Urol Res (1982) 10:209–211

Urological Research

Reduction of Exogenous Oxalate in Urine of Rats by Binding with Aluminium-oxyhydrate (Andursil®) and an Anion-exchanger (Colestid®) in the Intestinal Tract

C. Bannwart[1], V. Hagmaier[2], C. Simonet[2], G. Rutishauser[2], and H. Seiler[1]

[1] University of Basle, Institute of Inorganic Chemistry, and
[2] University of Basle, Division of Urology, Department of Surgery, Basle, Switzerland

Accepted: July 3, 1981

Summary. The influence of calcium carbonate, aluminium oxyhydrate (Andursil®) and an anion exchanger (Colestid®) on the absorption of oxalate from the intestine in rats was investigated. The animals were administered daily doses of 15mg oxalate as a ^{14}C-sodium-oxalate solution by means of a throat probe, and the substances of interest were mixed with the food. The intake of food and the ^{14}C-activity in the urine were measured during four urine-collecting periods of 3 days each. The quantity of the enterally administered oxalate excreted with urine has a negative correlation to the amount of the investigated test substances ingested with food.

Key words: Exogenous urinary oxalate, Aluminium oxyhydrate, Anion exchanger.

Introduction

There is little doubt that oxalate plays an important role in the formation of urinary stones. It appears that the amount of exogenous oxalate coming from intestinal absorption can exceed the amount of endogenous oxalate from metabolism. In the treatment of recurrent urolithiasis, the question of how to reduce the amount of exogenous oxalate in urine still exists.

Sierakowski [5] found from the data of an epidemiologic investigation a strong negative correlation between the amount of calcium in drinking water and the frequency of stone disease. In 1972 Marshall [3] observed that the excreted amount of oxalate in urine is diminished when the amount of calcium in the diet is increased.

There remains the paradox of influencing intestinal absorption of oxalate by increasing the intake of calcium when considering the possible therapeutic or prophylactic applications of this principle, since calcium is involved basically in the formation of stones. Moreover, the content of calcium in the blood is controlled exactly by sensitive mechanisms.

Another treatment for recurrent urolithiasis is to lower the calcium content of urine by means of diminishing the enteral absorption of calcium. In an earlier study in the rat, we showed that with this treatment signs of hyperparathyroidism developed when calcium is bound over a certain period by a cation exchanger in the intestine [2]. Therefore, prolonged reduction of urinary calcium by cation exchanger might result in secondary hyperparathyroidism and also hyperoxaluria.

Considering these facts, it appears that for the treatment of calcium oxalate urolithiasis, reduction of the oxalate content in the urine could be more successful and less harmful since oxalate itself is an important substance in the formation of stones. On the other hand oxalate is an end-product of metabolism, and its concentration in blood and urine is not actively regulated. Therefore, "hypo"-oxalaemia or "hypo"-oxaluria does not cause a counter-regulation to reach "normal" values. Consequently, new agents that could inibit intestinal oxalate absorption would seem warranted. To date, two anion-exchangers are available for this purpose and have been used to bind oxalate in the intestine. The administration of both Colestyramine (Quantalan®) [6] and Diethylaminoethanol-Cellulosa (DEAE-Cellulose) [4] resulted in a decrease of urinary oxalate.

Material and Methods

In this animal experiment we investigated the effect of two substances: aluminium oxyhydrate (Alox) and an anion exchanger (AE) and their ability to reduce oxalate absorption in the intestinal tract using the same principle as that established for calcium. Four groups of five female Wistar rats were used in the experiment; each rat was housed in a metabolic cage with free access to food and water. Over a period of 12 days each animal was administered a daily dose of 15 mg oxalate in a 3% solution of ^{14}C-labelled sodium oxalate. This solution was administered through a gastric tube during the period of food intake.

0300-5623/82/0010/0209/$01.00

Table 1. Additives to the food with respect to the collecting periods

Group	Addition to the food	Concentration of additive	Urine-collection period
I	Ca^{2+}	5%	1st–4th
II	Alox	2% 5%	1st and 2nd 3rd and 4th
III	AE	2% 5%	1st and 2nd 3rd and 4th

Table 2. Extreme values during 3 days. Influence of high and low quantities of intestinal oxalate binding substances on the exogenous urinary oxalate (in percentage of the administered dose of oxalate)

Uptake from food		Exogenous oxalate in urine
Ca:	130 mg	19.5%
	2,280 mg	0.7%
Alox:	120 mg	18.9%
	1,820 mg	1.5%
AE:	510 mg	11.6%
	1,690 mg	2.2%

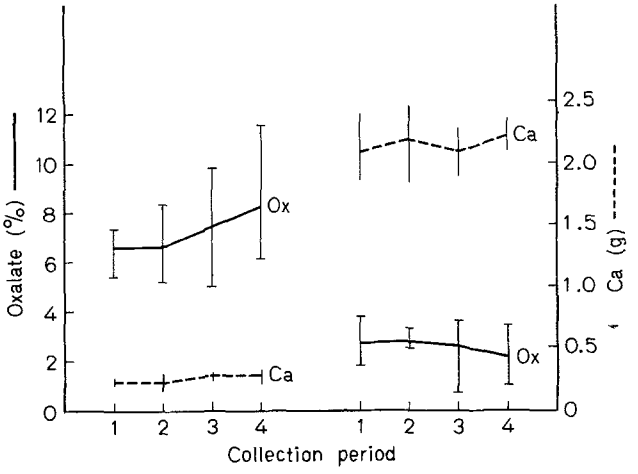

Fig. 1. Change of exogenous urinary oxalate (in percentage of the administered dose) caused by different Ca-ingestion. *Left:* food with normal Ca-content. *Right:* Ca-enriched food

