

Diabetic Ketoacidosis in Association with Second-Generation Antipsychotics

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INTRODUCTION

Diabetic Ketoacidosis

- DKA is a condition that is primarily seen in patients with type I diabetes and is caused by insufficient insulin levels.
- DKA manifests as rapid onset (<24 hours) abdominal pain, nausea, vomiting, polyuria, polydipsia, volume depletion, and eventually mental status changes and coma.¹
- DKA (and type I diabetes) typically first occur before 20 years old, peaking at 4-6 years and 10-14 years, but may occur at any age.¹

Aripiprazole

- Aripiprazole is a second-generation antipsychotic indicated for bipolar disorder, major depressive disorder, and schizophrenia.²
- It is similar to most second-generation antipsychotics in its adverse metabolic effects of dyslipidemia, hyperglycemia, and weight gain.³

CASE SUMMARY

History of Present Illness:

- 24-year-old black male presents to the Emergency Room with a 1-day history of abdominal pain, nausea and vomiting. He describes the abdominal pain as central before localizing to the left lower quadrant. He has been unable to keep any food down.
- He denies hematochezia, melena, or any changes in bowel habits. Remainder of ROS is negative. Patient states he usually has a morning blood sugar of 315 mg/dL.
- He reports first developing diabetes after 4 months of taking aripiprazole and methylphenidate for mood disorder at the age of 14. The patient was on these medications for 5 months before discontinuation. He was not trialed antipsychotics at any other point.

Social History:

- No illicit substance use

Medications:

- Metformin 1g twice per day

Physical Exam:

- Vitals: T 99.6F, HR 126, RR 22, BP 127/90, SpO2 100% on room air, BMI 23.4
- General: well nourished male in no apparent distress
- HEENT: dry mucous membranes
- Abdomen: scaphoid, nondistended, hypoactive bowel sounds; tenderness to palpation predominantly in the right lower quadrant with referred tenderness from the right upper and left lower quadrant; no rebound; localized peritoneal signs identified.
- Lungs, Heart and Extremities: unremarkable

Laboratory Data:

- CBC: WBC 12.4, absolute neutrophil count 11.0, otherwise WNL
- CMP: sodium 132, calcium 10.4, glucose 439, chloride 92, Bicarb 21
- Blood gas: pH 7.35, venous CO2 42, venous bicarb 23

Imaging:

- CT Abdomen Pelvis W Contrast: Impression - Radiopaque material is seen in the appendix which may be ingested radiopaque material or appendicoliths. The appendix near its base measures up to 12.8 mm and appendicitis should be considered. No abscess or free air. No obstructive uropathy. No bowel obstruction.



Image 1. CT abdomen pelvis with contrast

CLINICAL COURSE

- Two subcutaneous injections of Insulin Aspart U100 are administered to bring patient to an operable status, and patient is brought to the OR on day of admission.
- Laparoscopic appendectomy is performed without complications.
- Appendix pathology showed a markedly dilated appendiceal lumen with large amount of very firm, fecal material which is strictly lodged to occlude the distal 7.5 cm of the lumen.
- Following uncomplicated post-anesthesia care stay, patient is discharged home on the same day of presentation with prescriptions of ibuprofen, acetaminophen, tramadol and docusate. Follow-up appointment is scheduled for 1-2 weeks.
- Approximately 24 hours after discharge, patient returns to Alford ER with complaints of abdominal pain, nausea and vomiting.
- Laboratory results are shown below.
- Patient is admitted to Intensive Care Unit and started on insulin drip and broad-spectrum antibiotics. He is transitioned to subcutaneous Lantus and discharged in good condition after a 4-day hospital stay.
- This was the patient's first hospitalization for diabetic ketoacidosis or hyperglycemic emergency.

Serum Measurement	Value	Reference Range
Sodium	130	135 – 145 mmol/L
Potassium	4.8	3.5 – 4.9 mmol/L
Chloride	96	98 – 112 mmol/L
Bicarbonate	<10	24 – 34 mmol/L
Glucose	457	74 – 106 mg/dL
Ketones	Large	Negative
White Blood Cells	21.4	4.8 – 10.8 K/uL
Lactic Acid	2.9	0.4 – 2.0 mmol/L
Venous pH	7.12	7.32 – 7.42

