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SGLT2-RECEPTOR INHIBITORS-ASSOCIATED EUGLYCEMIC DIABETIC KETOACIDOSIS IN ONCOSURGICAL PATIENTS IN THE EARLY POSTOPERATIVE PERIOD: A CASE REPORT

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АННОТАЦИЯ

Relevance: *Administration of SGLT2-receptor inhibitors in oncosurgical patients with diabetes mellitus could lead to a formidable complication – the development of euglycemic diabetic ketoacidosis (EDKA) – a specific condition that is difficult to diagnose in a wide range of specialists. The lack of information about this complication and, thus, vigilance due to normal glucose levels complicates early detection of EDCA in surgical patients. Regarding oncosurgical patients, data on the prevalence of SGLT2-associated EDCA in the early postoperative period is limited. The presented clinical case highlights the significant risks of intraoperative surgical stress and prolonged fasting in patients on SGLT2 inhibitor therapy, as well as the difficulties in timely recognition of this condition.*

This paper aimed to *increase the alertness and raise the awareness of clinical specialists about the risk of EDCA development in oncosurgical patients after the administration of SGLT2 inhibitors in the early postoperative period, the importance of timely diagnosis of this condition, and the ways of its treatment, using the example of the described clinical case.*

Methods: *The article describes a clinical case of an oncosurgical patient who developed EDKA in the early postoperative period as a complication of SGLT2 inhibitors administration.*

Results: *In the early postoperative period following the administration of dapagliflozin, the patient developed EDKA, which was successfully managed through adequate hydration with balanced crystalloid solutions, correction of glycemia with intravenous insulin infusion and 10% glucose solutions, and the correction of acid-base and blood electrolytes balance.*

Conclusion: *This clinical case demonstrates the importance of early diagnosis and treatment of EDCA as a rare but dangerous complication of SGLT2 inhibitors in oncosurgical patients.*

Keywords: *euglycemic diabetic ketoacidosis (EDKA), SGLT2 inhibitors, Dapagliflozin.*

Introduction: SGLT2 inhibitors represent a new generation of oral antihyperglycemic agents for treating type 2 diabetes mellitus (T2DM). These medications lower blood glucose levels by inhibiting glucose reabsorption in the proximal renal tubules, thereby promoting glucosuria [1]. They are often preferred due to their cardiovascular and renal protective effects; however, their use has been associated with certain metabolic complications [2]. The most notable – though rare – of these is euglycemic diabetic ketoacidosis (EDKA), a condition that occurs with normal or near-normal blood glucose levels (<13.8 mmol/L or 250 mg/dL). EDKA arises from increased ketone production due to enhanced lipolysis and decreased insulin secretion, typically due to insufficient carbohydrate intake [3]. A similar condition, known as "starvation ketosis," is well-documented in non-diabetic patients. However, this form of ketoacidosis is atypical in diabetes, and normal blood glucose levels can delay diagnosis, leading to an increased risk of metabolic complications [4]. A particularly vulnerable subgroup includes oncology patients with diabetes who are undergoing surgical procedures. The postoperative period is characterized by numerous metabolic stressors, such as fasting, insulin resistance, and surgical stress responses, all of which can accelerate the onset of EDKA in patients taking SGLT2 inhibitors. Delayed recognition of this condition can lead to serious complications, including metabolic acidosis and hemodynamic instability [5]. Therefore, prevention, early detection, and timely management of this complication are crucial to improving patient outcomes [6].

Materials and methods: This article presents a case of euglycemic diabetic ketoacidosis (EDKA) in the early postoperative period in a patient of uro-oncological profile receiving SGLT2 inhibitor therapy. The patient was hospitalized at the Kazakh Institute of Oncology and Radiology (KazIOR), Almaty, Kazakhstan, in 2025. The patient provided signed informed consent for all procedures, as well as for the use of treatment outcomes

for scientific research, educational, academic, and promotional purposes.

