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Source / Izvornik: **Diabetology, 2023, 4, 499 - 506**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

https://doi.org/10.3390/diabetology4040043

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:184:297472

diabetology

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Brief Report

Educating Medical Students on How to Prescribe Anti-Hyperglycaemic Drugs: A Practical Guide

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Citation: Donker, E.M.; Belančić, A.; Piët, J.D.; Vitezić, D.; Tichelaar, J.; on behalf of the Clinical Pharmacology and Therapeutics Teach the Teacher (CP4T) Program and the Early Career Pharmacologists of the European Association for Clinical Pharmacology and Therapeutics (EACPT). Educating Medical Students on How to Prescribe Anti-Hyperglycaemic Drugs: A Practical Guide. *Diabetology* **2023**, *4*, 499–506. https://doi.org/10.3390/diabetology4040043

Academic Editor: Peter Clifton

Received: 1 September 2023
Revised: 26 October 2023
Accepted: 3 November 2023
Published: 7 November 2023

Abstract: In the light of the rapidly increasing global incidence of, and therapeutic arsenal for, diabetes type 2, this brief report underscores the need for advancements in clinical pharmacology and therapeutics (CPT) education with regard to diabetes type 2. We advocate for the comprehensive training of medical students and junior doctors in line with current guidelines, and emphasize the importance of teaching how to draw up individualized treatment plans based on patients' specific risk factors and conditions, such as cardiovascular risks, weight, and risk of hypoglycaemia. Within the curriculum, traditional teaching approaches should be replaced by innovative methods such as problem-based learning, which has been shown to be more effective in developing prescribing knowledge and skills. The inclusion of real-world experience and interprofessional learning via so-called student-run clinics is also recommended. Subsequently, innovative assessment methods like the European Prescribing Exam and objective structured clinical examinations (OSCE) are highlighted as essential for evaluating knowledge and practical skills. By adopting these educational advances, medical education can better equip future practitioners to adequately manage the complex pharmacological treatment of diabetes.

Keywords: education; clinical pharmacology and therapeutics; undergraduate; postgraduate

1. Introduction

Diabetes mellitus is a disease with a high global health burden [1]. With the alarming surge in people who are overweight and obese (with the latter encompassing 13% or 650 million people globally), more than 500 million individuals are currently diagnosed with diabetes type 2, and it is estimated that more than 1.3 billion people will have the disease by 2050 [1–3]. Diabetes type 2 is accompanied by a spectrum of associated health complications, such as microvascular (e.g., nephropathy, retinopathy, and neuropathy) and macrovascular diseases [4,5]. These complications significantly diminish patients' quality of life and increase the cost of healthcare, which affects high-, middle-, and low-income nations alike [6]. Consequently, there is an urgent need for better preventive strategies, optimal medicinal interventions, and more effective patient education.

Recent years have seen an increase in the number of therapeutic agents available for diabetes management, such as sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonists. This growing therapeutic arsenal makes prescribing challenging, especially for junior doctors who write out most hospital prescriptions, often without direct supervision [7,8]. Worryingly, studies suggest that junior doctors are responsible for the majority of prescribing errors [7–9], which can in part be explained by their limited prescribing competence early in their career [10–14], which do not improve in the year after graduation [11]. This highlights the need for improved teaching and training in prescribing for both medical students and junior doctors.

In this commentary, we focus on salient aspects of education in clinical pharmacology and therapeutics (CPT) with regard to diabetes type 2, one of the diseases considered essential in prescribing education [15]. We make a plea for efficacious pedagogical and assessment strategies, which may in turn help teaching professionals to update medical curricula, especially CPT modules and internal medicine [16].

2. What to Teach

First, although self-evident, it is essential to underscore the importance of a thorough education on diabetes type 2 and its management with anti-hyperglycaemic agents, based on the most recent (inter)national guidelines and evidence-based medicine, such as the guidelines jointly established by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) [17]. While we will not discuss these aspects further here, it is essential that students have a comprehensive understanding of the aetiology, pathophysiology, diagnostic criteria, evaluation, and potential complications and comorbidities associated with diabetes. Students need to learn that the initial approach to treating diabetes type 2 hinges on lifestyle recommendations, with an emphasis on factors such as physical activity, a balanced diet, weight management, smoking cessation, and limited alcohol consumption [18].

