both for and against the use of this class of drug in the acute setting of cardiology wards. The voting at the outset and after the debate is shown in Table 6. The counting of votes showed that several delegates had changed their minds and were now against the motion and therefore the motion was not carried.

The Chairperson remarked that he felt there was no winner or loser in this debate and that both speakers had increased our awareness and raised several issues which will impact on the safe prescribing of these drugs in the future. They both agreed that the advent of these drugs gives us an excellent opportunity to lower the burden of cardiovascular disease in type 2 diabetes in the community and that this was an excellent opportunity for diabetes, cardiology and colleagues in primary care to work together so that no one misses out on the huge benefits shown in several landmark clinical trials.

Acknowledgements

We are extremely grateful to the Red Hot Irons team for providing all the support for this meeting and debate and making available the transcripts of the debate for us to be able to write it up. We thank Professors Stephen Wheatcroft and John Wilding for their valuable comments on the manuscript.

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