Antibiotic-related serious adverse events during treatment of methicillin-susceptible Staphylococcus aureus bone and joint infections

Florent VALOUR1,2, Judith KARSENTY1, Anissa BOUAZII2, Florence ADER2,3, Michel TOD1, Sébastien LUG1,2, Frédéric LAURENT1,2, Christian CHIADIC2,3, Tristan FERRY2,3 on behalf of the Lyon BJJ study group

1: Infectious diseases department, Hospices Civils de Lyon; 2: Claude Bernard Lyon 1 University, INSERM U1111, International Center for Research in Infectiology; 3: Pharmacovigilance department; 4: Orthopedic surgery department; 5: National Reference Center for Staphylococci – LYON, France

Background: Combination antibiotic therapy is frequently recommended in MSSA BJI, but safety and risk factors for SAE are unknown.

Methods: Retrospective study (2005-2013) included 197 patients (SAE defined according to Common Terminology Criteria for Adverse Events (CTCAE)). The main exclusion criteria were re-operations, metastasis, or severe arthritis in patients > 60 years old (10.4%), enteral nutrition (9.4%), anticoagulation (9.4%), corticosteroids (13.7%), obesity (15.4%), chronic renal or liver failure (15.4%), and a delay in diagnosis of infection > 4 weeks (16.7%).

Results: Antibiotic-related serious adverse events occurred in 9 SAE among 102 patients (8.8%), median age: 60 years (44.5-75.3). Risk factors for rifampin-related SAE included obesity: HR 8.9, p=0.01. Obesity: HR 7.6; p=0.056. Age>60 year-old: HR 7.6; p=0.056. Prior history of BJI: HR 6.2; p=0.025. Charlson score > 2: HR 8.7; p=0.040. The individual risk for rifampin-related SAE (6.7%) was higher than for any other antibiotic. Respiratory (n=13), renal (n=6), acute kidney failure (n=1), central nervous system (n=3), infections (n=4), respiratory failure (n=3), and allergic reactions (n=3) were the most frequent SAE. The accumulated risk of rifampin-related SAE was 6.7% at 1 year, among 30 rifampin dosages, it was greater than 15%.

Conclusions: The rifampin-related SAE risk is extremely high in patients with factors favoring free rifampin: obesity, prior BJI, age > 60 years, and Charlson score > 2. The risk factors for rifampin-related SAE should be used to tailor the treatment. Further, for obese patients, rifampin dose adjustment is highly recommended. Rifampin should be used in patients with a lower risk of SAE. Further studies are needed to investigate the risk factors for rifampin-related SAE.