DISCUSSION

- This case describes a patient, complaining of abdominal pain, who is subsequently diagnosed with appendicitis and diabetic ketoacidosis. The antipsychotic use associated with new onset hyperglycemia, points towards this being a rare adverse complication of aripiprazole.
- While a majority of second-generation antipsychotics are associated with weight gain and development of glucose intolerance, antipsychotic induced hyperglycemic emergencies are rather uncommon (1-2 events per 1000 persons per year of exposure).⁴ However, the incidence of DKA in the population exposed to antipsychotics is tenfold higher relative to the general population.⁴
- Risk factors for antipsychotic associated DKA include average age younger than in general population of patients with diabetes type 2, gender imbalance with predominance of males, absence of autoimmune markers of diabetes, as well as the absence of significant weight gain.⁴
- Conversely, risk factors for development of Type 2 diabetes among this population includes pre-existing diabetes, diagnosis of schizophrenia, male gender, middle age, specific drug combinations, and polypharmacy.⁴
- While hyperglycemia and metabolic syndrome are common adverse effects, the risk of hyperglycemic emergencies precipitated by second generation antipsychotics are rare, but recognized, events.
- Hyperglycemic emergencies need to be considered in all patients starting or continuing second generation antipsychotic therapy, especially with the DKA mortality rate as high as 26% in this demographic.⁵
- This case also illustrates the prolonged effect antipsychotics may have on patients with only a short course of antipsychotics. Similar cases may be undocumented in literature.
- Preventative measures for patients include regular assessment of preexisting risk factors, avoidance of polypharmacy, and regular screening for diabetes in the first months of antipsychotic treatment.⁴

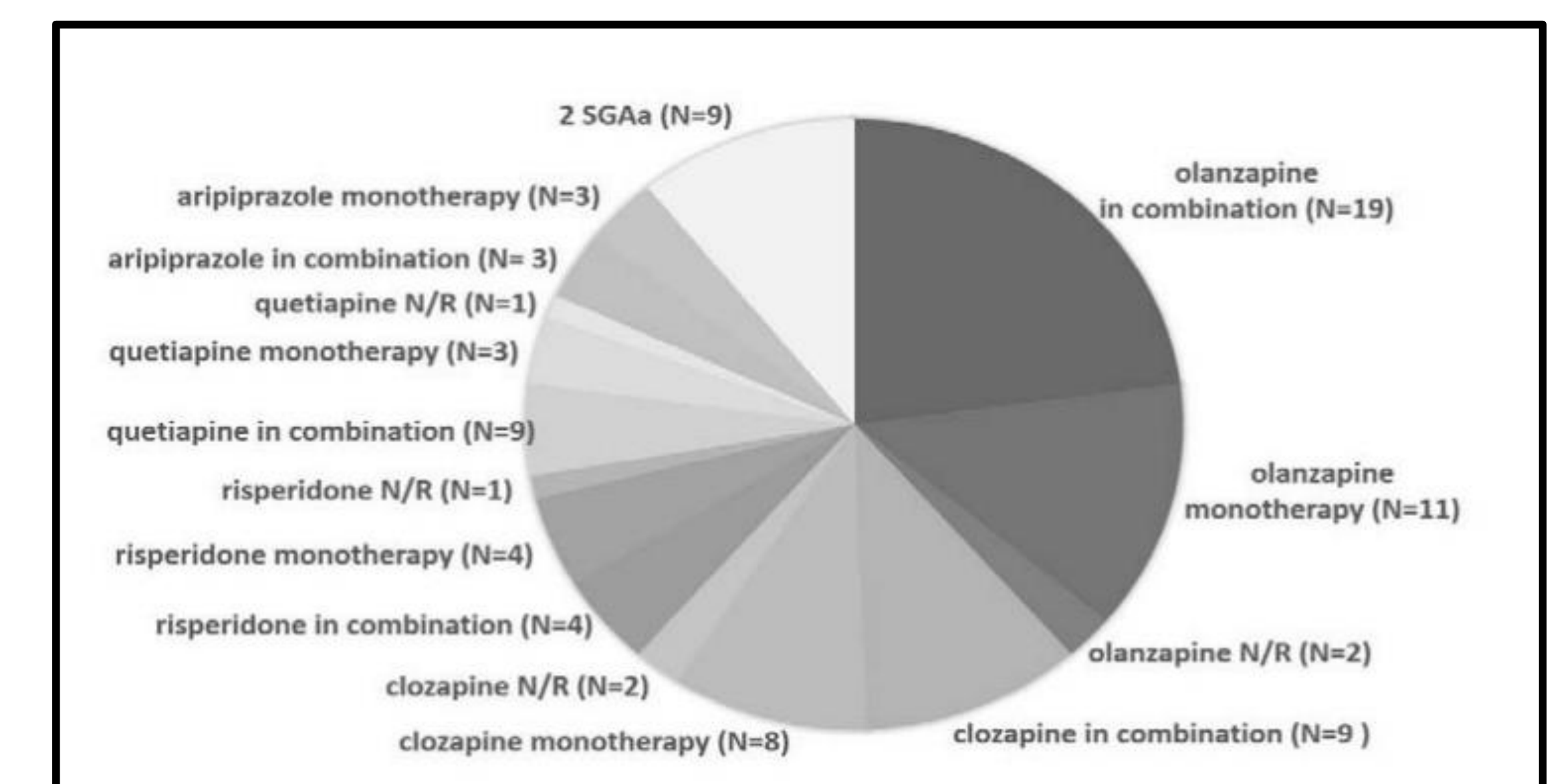


Image 2. Mono- and polypharmacy distribution of DKA cases⁴

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