Clinical case:

Patient Information: Patient D., a 56-year-old male, was admitted on a scheduled basis with a diagnosis of stage 1 bladder cancer (C-r of the bladder, stage 1). Comorbidities included: Grade 1 arterial hypertension, risk level 4 Type 2 diabetes mellitus (T2DM). The patient was scheduled to undergo transurethral resection of the bladder (TURB). Medical History: The patient had been followed by an endocrinologist for over 10 years for T2DM. Over the past year, he had been taking dapagliflozin (an SGLT2 inhibitor) at a dose of 10 mg/day. An endocrinologist who examined the patient during the pre-hospital phase identified no contraindications to surgery. An outpatient preoperative anesthesiology assessment was conducted at the polyclinic of KazIOR JSC (Almaty, Kazakhstan). The anesthesiologist recommended discontinuing dapagliflozin 72 hours (3 days) prior to surgery. A repeat evaluation was performed after hospital admission, one day before surgery. The anesthesiologist advised the attending physician to monitor and manage glycemic control and fluid balance. The surgical procedure was uneventful, lasting 50 minutes, and was performed under regional anesthesia – spinal anesthesia at the L3 - L4 level using a 27G needle, with 5 mL of 0.5% Bupivacaine Spinal solution.

Clinical Data: Laboratory tests conducted the day before admission revealed blood glucose of 13.5 mmol/L; other parameters were within normal limits. Only 500 mL of a balanced electrolyte solution was administered intravenously during surgery. No intraoperative blood glucose monitoring was performed. Postoperative observation in the recovery room was uneventful, and the patient was transferred to the specialty ward. The next day, routine tests showed 5.8 mmol/L of blood glucose. in the urinalysis, ketonuria was (++) and glucosuria (+). These findings were initially interpreted as a reaction to preoperative fasting. However, the patient's clinical condition deteriorated, with emerging signs of decompensated diabetes, and by the following morning, he was transferred to the intensive care unit (ICU). Further evaluation revealed severe metabolic acidosis, high anion gap due to ketones (28 mEq/L), normal blood glucose (6.4 mmol/L), normal lactate levels, significant glucosuria (++), and marked ketonuria (++++) (Table 1).

Table 1 – Laboratory Tests During Hospitalization

Hospitalization Day	Day 0	TURB* Surgery	Postoperative Day 1	ICU** Day 1	ICU Day 2	ICU Day 3
pH				7.11	7.29	7.41
Glucose (mmol/L)	13.5		5.8	6.4	11.6	5.9
HCO_3				7.6	24.3	29
pCO_2				12.9	46	44.3
Anion Gap				28	10	8
BE***				-24.9	1.3	5.9
Lactate				1.0	0.7	0.6
Ketonuria	abs.	++	+++	++++	+/-	abs.
Glucosuria	abs.	+	++	++	abs.	abs.

*Notes: *TURB – Transurethral Resection of the Bladder; **ICU – Intensive Care Unit; ***BE – Base Excess*

Diagnostics: Initially, the development of ketoacidosis was attributed to hypovolemia, but the patient showed no response to fluid resuscitation. It was further revealed that the patient had consumed almost no food since admission due to a poor appetite, had not maintained proper hydration, and his diabetes was being managed with insulin based on glucose levels alone, without carbohydrate supplementation. This combination of clinical information and laboratory findings led to the suspicion of euglycemic diabetic ketoacidosis (EDKA) in the context of ongoing SGLT2 inhibitor therapy.

Treatment: The patient was started on adequate intravenous fluid therapy using balanced crystalloids, and a continuous intravenous insulin infusion was initiated at a starting dose of 0.1 IU/kg/day. Glycemic levels were closely monitored and corrected accordingly, with a 10% glucose infusion to prevent hypoglycemia. Ongoing monitoring included acid-base balance and electrolyte levels.

