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Case Report

Arginine Induced Metabolic Acidosis and Acute Kidney Injury -

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ABSTRACT

Over the last few years, with the growing date on the internet and social media, patients are moving toward the use of alternative medicine and supplements for various medical conditions. Unfortunately, awareness in terms of side effects and proper dosing is not well known to users. In this case report we present a case were a nurse was using an over the counter supplement to treat her medical condition for years, yet when the desired results were not achieved she overdosed ending up with non-anion gap metabolic acidosis and acute kidney injury requiring admission to intensive care unit and treated with hydration and Sodium Bicarbonate drip.

Keywords: Arginine; Hypertension; Arginine overdose; Acute kidney injury; Non anion gap metabolic acidosis; Hypertension

INTRODUCTION

Over the last few years, with the widespread of data on the internet and the growing use of alternative medicine, Over The Counter (OTC) supplements have been used widely, Arginine (Arg) among which has been used for various medical conditions. Under the appropriate dose and chemical form, it is not toxic to cells [1]. Up until writing this case report, no data was available on what to be considered a safe dose for healthy adults or with various underlying clinical issues. High doses > 9 gm/day are associated with adverse effects in some subjects [2]. On the contrary Arginine, dosing is studied well in the pediatric population with its long history of use with different inborn metabolic diseases.

In this case report, we discuss the case of a middle-aged female who presented with a non-anion gap metabolic acidosis and acute kidney injury secondary to a high dose of Arginine-monohydrochloride (Arg-HCL) corrected shortly with Sodium Bicarb ($NaHCO_3$) infusion and hydration.

CASE PRESENTATION

65 years old female patient with only Hypertension (HTN) as a chronic medical disease, patient self-treated her HTN with OTC Arg supplement for more than 10 years. Initially, the patient reported acceptable results with blood pressure ranges less than 140 mmHg systolic. As a nurse, the patient was self-medicating adjusting her dose as she finds appropriate for achieving the desired goal.

Not followed by an experienced health provider, patient's blood pressure was not properly controlled over the course of the last 3 - 4 years with readings exceeding 160 mmHg systolic. At diagnosis patient was using 5 mg daily, and as her blood pressure was getting uncontrolled she increased her dose gradually, in the last month prior to presentation, she reported using 3 to 4 tablets 3 times per day, making a total of 45 - 60 mg/day yet failed to achieve proper control of blood pressure.

3 days prior to presentation, the patient started to feel progressively weak with decreased energy. On the day of presentation patient presented to work disoriented to time and place with bizarre behavior and inappropriate verbal responses. Upon arrival to ED, Initial vital signs Blood pressure of 154/78, Heart rate 81, Temperature 97.8 oral and saturating 97% on room air, Glasgow-Coma scale 14/15 losing one point for inappropriate verbal responses, otherwise complete physical exam was unremarkable. Lab workup showed a Non-Anion Gap Metabolic acidosis, with elevated Creatinine (Table 1).

Arg overdose revealed from clinical history, the patient received fluid bolus with 2 liters crystalloids and soon after was started on NaHCO3 infusion (150 meq $NaHCO_3$ in 1 Liter Dextrose 5% water at 150 ml/Hr). Patient's general condition improved gradually over the next few hours till completely resolved on day two of admission, the patent was started on Amlodipine for management of her hypertension. General condition continued to improve till normalized both clinically and on lab workup and the patient was discharged on day 3 in good general condition.

DISCUSSION

L-Arginine, available over the counter Amino Acid supplement, used by patients for various medical conditions including but not limited to Congestive Heart Failure (CHF), chest pain, high blood pressure, coronary artery disease, and decreased mental capacity in the elderly (senile dementia), erectile dysfunction and male infertility are also among other uses [3].

Several studies showed that diets rich in proteins help control blood pressure even in patients with high salt intake, Including Dietary Approach to Stop Hypertension (DASH) diet [4,5], Optimal Macronutrient Intake Trial for Heart Health (Omni Heart) [6], Multiple Risk Factor Intervention Trial (MRFIT) [7] and the International Study of Salt and Blood Pressure (INTERSALT) [8] studies, have shown that increased protein intake is associated with a decrease in blood pressure. One component of protein that may explain its antihypertensive properties is arginine.

Experimental and human clinical data suggest that L-Arginine treatment produces a modest decrease in blood pressure in normotensive individuals and individuals with some forms of hypertension [9]. Oral supplementation with L-arginine increases the level of arginine, citrulline, and TAS in patients with mild arterial hypertension. It confirms that increased concentrations of

Table 1: Patient's abnormal lab results on admission and on discharge.

