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Primary hyperparathyroidism and nephrolithiasis

Hyperparathyroïdie primaire et lithiases

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Abstract

Calcifications in the kidneys may occur in the parenchyma (nephrocalcinosis), pelvis renis (nephrolithiasis) or ureters (ureterolithiasis). Several factors may protect against stone formation or promote precipitation of stones. Most stones contain calcium, and the hypercalciuria seen in primary hyperparathyroidism is a contributing factor to stone formation in the kidneys and urinary tract. In early case series, renal stone formation was frequent, whereas the proportion of patients with symptomatic renal stones has declined in recent years. However, a substantial proportion of patients presents with asymptomatic nephrocalcinosis or nephrolithiasis. Before diagnosis and treatment of primary hyperparathyroidism, renal stone events are more frequent than in the general population. However, even after surgical cure, an increased rate of renal stone events may be seen. This may to some extent be the result of stones or calcifications already present at the time of diagnosis or sequelae to prior stones such as infections or ureter strictures.

Keywords: Nephrolithiasis; Nephrocalcinosis; Hyperparathyroidism

Résumé

Les calcifications rénales peuvent survenir au sein du parenchyme (néphrocalcinose), des cavités rénales (néphrolithiases) ou dans les uretères (urétérolithiases). Plusieurs facteurs sont susceptibles de protéger contre la formation de calculs, d'autres contribuent à leur constitution. La plupart des lithiases ont un contenu calcique, et l'hypercalciurie observée dans l'hyperparathyroïdie est un facteur prédisposant à la formation de calculs des reins et du tractus urinaire. Dans les séries initiales d'hyperparathyroïdies, la constitution de calculs rénaux était fréquente, mais la proportion de patients souffrant de lithiases rénales symptomatiques s'est maintenant réduite. Cependant, un nombre significatif de patients présente une néphrocalcinose et des lithiases rénales asymptomatiques. Avant que ne soit établi le diagnostic et débuté le traitement de l'hyperparathyroïdie primaire, les évènements lithiasiques rénaux sont plus fréquents que dans la population générale. Cependant même après la cure chirurgicale de l'hyperparathyroïdie, persiste encore un risque accru de survenue de lithiases. Dans une certaine mesure, ceci peut résulter de lithiases ou de calcifications déjà présentes au moment du diagnostic, ou apparaître comme les séquelles de lithiases antérieures, liées par exemple à l'infection ou à des rétrécissements urétéraux.

Mots clés : Lithiases rénales ; Néphrocalcinose ; Hyperparathyroïdie

1. Introduction

Many factors may contribute to stone formation in the renal pelvis (nephrolithiasis) or ureters (ureterolithiasis) or to calcifications in the kidney parenchyma (nephrocalcinosis). However, protective factors also exist [1]. Most stones are calcium containing. This narrative review will focus on calcifications in the kidney parenchyma (nephrocalcinosis), renal pelvis (nephrolithiasis) and ureters. The main factor behind the calcifications is believed to be the increased calcium excretion in the urine [2]. However, other factors may also contribute such as dehydration brought about be nausea and the osmotic diuretic effect of the high calcium levels.

2. Basal physiology

Fig. 1 shows the normal calcium fluxes and an example of primary hyperparathyroidism. Usually calcium is absorbed in