Results: Ketoacidosis resolved within 48 hours (see dynamics in Table 1). The patient was subsequently switched to a subcutaneous insulin regimen. No recurrence of EDKA occurred during the remainder of the hospital stay.

The timeline of the clinical case is presented in Table 2.

Table 2 – Clinical Timeline of EDKA in a Uro-oncological Patient on SGLT2 Inhibitor Therapy

Date	Event	Note
14.01.2025	Pre-hospital endocrinology consultation	Type 2 diabetes diagnosed; no contraindications for surgery
17.01.2025	Outpatient preoperative anesthesiology assessment	The patient underwent an anesthesiology consultation, during which discontinuation of dapagliflozin was advised
20.01.2025	Admission – Day 1 of planned hospitalization	Repeat anesthesiology evaluation; 2.5 days since dapagliflozin withdrawal
21.01.2025	TURB* surgery	Duration: 50 minutes Anesthesia: SA**
22.01.2025	Postoperative care in specialty ward	
23.01.2025	Transferred to ICU*** with signs of DM^ decompensation	ICU*** Day 1 - Intensive therapy and monitoring initiated
24.01.2025	ICU*** Day 2	Ongoing intensive care, continuous monitoring, and correction of acid-base status and glycemic control
25.01.2025	ICU*** Day 3	Clinical stabilization; resolution of ketoacidosis; transfer to a ward for further treatment
01.02.2025	Patient discharged	

*Notes: *TURB – Transurethral Resection of the Bladder; **SA – Spinal Anesthesia; ***ICU – Intensive Care Unit; ^DM – Diabetes Mellitus*

Discussion: SGLT2 receptor inhibitors (gliflozins) act on mechanisms in the proximal renal tubules responsible for reabsorbing filtered sodium and glucose. Clinically, this results in reduced blood glucose levels and increased urinary sodium excretion. These agents are widely used for glycemic control in diabetes, reducing cardiovascular event risk in diabetic patients, and treating heart failure. However, alongside their benefits, SGLT2 inhibitors carry risks, including genitourinary infections, acute kidney injury, skeletal fractures, and, notably, ketoacidosis at relatively normal blood glucose levels [7]. Their use also increases perioperative risks, as documented in multiple case reports of EDKA in surgical patients, highlighting the importance of recognizing this class of hypoglycemic agents as a potential perioperative risk factor [8]. In a prospective study involving 759 surgical patients, the incidence of postoperative SGLT2i-induced ketoacidosis was 0% (95% CI: 0 - 0.4%) [9]. Case reports have documented instances of EDKA occurring in the postoperative period. For example, a 58-year-old woman developed EDKA 48 hours after her last dose of empagliflozin and one day post-neurosurgery [10]. In a broader context, a study involving cardiac surgery patients reported a 70.8% incidence of ketoacidosis associated with SGLT2 inhibitor use [11]. However, this high rate may not be directly extrapolatable to populations undergoing cancer surgery due to differing patient characteristics and responses to surgical stress.

Patients undergoing bowel preparation prior to surgery, as well as cancer patients, are often subject to prolonged periods of reduced caloric intake. This can lead to energy depletion and dehydration, particularly when combined with SGLT2 inhibitor therapy. These factors may contribute to the development of EDKA even before the onset of surgical stress [7]. The perioperative period is marked by various physiological disturbances, including dehydration due to fasting, restricted intake, and increased metabolic demand following surgery, all of which favor ketosis. Moreover, surgical stress triggers a catecholamine surge, stimulating gluconeogenesis, lipolysis, and ketogenesis [12]. A normal blood glucose level may mask the onset of EDKA, complicating its early detection. Therefore, clinicians must maintain a high index of suspicion for EDKA in patients on SGLT2 inhibitors [13]. Pre- and postoperative fasting and stress-induced metabolic shifts further exacerbate the ketogenic potential of SGLT2 inhibitors [14]. According to the literature, preoperative discontinuation of SGLT2 inhibitors and careful perioperative monitoring can reduce the risk of developing EDKA; however, the optimal duration of drug withdrawal remains a matter of debate [6]. Current updated guidelines suggest withholding SGLT2 inhibitors for 3-4 days prior to scheduled surgery [7].