	Admission	Discharge	Reference
pH	7.15↓		7.32 - 7.45
PCO_2	14↓		35 - 45 mmHg
HCO_3	< 5 ↓	27	22 - 24 mmol
creatinine	2.4↑	1.0	0.6 - 1.3 mg/dL
Blood Urea Nitrogen	87↑	40↑	7- 21 mg/dL
Na	137	139	136 - 144 mmol/L
K	3.4↓	3.6	3.6 - 5.1 mmol/L
Anion Gap	14	7	5.5 - 14.6 mmol/L
Phosphorus	1.8	5.3	2.3 - 7 mg/dL
Mg	1.8	2.9↑	1.8 - 2.5 mg/dL
Glucose	123	143↑	70 - 100 mg/dL
Venous Lactate	0.7		< 2.0 mmol/L
Chloride	118↑	105	97 - 107mmol/L

this amino acid lead to a reduction of oxidative stress by stimulating NO biosynthesis helping in control of moderate hypertension [10] (Figure 2).

Arginine is available in different chemical structures, among which is Arg-HCL, HCL group is added to improve solubility, Side effects of supplement are largely related to the HCl group resulting in a rapid drop in pH causing metabolic acidosis leading to hyperkalemia from displacement of intracellular potassium, which was the case in our patient but on the contrary she had hypokalemia [11,12].

Arginine as a cationic amino acid markedly impairs bicarbonate reabsorption in the proximal convoluted tubules, hence inducing proximal renal tubular acidosis with hypophosphatemia without a renal phosphate leak. Infusion of arginine monohydrochloride causes profound impairment of bicarbonate reabsorption, Also the effect of cationic amino acids in HCL generation contribute to overall metabolic acidosis [13].

As noticed from title, acute kidney injury with preserved urine output was diagnosed on basis of Kidney Disease Improving Global Outcomes (KDIGO) guidelines [14], as revealed from history the elevated Creatinine was attributed to combined effect of dehydration and increased production as a by-product from Arg Metabolism, no other cause was clear from encounter, Few casereports attributed acute kidney injury with use of creatine-containing supplements, yet Arg was part of the chemical composition of the supplement but not discussed as direct cause (Figure 1) [3] [14-16].

CONCLUSION

Management is mainly supportive with Intravenous (IV) $NaHCO_3$ and hydration with correction of electrolyte abnormalities, this patient was lucky enough to reverse damage but case reports of fatal dose have been reported in the pediatric population. Proper control and proper understanding of supplement use and doses should be implemented, as so believed innocent can't be fatal.

Data available on potential effects of arginine are directed more towards the effects of arginine infusion rather than dose effects. Effects in the pediatric population are more investigated on contrary to adults with most data available in basic biochemistry literature [17,18].

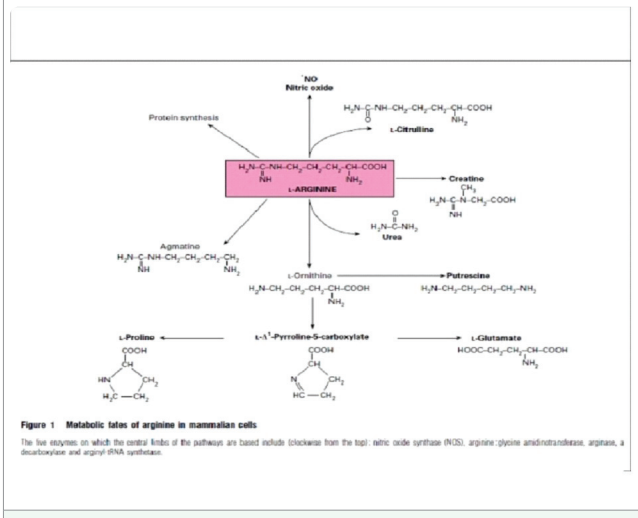

Figure 1 Matabolic fates of arginine in mammalian cells

The five enzymes on which the central limbs of the pathways are based include (clockwise from the top): nitric oxide synthase (NOS), arginine:glycine amidinotransferase, arginase, a decarboxylase and arginyl-tRNA synthetase.

Figure 1:

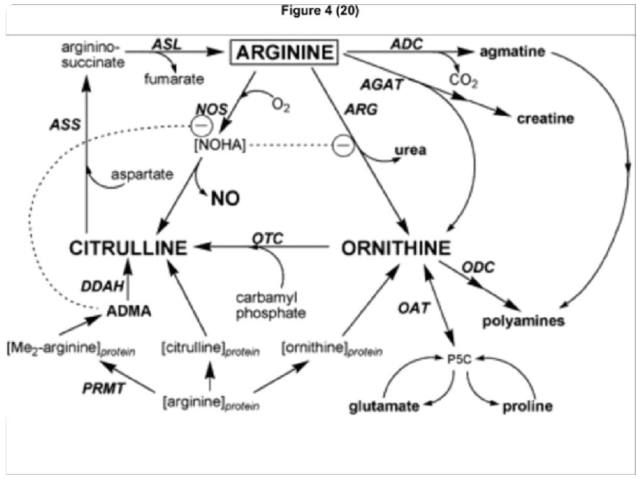

Figure 2:

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