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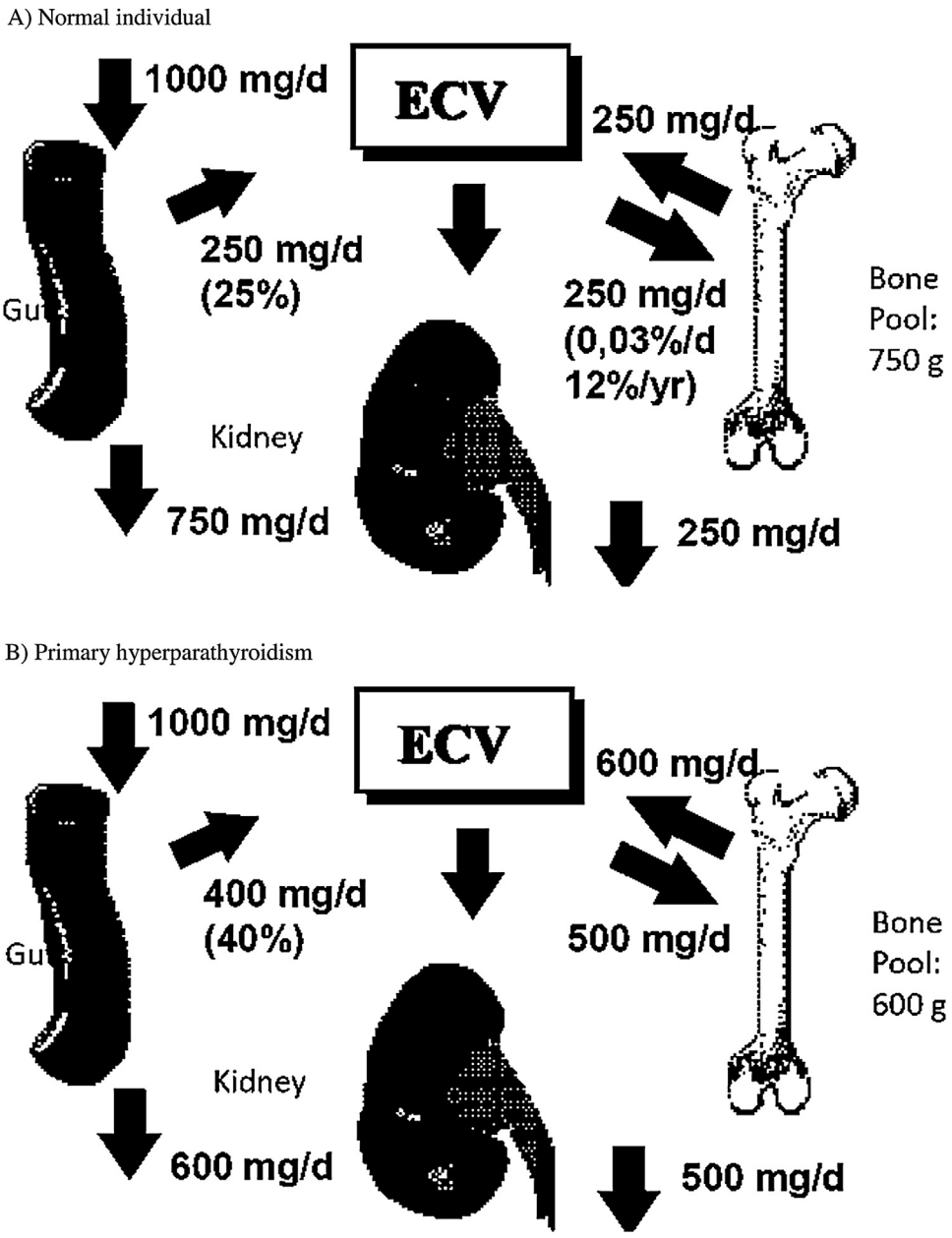

Fig. 1. Example of calcium flux in a normal person and in primary hyperparathyroidism; ECV: extracellular volume. A. Normal individual. B. Primary hyperparathyroidism.

the intestine, deposited and resorbed from the skeleton and filtered in the glomerulus in the kidney. A large re-absorption of calcium takes place in the kidney (see Table 1 for a hypothetical example).

In primary hyperparathyroidism, more calcium is re-absorbed from the skeleton through the effects of parathyroid hormone (PTH) on the osteoclasts. However, an increased calcium absorption in the intestine may also play a role as PTH activates the one-alpha-hydroxylase enzyme, which increases the levels of activated vitamin D (1,25-dihydroxy-vitamin D), which in turn may increase intestinal calcium absorption thus further contributing to the calcium load in the kidney. In the kidney, PTH may increase calcium re-absorption, but as PTH only works in parts of the tubuli, e.g. through stimulation of TRPv5 in the distal tubulus [1], the increased filtration of calcium in the glomerulus may overpower the capacity for calcium absorption further downstream in the tubuli leading to an increased net excretion although the calcium/creatinine clearance ratio if increased (Table 1).

Under normal circumstances, total plasma calcium is around 2.20–2.55 mol/l with an ionised plasma calcium of 1.18–1.32 mmol/l. This is because approximately 50% of the total calcium is "free". Calcium is filtered in the glomerulus as other ions. At a glomerular filtration of 90 ml/min and a "free" ionised plasma calcium of 1.20 mmol/l. The filtration is thus 155.5 mmol of calcium per day (or 6221 mg). With an excretion of 4%, the total daily excretion is around 249 mg in the urine (Fig. 1). The normal urine calcium excretion is around