Intraoperative management in diabetic patients also requires attention: glucose monitoring, administration of glucose-containing solutions, and insulin therapy are crucial [8].

Continuous blood gas monitoring is essential for early identification and correction of metabolic acidosis. Nutritional support, including adequate carbohydrate intake, is advised to reduce postoperative ketone production [15]. Fluid resuscitation, insulin therapy, and careful ketone monitoring are the cornerstones of both the prevention and management of EDKA in postoperative patients [16]. Educating patients and healthcare providers on early EDKA symptoms — such as nausea, fatigue, and abdominal pain — is vital for timely intervention [4]. Skilled endocrinology consultation in the perioperative setting is crucial for patients on SGLT2 inhibitors undergoing surgery, facilitating prevention, early detection, and appropriate management [8]. A multidisciplinary perioperative ap-

proach involving endocrinologists, anesthesiologists, and surgeons is essential to minimize the risk of this potentially life-threatening complication [17].

Conclusion: The presented clinical case highlights the importance of recognizing EDKA as a potential complication associated with using and discontinuing SGLT2 inhibitors in the days leading up to surgery and during the early postoperative period. It is essential to provide patients with low-dose insulin and carbohydrate support during surgery to suppress ketogenesis, along with close monitoring of laboratory parameters to minimize the risk of EDKA, which can significantly complicate postoperative recovery.

There is a clear need to develop standardized perioperative management protocols for patients with diabetes who are taking SGLT2 inhibitors in order to reduce the risk of EDKA while preserving the therapeutic benefits of these agents in diabetes care. Physician education and patient awareness may also be crucial in preventing or mitigating the consequences of this potentially serious complication.

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АҢДАТПА

ОПЕРАЦИЯДАН КЕЙІНГІ ЕРТЕ КЕЗЕҢДЕ ОНКОХИРУРГИЯЛЫҚ БЕЙІНДЕГІ ПАЦИЕНТТЕРДЕ SGLT2-РЕЦЕПТОРЛАР ИНГИБИТОРЛАРЫМЕН ЕМДЕУ АЯСЫНДА ЭУГЛИКЕМИЯЛЫҚ ДИАБЕТТІК КЕТОАЦИДОЗ: КЛИНИКАЛЫҚ ЖАҒДАЙ

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Өзектілігі: *қант диабетімен ауыратын онкологиялық науқастарға SGLT2 рецепторларының ингибиторларын енгізу ауыр асқынуларға әкелуі мүмкін-эвгликемиялық диабеттік кетоацидоздың (EDKA) дамуы - көптеген мамандарда диагноз*

қою қиын болатын ерекше жағдай. Мұндай асқыну туралы ақпараттың болмауы және сәйкесінше глюкозаның қалыпты деңгейіне байланысты сергектік хирургиялық науқастарда ЭДКА-ны ерте анықтауды қиындатады. Операциядан кейінгі ерте кезеңдегі онкологиялық науқастардың контекстінде SGLT2-мен байланысты EDCA таралуы туралы деректер шектеулі. Біздің клиникалық жағдайымыз SGLT2 ингибиторлық терапиясын қабылдаған емделушілерде операция ішілік хирургиялық стресстің және ұзақ уақыт ораза ұстаудың елеулі қауіптерін, сондай-ақ бұл жағдайды уақтылы танудағы қиындықтарды көрсетеді.