Students must be familiar with the distinct classes of drugs available for the treatment of diabetes (e.g., biguanides, thiazolidinediones, α-glucosidase inhibitors, sulfonylurea derivatives, glinides, SGLT2 inhibitors, DPP-4 inhibitors, GLP-1 receptor agonists, dual GIP and GLP-1 receptor agonists, and insulin). Table 1 gives the key pharmacodynamic attributes of each drug class, highlighting potential benefits/concerns, prevalent or perilous adverse events, and contraindications. Broadly speaking, when prescribing anti-hyperglycaemic agents, prescribers must be cognizant of differences in drug efficacy/effectiveness (where efficacy is based on randomized controlled trial data and effectiveness on real-word experience), particularly with respect to lowering HbA1c levels, fluctuations in weight, and the risk of hypoglycaemia. For example, weight reduction is associated with better outcomes in terms of metabolic and glycaemic control, disease-modifying effects, cardiometabolic disease, and quality of life determinants [19]. Drug–drug interactions are reported in the Summary of Product Characteristics (SmPC) of all individual drugs. In general, two important interactions are those of drugs associated with a high risk of causing hypoglycaemia given in combination with drugs that can mask the symptoms of hypoglycaemia (e.g., the beta-blocker propranolol) or drugs that can worsen glycaemic control (e.g., corticosteroids) [20,21].

Equipped with the foundational knowledge outlined above, students should be able to understand and implement current (local) guidelines. This proficiency should empower them to write specific prescriptions tailored to the individual patient (i.e., desired drug with correct dosage). A pivotal understanding they must internalize is the difference in treatment strategies for patients with or without a high risk of cardiovascular disease. Notably, SGLT2-inhibitors (i.e., empagliflozin and canagliflozin) and GLP-1 receptor agonists (e.g., semaglutide, liraglutide and dulaglutide) have demonstrated additional efficacy in reducing major adverse cardiovascular events (MACE) in patients at high cardiovascular risk (e.g., those with a stroke or myocardial infarction in their medical history) [17]. Fur-

thermore, students should base their decision-making on a comprehensive risk/benefit assessment, selecting the optimal therapeutic strategy tailored to the circumstances of an individual patient, such as treating professional drivers with drugs that carry a low risk of hypoglycaemia, considering alternatives to insulin for patients with a needle phobia, or opting for gliclazide 80 mg extended-release tablets for patients with irregular eating patterns, instead of 30 mg extended-release tablets. Moreover, when the most appropriate drug therapy is chosen, students have to be knowledgeable about what information should be provided to the patient (with or without a consultation with a pharmacist), and what the correct follow-up management approach is. Although beyond the scope of this paper, students should also be taught about the cardiovascular risk factors associated with diabetes and their treatment, such as hypertension (e.g., preferably renin–angiotensin system inhibitors in patient with diabetes) [22], and hypercholesterolemia (e.g., statins) [23].

Table 1. Overview of anti-hyperglycaemic drug classes with potential benefits and risks.

Anti-Hyperglycaemic Class	Pharmacodynamics	Efficacy *	Safety Profile **	Hypoglycaemic Risk	Weight Change ***	Potential Cardio-Renal Benefits	Contraindications/Special Considerations	Costs
Biguanides	- Inhibition of gluconeogenesis and glycogenolysis - Increase in insulin sensitivity - Delay in the absorption of glucose in the small intestine	++	- GI ADRs - Lactic acidosis	Low	↔	MACE: potential benefit	- Acute metabolic acidosis - eGFR < 30 mL/min - Decompensated heart failure, recent myocardial infarction, shock - Hepatic insufficiency	Low
Thiazolidinediones ****	- PPAR-γ activation	++	- Oedema - Congestive heart failure - Hepatogram alteration	Low	↑	MACE: potential benefit HF: increased risk	- (History of) heart failure - Hepatic insufficiency - Existing or recovered bladder cancer	Low
α-gluconidase inhibitors	- Inhibition of intestinal α-glucosidase	+	- GI ADRs	Low	↔	Neutral	- Inflammatory bowel disease - Colon ulceration - Partial bowel obstruction - Hepatic insufficiency - eGFR <30 mL/min	Low
Sulfonylurea derivates	- β-cytotropic drugs (glucose-independent stimulation)	++	- Hypoglycaemia - GI ADRs - Skin and subcutaneous tissue disorders	High	↑	Neutral	- C-peptide negative DM - Hepatic insufficiency - Severe impairment of renal function (≥G3b); does not apply for gliquidone (dose adjustment per renal function not needed)	Low
Glinides	- β-cytotropic drugs (glucose-independent stimulation)	++	- Hypoglycaemia - GI ADRs	Intermediate	↑	Neutral	- C-peptide-negative DM - Hepatic insufficiency	Low
SGLT2 inhibitors	- Competitive inhibition of SGLT2; renal mechanism	+(+)	- Urinary tract infection - Genital infection - Polyuria, pollakisuria, volume depletion - Euglycaemic ketoacidosis (rare) - Fournier gangrene (extremely rare)	Low	↓	MACE: benefit for canagliflozin and empagliflozin HF: benefit for dapagliflozin and empagliflozin DKD: benefit for canagliflozin, dapagliflozin and empagliflozin	- Recurrent urinary infections Considerations: - Euglycaemic ketoacidosis (rare) - Fournier gangrene (extremely rare)	High

