

# Where is the Gap Coming from?

Myriam C Vela-Ortiz<sup>1,\*</sup>, Yanfang Guan<sup>1</sup>, Sukhminder Singh<sup>1</sup>, Vinay Rupashree<sup>2</sup>, Richard Snyder<sup>2</sup>

<sup>1</sup>Medical Resident, Internal Medicine Residency, Easton Hospital, Department of Medicine

<sup>2</sup>Internal Medicine Residency, Easton Hospital, Department of Medicine

\*Corresponding author: [cristiveo1986@gmail.com](mailto:cristiveo1986@gmail.com)

Received April 26, 2015; Revised July 24, 2015; Accepted July 26, 2015

**Abstract** A 52 year old male with history of alcohol abuse presented to the hospital with metabolic acidosis, he reported consuming a bottle of Listerine for the past two months. On admission he high anion gap and osmolar gap. Given the severe acidosis the patient was started on a bicarbonate drip and also Fomepizole. Later the assays for ethylene glycol and methanol came back negative. Clinicians should have a high index of suspicion for Listerine use and other over the counter products in patients with a history of ethanol abuse, especially when they present with high anion gap and osmolar gap.

**Keywords:** anion gap acidosis, fomepizole, intoxication, listerine, osmolar gap

**Cite This Article:** Myriam C Vela-Ortiz, Yanfang Guan, Sukhminder Singh, Vinay Rupashree, and Richard Snyder, "Where is the Gap Coming from?." *American Journal of Medical Case Reports*, vol. 3, no. 9 (2015): 276-277. doi: 10.12691/ajmcr-3-9-3.

## 1. Background

The presence of a high anion gap metabolic acidosis often requires measurement of the osmolar gap as part of the diagnostic evaluation. The most common etiologies of an elevated gap include methanol and/or ethylene glycol poisoning. Elevation of the osmolar gap in the absence of an elevated anion gap is highly suspicious for isopropyl alcohol ingestion. Other medical conditions such as diabetic ketoacidosis, lactic acidosis, and advanced chronic kidney disease can also produce a less pronounced elevation in the osmolar gap.

We describe a patient who presented with both a significant elevated anion gap and osmolar gap in whom the methanol and ethylene glycol assays were both negative. The elevation in both the anion and osmolar gaps were felt to be due to excessive Listerine consumption. Of note, the patient had a history of chronic Listerine ingestion.

## 2. Case Report

A 52 year old African American male with a history of alcohol abuse presented with nausea and vomiting. He reported consuming a bottle of Listerine daily for the past two months. On admission his vitals were stable. Labs demonstrated a pH of 6.9, pCO<sub>2</sub> 13 mmHg. The sodium was 137 meq/L, potassium 4.6 meq/L, chloride 105 meq/L, carbon dioxide 7 meq/L, BUN 13 mg/dl, creatinine 1.5 mg/dl, and glucose 111 mg/dL. His lactic acid was 16.5 mmol/L, lipase 46 U/L, AST 60 U/L and ethanol level 80 mg/dL. The measured serum osmolality was 352; his calculated osmolality was 296 with an osmolar gap of 56. His anion gap was 31.

The patient was initially started on a continuous bicarbonate infusion. Fomepizole was also administered acutely as there was concern for possible methanol and/or ethylene glycol ingestion. He was admitted to the Intensive Care Unit where he received continued supportive care and resuscitation measures with IV fluids with bicarbonate. The patient's acidosis improved thus avoiding the need for hemodialysis.

His blood work after the noted interventions revealed an improvement in his metabolic parameters including a pH of 7.2 (from 6.9), pCO<sub>2</sub> of 25.5 mmHg from 13 mmHg, base excess - 15.2 from - 26.5, and bicarbonate of 11.6 meq/L from 7 meq/L.

His ethylene glycol and methanol levels were negative.

## 3. Discussion

This case illustrates the need to consider all causes in a patient who presents with a significant metabolic acidosis, high anion gap and also elevated osmolar gap, even after the formula was corrected for alcohol in whom methanol and ethylene glycol levels are negative. The uniqueness of this case lies in the fact that the patient had a significant history of chronic Listerine ingestion. The high anion gap and the elevated osmolar gap were thought to result from the over consumption of Listerine or its components. Although their concentration in Listerine is minimal when compared to the ethanol concentration, there have been case reports of death and cardio pulmonary arrest in the literature related to mouthwash ingestion. Note that the majority of these cases occurred in the pediatric population where the ingestion was mostly accidental rather than a conscious act as in most adults who are searching for the ethanol component of mouthwash. [1,2] In comprehensive literature search, there is only one other

case report in the medical literature of mouthwash ingestion associated with elevated anion gap and osmolar gap not related to alcohol and our case reported here.

We performed a review of the medical literature and found another case report in which a 46 year old white female with a history of schizoaffective disorder and alcohol abuse presented with cardiopulmonary arrest after consuming a large amount of Listerine in an apparent suicide attempt. The patient had a significant metabolic acidosis, elevated anion gap of 42 mEq/L, ethanol level of 125 mg/dL, measured osmolality of 342 mOsm/L, including ethanol was 312 mOsm/L, with a gap of 30 mOsm/L. In this case the laboratory discarded the methanol and ethylene glycol samples. Once extubated and recovered she stated that she frequently drank mouthwash up to five bottles daily. [2] In our case the methanol and ethylene glycol samples were negative but the osmolar Gap remained elevated even when corrected for the ethanol concentration.

