中文題目：服用鈉-葡萄糖共同轉運蛋白 2 抑制劑的第二型糖尿病人由於間歇性斷食引發正常血糖值糖尿病酮酸血症

英文題目：Euglycemic diabetic ketoacidosis precipitated by intermittent fasting in type 2 diabetes treated with sodium-glucose cotransporter 2 inhibitor

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Introduction: The use of sodium-glucose cotransporter 2 (SGLT2) inhibitors grew rapidly in recent years for its advantages of improved cardiovascular and kidney outcomes in type 2 diabetes. However, warnings of increasing risks of euglycemic diabetic ketoacidosis (DKA) had been announced by the U.S. Food and Drug Administration (FDA) in 2015. Here we reported a case of euglycemic DKA precipitated by intermittent fasting in type 2 diabetes treated with SGLT2 inhibitors for about half year and discussed its clinical implications.

Case presentation: A 57-year-old man with type 2 diabetes for about six years, hypertension, and dyslipidemia presented to the emergency rooom with nausea and vomiting for one day. Accompanied symptoms included poor appetite, dyspnea and dysuria. In addition to pioglitazone, glimepiride, and metformin, empagliflozin was prescribed about half year ago as the antidiabetic regimen. The patient's body mass index was 39.6 kg/m^2. His laboratory data at our emergency department revealed metabolic acidosis, with a venous blood gas showing a nadir pH of 7.085, with $HCO3^-$ level of 6.9mmol/L and PCO_2 level of 23.7mmHg. The anion gap was 21.7. The serum ketone level was elevated to 5.8mmol/L (reference range <0.6mmol/L). An urinalysis revealed glycosuria (4+) and ketonuria (4+). His blood sugar level initially was 202mg/dL. He mentioned that he took medications as usual, and started intermittent fasting with reduced carbohydrate intake about two days prior to admission, in the hope to lose body weight. A diagnosis of euglycemic diabetic ketoacidosis was made, presumably related to SGLT2 inhibitor therapy.

Discussion: DKA is characterized by the triad of hyperglycemia, anion gap metabolic acidosis, and ketonemia. The diagnosis of euglycemic DKA could be possibly delayed due to the relatively normal glucose levels (usually meaning plasma glucose <250 mg/dL) at the time of becoming acidemic. SGLT2 inhibitors increase the renal excretion of glucose, thereby lower elevated blood glucose levels, leading to decreased insulin and increased glucagon secretions to promote lipolysis and ketogenesis. The possible precipitating factors include acute illness, such as infection and surgery, reduced oral intake, and reduced insulin dosage. In our case, the patient developed euglycemic DKA about half year after SGLT2 inhibitor use. Because the median time to DKA after initiation of SGLT2 inhibitor was 2 weeks (ranging from 1-175 days), we postulated that reduced carbohydrate intake was the major precipitating factor for the patient to develop euglycemia DKA. For diabetes treated with SGLT2 inhibitor, patients must be educated about the treatment risks and the strategies to prevent these risks.

Conclusion: This case of SGLT2 inhibitor associated euglycemic DKA implicated the clinicians to make precautions to avoid life threatening medical emergencies when prescribing SGLT2 inhibitor.