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Amoxicillin crystalluria: an emerging complication with an old and well-known antibiotic

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Background: Amoxicillin is a drug that can crystallize in the urinary tract and lead to macroscopic hematuria and acute renal insufficiency (ARI). However, amoxicillin crystalluria is a rare event, whose incidence remains unknown. Over 10 years (09/2004–09/2014), we managed a cohort of 2348 patients with osteoarticular infections. Among 228 patients who received high-dose intravenous (IV) amoxicillin, fewer than one per year developed amoxicillin crystalluria with ARI. During the past year we observed an important increase of this complication. The aim of our study is to describe the current incidence of amoxicillin crystalluria with ARI, to describe the clinical signs of this complication, its treatment and outcome.

Material/methods: We conducted a retrospective mono-centric cohort study in a French Referral Center for treatment of Bone and Joint Infections between September 1st 2014 and October 31st 2015. All the patients treated with IV high-dose amoxicillin (≥ 6gram/24h for at least 48 hours) developing ARI and signs of crystalluria (macroscopic hematuria, oliguria, intense burning during urination, abdominal or lumbar pain) were included.

Results: Among 285 patients, 56 received IV amoxicillin. Ten (18%) develop ARI associated with signs of amoxicillin crystallisation. For these 7 women and 3 men, median age 70 [range 47–86] years, median initial creatininemia was 58 [range 45–116] □mol/L. Eight patients had received 12 gram (g), one 9 g and one 15 g of amoxicillin per 24 hours. IV amoxicillin was administered in 3, 4 or 6 infusions over 60–120 min, with a unit doses of 4, 3, 2 or 2.5 g, to four, four, three or one patient respectively. The first clinical manifestations (macroscopic hematuria for all patients, oliguria for seven, intense burning during urination for three, abdominal or lumbar pain for two) appeared within 15 [range 1–27] days after starting amoxicillin. ARI became manifest a median of 2 [range 0–3] days after the first clinical signs. Median maximum creatininemia was 411 [range 153–728] □mol/L. For all patients, treatment consisted of amoxicillin withdrawal, IV hydration and urine alkalinisation. A JJ ureteral stent was placed to treat renal pelvis dilatation in 2 patients. Complete recovery of previous renal function was obtained in all patients within a median of 13 [range 1–24] days.

Conclusions: The sharp rise of this complication over the past year, while our prescription modalities have not changed, leads us to think that it is related either to an increase of urinary amoxicillin

concentrations, eg. by another drug or infusion solution, or to the manufacture of the drug. Further studies are warranted to answer that question.