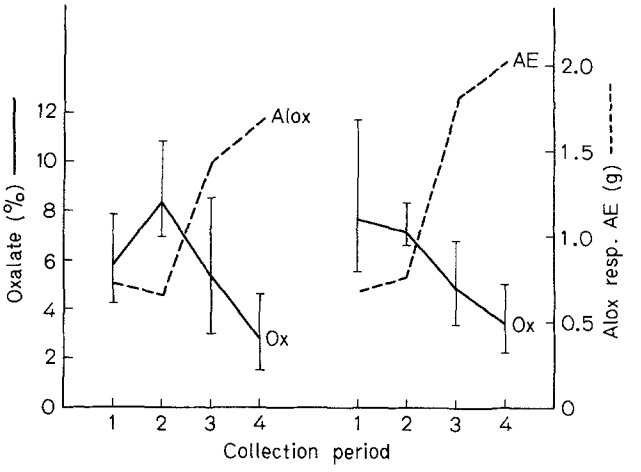

Fig. 2. Change of exogenous urinary oxalate (in percentage of the administered dose) caused by ingestion of Alox resp. AE with the food. *Left:* food with Alox. *Right:* food with AE

The control group was fed a standard diet for rats (NAFAG No. 900, Gossau, Switzerland) with a calcium content of 0.9%. The three experimental groups were fed the same standard diet mixed with the substances as listed in Table 1.

The urine was collected during four periods, each period of 3 days duration. The ^{14}C-activity in the urine was measured by liquid scintillation counting [1]. The intake of food for each animal during each of the four collecting periods was also measured.

Calcium enrichment of the food was obtained by calcium carbonate. The additive aluminium oxyhydrate (Alox) in a commercially available form was used as an antacid drug (Andursil®). The additive anion-exchanger (AE) in the chloride form is commercially available as a cholesterine-reducer (Colestid®).

Results

Figure 1 shows the content of exogenous oxalate in urine during four collection periods as a percentage of the total dose administered in that period. The amount of calcium ingested during a single three-day period clearly has an influence on the amount of oxalate excreted in the urine. As the calcium content in the food was elevated, the amount of exogenous oxalate which appeared in the urine decreased considerably.

A similar effect on the exogenous urinary oxalate could be observed when either Alox or AE was administered with the food (see Fig. 2). There was a strong negative correlation between the amount of these additives taken in with the food and the amount of exogenous urinary oxalate.

Table 2 demonstrates also the influence of the amount of the administered substances on the exogenous urinary oxalate. An extremely high supply administered during a three-day period caused an extremely low content of exogenous oxalate in urine and vice versa. A twenty-fold reduction of exogenous urine oxalate was achieved nearly linearly if the intake of one of the effective substances was increased by approximately the same amount.

Discussion

The well known fact that increasing amounts of ingested calcium cause a decrease in exogenous urinary oxalate,

while the oxalate ingestion remains more or less constant, is due to an increased formation of non-absorbable calcium oxalate in the intestine.

The use of aluminium oxyhydrate is based on its property to act as an anion exchanger in the alkaline environment of the intestine, as well as to adsorb and carry off microcrystalline precipitates such as calcium oxalate.

The anion exchanger is in equilibrium with the anions with which it is to exchange. This means that the anions are bound to the exchanger in proportion to their relative concentrations. Higher charged anions are preferred to those with a lower negative net charge. During the exchange process the anion exchanger releases chloride ions and, since it is in the form of a permeable high polymer, it also adsorbs and coprecipitates microcrystalline precipitates.

The results of this study suggest that a reduction of the exogenous urinary oxalate can be obtained succesfully by the administration of a relatively harmless drug such as aluminium oxyhydrate. Such drugs have been in use for many years and administered over long periods of time without any serious side effects.

References

1. Bannwart C, Hagmaier V, Rutishauser G, Seiler H (1979) Absorption of oxalic acid in rats by means of a ^{14}C method. Eur Urol 5:276
2. Hagmaier V, Flückiger B, Scholer A, Remagen W, Rutishauser G (1979) Influence of an orally administered calcium-binding cation exchanger on calcium metabolism in the rat. Urol Res 7:277
3. Marshall RW, Cochran M, Hodgkinson A (1972) Relationships between calcium and oxalic acid intake in the diet and ther excretion in the urine of normal and renal-stone-forming subjects. Clin Sci 43:91
4. Pinto B, Bernshtam J (1977) Diethylaminoethanol-cellulose in the treatment of absorptive hyperoxaluria. J Urol 119:630
5. Sierakowski R, Hemp G, Finlayson B (1976) Waterhardness and the incidence of urinary calculi. In: Finlayson B, Thomas WC (eds) Colloquium on Renal Lithiasis. The University of Press of Florida, Gainesville, p 213–220
6. Smith LH, Fromm H, Hofmann AF (1972) Acquired hyperoxaluria, nephrolithiasis, and intestinal disease. N Engl J Med 286:1371

Dr. C. Bannwart
Institut für Anorganische
Chemie der Universität Basel
Abteilung Analytik
Spitalstrasse 51
CH-4056 Basel