It remains unknown whether other Listerine components could account for the elevated osmolar gap. Sorbitol is present in Listerine, and has been proposed to be the etiology for acidosis, but previous studies have shown that sorbitol itself won't increase the anion gap. The reported metabolic side effect from sorbitol use has been hypernatremia, and in theory, sorbitol would elevate the osmolar gap. [3] Minoche et al nonetheless studied the effects of ingested sorbitol and did not find change in the serum osmolality. Here again elevation in sodium and phosphate was described [4].

Menthol is another of Listerine components, but it has not been described as a toxic substance [5].

The concentration of ethanol in Listerine is approximately twenty-seven percent usually making it the main contributor to the osmolar gap. Consumption of large doses of the phenolic compounds such as thymol, eucalyptol, menthol as well as methyl salicylate have been reported in the medical literature to cause a metabolic acidosis while not increasing the osmolar gap [5].

The side effects of methyl salicylate, also present in Listerine have been described. The substance is hydrolyzed to salicylate, and the major side effects of salicylates include gastrointestinal, central nervous system, hematologic, and metabolic acid base disturbances [6].

Thymol, another one of Listerine components, has side effects including gastric pain, nausea, vomiting, central hyperactivity, occasional convulsions, coma, cardiac and respiratory collapse.

Other germicidal and denaturing components such as phenol, present in Listerine could possibly explain the deterioration and laboratory abnormalities seen in our patient, but this has not been described in the literature as of yet.

Clinicians should have a high index of suspicion for Listerine use in anyone with a history of ethanol abuse who present with a high anion gap metabolic acidosis and high osmolar gap. Patients with a history of alcoholism, may try to ingest different substances that contain ethanol and that are not intended for consumption, and other sources besides the well known methanol, isopropyl, and ethylene glycol should be sought and inquired about,

specially when over the counter products like mouthwash are so readily available. [2] Mouthwash ingestion has been observed in settings in which availability for alcoholic beverages might be restricted like in the hospital setting, prisons, or military establishments [1].

Nonalcoholic beverage usage has been described with substances like mouthwash, aftershave lotion and alcohol based fuels. A case series from NBA patients was taken and showed that 10 to 15 % of alcoholic hospitalized patients in detoxification units had consumed NBA, and half of them were regular consumers. [7] Many fatalities have been reported in association with ethanol consumption from a variety of commercial products, which contain high levels of ethyl alcohol but are not designed for consumption, and that are easily purchased, the awareness that alcohol containing products can be fatally abused is essential to detect as an unconventional ethanol source [8].

The metabolic abnormalities present in our patient are thought to be secondary to the chronic ingestion of Listerine, although an acute overconsumption on the day of presentation cannot be ruled out. It has been described in the literature that the occasional or even chronic ingestion of mouthwash would not cause health effects above the effects of ethanol alone. [5]. It is plausible and conclusive that the exposure to mouthwash may cause effects, which are not solely explained by ethanol exposure alone.

#### 4. Educational Paragraph

A high anion gap metabolic acidosis with a high osmolar gap in a patient in whom other toxins like methanol and ethylene glycol are ruled out should raise the suspicion to the consumption of nonalcoholic beverages like Listerine, as it can have life threatening effects, prompt treatment for the acidosis is recommended.

#### References

- [1] Lachenmeier, D.W., et al., What happens if people start drinking mouthwash as surrogate alcohol? A quantitative risk assessment. *Food Chem Toxicol*, 2013. 51: p. 173-8.
- [2] Westermeyer, R.R. and R.N. Terpolilli, Cardiac asystole after mouthwash ingestion: a case report and review of the contents. *Mil Med*, 2001. 166(9): p. 833-5.
- [3] Farley, P.C., K.Y. Lau, and S. Suba, Severe hypernatremia in a patient with psychiatric illness. *Arch Intern Med*, 1986. 146(6): p. 1214-5.
- [4] Minocha, A., et al., Effect of activated charcoal in 70% sorbitol in healthy individuals. *J Toxicol Clin Toxicol*, 1984. 22(6): p. 529-36.
- [5] Dirk W. Lachenmeier , Y.B.M., Mariya Markova , Thomas Kuballa , Jürgen Rehm, What happens if people start drinking mouthwash as surrogate alcohol? A quantitative risk assessment. *Food Chem Toxicol*, 2013. 51: p. 173-178.
- [6] Chan, T.Y., Potential dangers from topical preparations containing methyl salicylate. *Hum Exp Toxicol*, 1996. 15(9): p. 747-50.
- [7] Egbert, A.M., et al., Alcoholics who drink mouthwash: the spectrum of nonbeverage alcohol use. *J Stud Alcohol*, 1985. 46(6): p. 473-81.
- [8] Sperry, K. and R. Pfalzgraf, Fatal ethanol intoxication from household products not intended for ingestion. *J Forensic Sci*, 1990. 35(5): p. 1138-42.