Зерттеудің мақсаты: *SGLT2 тежегіштерін енгізумен байланысты операциядан кейінгі ерте кезеңде онкологиялық науқастарда EDCA даму қаупі туралы клиникалық мамандардың қырағылығы мен хабардарлығын арттыру; осы жағдайды уақтылы диагностикалаудың маңыздылығы, сондай-ақ осы клиникалық жағдай мысалында оны емдеу жолдарын зерттеу.*

Әдістері: *Мақалада операциядан кейінгі ерте КЕЗЕҢДЕ ЭДКА дамыған онкологиялық науқастың клиникалық жағдайы SGLT2 тежегіштерін енгізудің асқынуы ретінде сипатталған.*

Нәтижелері: *Операциядан кейінгі ерте кезеңде дапаглифлозинді қабылдағаннан кейін науқасқа ЕДКА диагнозы қойылды, содан кейін ол теңдестірілген кристаллоидты ерітінділермен адекватты гидратациямен, ішілік инсулинмен және 10% глюкоза ерітіндісімен гликемияны түзетумен, қышқыл-негіз балансын және қан электролиттерін түзету арқылы сәтті емделді.*

Қорытынды: *Біздің клиникалық жағдайымыз онкохирургиялық науқастарда SGLT2 тежегіштерінің сирек, бірақ қауіпті асқынуы ретінде EDCA-ны ерте диагностикалау мен емдеудің маңыздылығын көрсетеді.*

Түйінді сөздер: *эугликемиялық диабеттік кетоацидоз (ЭДКА), SGLT2 ингибиторлары, Дапаглифлозин.*

АННОТАЦИЯ

ЭУГЛИКЕМИЧЕСКИЙ ДИАБЕТИЧЕСКИЙ КЕТОАЦИДОЗ НА ФОНЕ ТЕРАПИИ ИНГИБИТОРАМИ SGLT2-РЕЦЕПТОРОВ У ПАЦИЕНТОВ ОНКОХИРУРГИЧЕСКОГО ПРОФИЛЯ В РАННЕМ ПОСЛЕОПЕРАЦИОННОМ ПЕРИОДЕ: КЛИНИЧЕСКИЙ СЛУЧАЙ

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Актуальность: *Прием ингибиторов SGLT2-рецепторов у пациентов онкохирургических профилей с сахарным диабетом 2 типа может сопровождаться грозным осложнением – развитием эугликемического диабетического кетоацидоза (ЭДКА). Данное специфическое осложнение вызывает трудности в диагностике у многих специалистов. Недостаточная информированность о таком осложнении и, соответственно, отсутствие настороженности из-за нормального уровня глюкозы затрудняет раннее выявление ЭДКА у хирургических пациентов. В отношении онкохирургических пациентов данные о распространенности SGLT2-ассоциированного ЭДКА в раннем послеоперационном периоде ограничены. Представленный клинический случай дополняет объем сведений, подчеркивающих значительные риски, возникающие при интраоперационном хирургическом стрессе и длительном голодании у пациентов с терапией ингибиторами SGLT2, а также трудности своевременного распознавания данного состояния.*

Цель исследования *– повышение настороженности и информированности клинических специалистов о риске развития ЭДКА у онкохирургических пациентов на фоне приема ингибиторов SGLT2 в раннем послеоперационном периоде, важности своевременного диагностирования данного состояния, а также способах его лечения на примере данного клинического случая.*

Методы: *В статье описан случай ЭДКА у пациента онкохирургического профиля в раннем послеоперационном периоде на фоне приема ингибиторов SGLT2.*

Результаты: *В раннем послеоперационном периоде после приема препарата Дапаглифлозин у пациента был диагностирован ЭДКА, который был успешно купирован с помощью адекватной гидратации сбалансированными кристаллоидными растворами, коррекции гликемии внутривенной инфузией инсулина и растворов глюкозы 10%, коррекции кислотно-щелочного баланса и электролитов крови.*

Заключение: *Данный случай демонстрирует важность своевременной диагностики и коррекции ЭДКА как редкого, но опасного осложнения приема ингибиторов SGLT2 у пациентов онкохирургического профиля.*

Ключевые слова: *эугликемический диабетический кетоацидоз (ЭДКА), ингибиторы SGLT2, Дапаглифлозин.*

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