Table 1. *Cont.*

Anti-hyperglycaemic Class	Pharmacodynamics	Efficacy *	Safety Profile **	Hypoglycaemic Risk	Weight Change ***	Potential Cardio-Renal Benefits	Contraindications/Special Considerations	Costs
DPP-4 inhibitors	- β-cytotropic drugs (glucose-dependent stimulation); - ↑insulin/glucagon ratio	+	- Very good safety profile and tolerability - ADRs are occasional and not typical	No	↔	HF: potential risk of saxaglitptin	- Consider discontinuation in case of acute pancreatitis	High
GLP-1 receptor agonists	- β-cytotropic drugs (glucose-dependent stimulation); - ↑insulin/glucagon ratio	++(+)	- GI ADRs	No	↓(↓)	MACE: benefit for dulaglutide, liraglutide and semaglutide DKD: potential benefit for dulaglutide, liraglutide, and semaglutide (secondary outcomes)	- Gastroparesis - Consider discontinuation in case of acute pancreatitis	High
Insulin (human and analogues)	- Tyrosine kinase receptor activation	++(+)	- Hypoglycaemia - Lipodystrophy - Somogyi effect - Injection site reactions	High	↑	Neutral	- Injection site reactions - Higher risk of hypoglycaemia with human insulin vs. analogues	High

* + Intermediate (HbA1c↓ 0.5–1.0%), ++ High (HbA1c↓ 1.0–1.5%), +++ Super high (HbA1c↓ >1.5%); ** Check the Summary of Product Characteristics for information regarding individual ADR frequency; *** ↓↓ high loss, ↓ loss, ↔ neutral, ↑ gain; **** Benefit in non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. PPAR-γ Peroxisome proliferator-activated receptor gamma; SGLT2 sodium-glucose cotransporter-2; DPP-4 dipeptidyl peptidase 4; GLP-1 glucagon-like peptide-1; GI gastrointestinal; ADR adverse drug reaction; MACE major adverse cardiovascular events; HF Heart failure; DKD diabetic/chronic kidney disease; eGFR estimated glomerular filtration rate; DM Diabetes Mellitus.

The economic dimensions of care, encompassing both the direct costs of medications and the nuances of national or local health insurance reimbursement, are also important within diabetes education, and students should understand this. The general principle is that newer anti-hyperglycaemic drugs are more expensive than older drugs. In the Netherlands, for example, the cost of one tablet of metformin (500 mg) is EUR 0.02 compared with that of EUR 23.84 for one injection of semaglutide (0.25 mg) [24].

Lastly, students need to learn how to interpret new findings and information. They need to become well versed in the principles of evidence-based medicine and understand the distinctions between primary and secondary outcomes (e.g., secondary outcomes often lack sufficient power). In diabetes research, cardiovascular outcomes (MACEs) have often been a secondary concern, despite the recommendations of the Food and Drug Administration and the European Medicines Agency.

In summary, we advocate that students should be able to draw up an individualized therapeutic strategy for patients with diabetes, with a view to achieving the glycaemic target and reducing the risk of cardiovascular disease. The treatment plan should provide clear information about the medication, its route of administration, correct dosage, and any adjustments made on the basis of renal or hepatic function, patient preferences, age, concurrent health conditions, co-administered drugs, frailty, and cost implications.

