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Fournier Gangrene Associated With Sodium–Glucose Cotransporter-2 Inhibitors: A Review of Spontaneous Postmarketing Cases

Article, Author, and Disclosure Information

Abstract

Background: Use of sodium–glucose cotransporter-2 (SGLT2) inhibitors has been associated with Fournier gangrene (FG), a rare urologic emergency characterized by necrotizing infection of the external genitalia, perineum, and perianal region.

Objective: To describe and compare reported cases of FG in diabetic adults receiving treatment with SGLT2 inhibitors or other antiglycemic agents.

Design: Descriptive case series.

Setting: U.S. Food and Drug Administration (FDA) Adverse Event Reporting System and published case reports.

Patients: Adults receiving SGLT2 inhibitors or other antiglycemic agents.

Measurements: Clinical and laboratory data.

Results: The FDA identified 55 unique cases of FG in patients receiving SGLT2 inhibitors between 1 March 2013 and 31 January 2019. The patients ranged in age from 33 to 87 years; 39 were men, and 16 were women. Time to onset after

initiation of SGLT2-inhibitor therapy ranged from 5 days to 49 months. All patients had surgical debridement and were severely ill. Reported complications included diabetic ketoacidosis (n = 8), sepsis or septic shock (n = 9), and acute kidney injury (n = 4). Eight patients had fecal diversion surgery, 2 patients developed necrotizing fasciitis of a lower extremity that required amputation, and 1 patient required a lower-extremity bypass procedure because of gangrenous toes. Three patients died. For comparison, the FDA identified 19 FG cases associated with other antiglycemic agents between 1984 and 31 January 2019: metformin (n = 8), insulin glargine (n = 6), short-acting insulin (n = 2), sitagliptin plus metformin (n = 2), and dulaglutide (n = 1). These patients ranged in age from 42 to 79 years; 12 were men, and 7 were women. Two patients died.

Limitation: Inability to establish causality or incidence, variable quality of reports, possible underreporting, and confounding by indication.

Conclusion: FG is a newly identified safety concern in patients receiving SGLT2 inhibitors. Physicians prescribing these agents should be aware of this possible complication and have a high index of suspicion to recognize it in its early stages.

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