Enteral nutrition formulas with higher oxalate content may contribute to higher oxalate absorption and urinary excretion in patients requiring nutrition support

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Introduction & Objective

Patients requiring oral and/or enteral nutrition support (delivered via nasogastric tube or via direct entry to the stomach or upper intestine) to meet their nutrient needs have a relatively high incidence of calcium oxalate (CaOx) kidney stones

In fact, **evidence suggests the incidence of CaOx stones in this population is higher than in the general population**[1,2]

Dietary oxalate, if excessive, contributes to hyperoxaluria and CaOx stones, especially when:

1. It is unopposed by concomitant calcium intake
2. Gastrointestinal malabsorption is present
3. Oxalate degrading gut bacteria are absent

Enteral nutrition formulas are frequently built up from corn and/or soy, both of which contain ample oxalate; **patients on nutrition support have been observed to have high urinary oxalate excretion**[3]

The oxalate load of enteral nutrition formulas is of interest as patients who rely on nutrition support have limited means to alter their diets and as, depending on energy needs, require a liter or more of formula daily

The oxalate content of enteral nutrition formulas is unknown

OBJECTIVE

We assessed commonly used adult and pediatric enteral nutrition formulas for oxalate content using ion chromatography

Methods

Sample selection. Enteral nutrition formulas were selected from our hospital's adult and pediatric formularies; completely elemental (hydrolyzed) formulas or modular products were excluded

Some formulas were designed for use in tube feeding applications only; others were designed for both oral intake and tube feeding

Sample preparation. 5 mL aliquots of formula were diluted with 5 mL 0.1 M HCl and vortexed for 1 min at room temperature. Each solution was heated for 1 hour in a water bath set at 70ºC. Heated samples were centrifuged for 30 min at 4,000 rpm. Supernatants were filtered and refrigerated until analysis (within 5 days). Samples were prepared in triplicate.

Chromatographic method. Samples were injected into a separation system consisting of a pre-column and an analytical column heated at 45ºC. Mobile phase was $NaHCO_3$ and $NaCO_3$ (1.0 and 3.2 mmol/L, respectively). Flow rate was 0.7 mL/min. Oxalate standards were prepared and used to create a calibration curve (**Figure 1**). Resolution of the oxalate peak was satisfactory (**Figure 2**). Quality control results were acceptable (**Table 1**).

Figure 1. *Calibration curve*

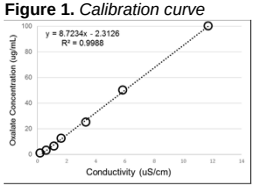

Figure 2. *Peak separation*

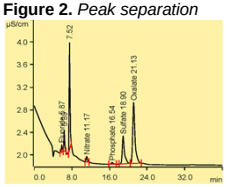

Table 1. ***Quality control results from methods development for analysis of oxalate by ion chromatography***

Limit of detection	0.23 ppm
Limit of quantification	0.77 ppm
R^2	0.999
Sample spike recovery	Within 94%
Within-batch reproducibility	Within 91%

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Results

- **Overall, <u>oxalate content ranged from 4.4 ± 0.36 to 140 ± 19 mg oxalate</u>** per liter of formula
- Of 35 formulas analyzed, the complex matrix of 9 resulted in inconsistent results over several trials and high coefficients of variation (CV) and were thus excluded
- Of remaining formulas (n=26), **oxalate content tended to be higher in flavored formulas** and in those providing full nutrition support (i.e., 100% of macronutrient and micronutrient needs)

*A chromatogram from analysis of an enteral nutrition formula (**Figure 3**), and data and comments re: sample variability (**Table 2**) are shown*

Figure 3. *Sample chromatogram*

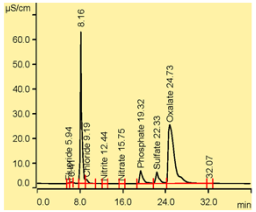

Table 2. *Data showing analytical variability and oxalate content of oral vs. enteral-only formulas*

	Oral & enteral n=15	Enteral-only n=11	*P*-value	Comment
Oxalate	45 mg/L (range 7.8-99)	46 mg/L (range 4.4-140)	0.92	Depending on calcium content, calcium-to-oxalate ratios vary widely
CV	21.3% (median 22.6%)	16.3% (median 14.4%	0.32	Analyses of oral formulas may result in higher CV due to use of flavors and other taste-enhancing properties
SD	7.0 (median 4.8)	5.5 (median 3.6)	0.45	Oral formulas may have higher SD during replicate analysis due to more complex matrices related to above

Clinical impact. Excluding formulas with no calcium (n=4), **formulas in the highest tier for oxalate (68-140 mg/L) had more bioavailable oxalate** than those with lower oxalate content (calcium:oxalate ratio 16 vs. 85, respectively; *P* = 0.04 for difference). **Patients relying on these formulas would thus be at higher risk for hyperoxaluria and CaOx stones** depending on the presence of other factors regulating oxalate absorption.

Discussion

The oxalate content of some tube feeding formulas is very high

- **Depending on the formula, anywhere from 5-360 mg oxalate daily could be provided** as many patients require 1 liter or more of formula daily
- In some patients, **dietary oxalate may thus account for a large percentage of urine oxalate,** especially if higher endogenous production and/or if higher oxalate bioavailability (due to lower calcium intake, lower bacterial degradation of oxalate in the digestive tract, or both)

Strategies to reduce oxalate absorption in patients on nutrition support should be utilized and may include reducing urine supersaturation by flushing more fluids through the tube feeding system, calcium supplementation with bolus feeds, and efforts to enhance bacterial oxalate degradation

<u>Literature cited</u>

1. Johnson EK, Lightdale JR, Nelson CP: Risk factors for urolithiasis in gastrostomy tube fed children: a case-control study. Pediatrics 2013;132(1): e167-74.
2. Smith PJ, Basravi S, Schlomer BJ, Bush NC, Brown BJ, Gingrich A, Baker LA: Comparative analysis of nephrolithiasis in otherwise healthy versus medically complex gastrostomy fed children. J Pediatr Urol 2011;7(3): 244-7.
3. Gnessin E, Handa SE, Krieg CB, Lingeman JE: Metabolic characteristics of patients who use tube feeding as their primary dietary source. J Urol 2010;183(4): E509-10 [meeting abstract].