3. How to Teach

Traditional teaching methods have focused on lectures and self-study, methods that are still common in European universities [25]. However, emerging pedagogical strategies provide innovative alternatives for teaching and training CPT. For instance, problem-based learning has proven more effective than traditional methods in equipping medical

students with prescribing knowledge and skills [26–29]. The problem-based approach, in combination with the effective World Health Organisation (WHO)'s six-step model which is currently under revision [30–33], is designed to foster active and collaborative learning by situating learning in real-world contexts or problems [34,35]. For instance, students can learn about anti-hyperglycaemic agents in small group-based discussions of real or hypothetical cases. This approach is particularly effective in the bachelor phase [26]. Supplementary Materials File S1 gives an example case that can be used for such discussions. More cases can be found on the European Open Platform for Prescribing Education (https://www.prescribingeducation.eu/, accessed on 6 November 2023) [36].

The learning context is also important for improving educational outcomes [37]. An enriched learning context, such as one incorporating responsibilities for patient care, significantly improves the prescribing competence of medical students. Competence also improves when students move from studying case-based scenarios to analysing real patient records and preparing for therapeutic consultations [38]. Carrying out real-life consultations helps students to refine their prescription writing abilities. While real-life teaching should be available in the master's degree phase at the latest, it is more effective if it is incorporated during the bachelor's degree phase via, for example, so-called student-run clinics (SRC), which have proven effective in increasing the prescribing competence of medical students [39–44]. In SRCs, students have early exposure to prescribing and taking on authentic patient care responsibilities while assisting physicians in their prescribing tasks [45,46]. SRCs for diabetes management are already available in the United States [46–48], and a SRC for cardiovascular risk management has proven beneficial to patients, students, and general practitioners in the Netherlands [43].

Furthermore, we believe that the interprofessional nature of clinical practice should be mirrored in CPT education. Typically, in diabetes management, the healthcare team comprises different professionals, such as physicians, specialist nurses, and pharmacists. Promoting interprofessional learning in (pre-)clinical stages could help students to understand the role of other health professionals, which might facilitate better interprofessional collaboration in the future. SRCs are a feasible way to incorporate this interprofessional learning [41,44].

Lastly, it is essential to assess students' knowledge and skills regarding the safe and effective prescription of anti-hyperglycaemic drugs. This assessment should not only include theoretical knowledge (e.g., contraindications and interactions) but also practical skills, such as the ability to prescribe or conduct therapeutic consultations. Standardized examinations such as the European Prescribing Exam (https://www.prescribingeducation.eu/, accessed on 6 November 2023) are suitable for assessing both knowledge and the ability to prescribe [49], while objective structured clinical examinations (OSCE) can effectively gauge practical skills [50,51]. Diabetes management is one of the eight main topics of the European Prescribing Exam and is assessed on all levels of Miller's pyramid [49]. OSCEs encourage students' deeper understanding of diabetes management and the reasons why they choose a specific drug.

In summary, CPT education must evolve to incorporate problem-based learning, hands-on experience, and interprofessional collaboration. This will help to prepare medical students better for the demands of their future roles, particularly regarding the prescription of critical therapeutics such as anti-hyperglycaemic drugs.

4. Conclusions and Future Direction

In conclusion, CPT education on diabetes management must evolve to align it with current guidelines, to emphasize the need for a comprehensive understanding of the disease, and to encourage students to make tailored treatment plans. Problem-based learning, real-world experience, and interprofessional learning should shape teaching strategies, preparing students to navigate the complexity of prescribing anti-hyperglycaemic agents in clinical practice. Innovative assessment methods, including the European Prescribing Exam and OSCEs, are crucial to the evaluation of knowledge and practical skills. By embracing

these advances, educational institutions can empower (future) healthcare practitioners to effectively manage the pharmacological treatment of diabetes.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/diabetology4040043/s1, File S1: Example case.

Author Contributions: Conceptualization, E.M.D., A.B. and on behalf of the Clinical Pharmacology and Therapeutics Teach the Teacher (CP4T) Program and the Early Career Pharmacologists of the European Association for Clinical Pharmacology and Therapeutics (EACPT); writing—original draft preparation, E.M.D., A.B. and J.D.P.; writing—review and editing, all authors; visualization, E.M.D. and A.B.; supervision, D.V. and J.T. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by Erasmus +, grant number 2022-1-NL01-KA220-HED-000088069.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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