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Short communication

Pristinamycin-induced arthralgia and myalgia: Analysis of the French Pharmacovigilance Database

Arthralgie et myalgie sous pristinamycine : analyse de la Base nationale de pharmacovigilance

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Abstract

Introduction. – Pristinamycin is an antibiotic of the streptogramin family; few adverse effects of this drug are reported, only cutaneous and digestive ones. Arthralgia and myalgia may however be observed although not mentioned in the summary of product characteristics.

Objective. – Description and analysis of cases of pristinamycin-induced arthralgia and/or myalgia registered in the French database of pharmacovigilance.

Method. – We carried out a targeted search of the database, selecting case patients presenting with arthralgia and muscle pain and excluding those associated with sensitivities or allergies to pristinamycin.

Results. – We retrieved 15 case patients of pristinamycin-induced arthralgia and myalgia. Pristinamycin was the only potentially incriminated drug for seven case patients.

Conclusion. – Although not serious, this adverse effect deserves to be better known by physicians to optimize therapeutic management.

Keywords: Arthralgia; Myalgia; Pristinamycin

Résumé

Introduction. – La pristinamycine est un antibiotique de la famille des streptogramines pour lequel peu d'effets indésirables sont décrits, essentiellement cutanés et digestifs. Cependant, des arthralgies et des myalgies sont possibles bien que non mentionnées dans le résumé des caractéristiques du produit.

Objectif. – Description et analyse des cas d'arthralgie et/ou de myalgie sous pristinamycine enregistrés dans la Base nationale de pharmacovigilance française.

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Méthode. – Nous avons effectué une requête ciblée dans la Base nationale de pharmacovigilance française, en sélectionnant les cas d'arthralgie et de douleurs dans les muscles, et en excluant ceux associés à des hypersensibilités ou à des allergies à la pristinamycine.

Résultats. – Nous avons retrouvé 15 cas d'arthralgie et/ou de myalgie sous pristinamycine. La pristinamycine était le seul médicament suspect pour sept cas.

Conclusion. – Bien que non grave, cet effet indésirable mériterait d'être mieux connu des cliniciens afin d'optimiser la prise en charge thérapeutique.

Mots clés : Arthralgie ; Myalgie ; Pristinamycine

1. Introduction

Pristinamycin is an antibiotic of the streptogramin family, also known as synergistins. Pristinamycin has been on the French market since 1973 under the trade name Pyostacine®. Following unexpected unfavorable efficacy results observed in a clinical trial of patients presenting with tonsillitis, the benefit/risk ratio of pristinamycin was reviewed and led to the restriction of indications in July 2012 [1]. The use of pristinamycin is now limited to the following indications: acute maxillary sinusitis, acute exacerbations of mild to moderate chronic bronchitis and community-acquired pneumonia, and skin and soft tissue infections. Nevertheless, the actual benefit of pristinamycin remains substantial [1]. Pristinamycin-related adverse effects – mentioned in the summary of product characteristics (SmPC) – are few: gastrointestinal disorders, skin disorders, or hypersensitivity.

A case of pristinamycin-induced arthralgia was recently observed in our pharmacovigilance center. This adverse effect has been well documented for another antibiotic of the streptogramin family, i.e. the combination of quinupristin/dalfopristin. Arthralgia is, however, not mentioned in the SmPC of pristinamycin. Quinupristin/dalfopristin used to be on the market under the trade name Synercid®, but it is no longer commercialized in France. We aimed to describe and analyze all cases of pristinamycin-induced arthralgia and/or myalgia recorded in the National Pharmacovigilance Database.

2. Methods

A search targeted on pristinamycin was carried out on the National Pharmacovigilance Database on June 30, 2016. The database includes case patients notified to the French regional centers for pharmacovigilance (French acronym CRPV) and recorded since the creation of the database on January 1, 1983. We used the MedDRA search terms [Preferred Terms (PT)] "arthralgia" and [high-level group terms (HLGT)] "muscle pain".

We included patients presenting with joint pain and/or muscle pain whether or not combined with other adverse effects, but we excluded patients also presenting with hypersensitivity or pristinamycin allergy. Data collected included sex and age of patients, localization and severity of arthralgia and/or myalgia, time to symptom onset following pristinamycin initiation, discontinuation or continued treatment, evolution of symptoms and time to regression, introduction or not of a symptomatic treatment, potential additional examinations.

3. Results

A total of 28 case patients with pristinamycin involvement were retrieved from the National Pharmacovigilance Database. Thirteen patients were excluded because arthralgia was associated with hypersensitivity and rash, fever, purpuric or maculopapular rash, vascular purpura, generalized edema, urticaria, or acneiform eruptions. Pristinamycin was the only potentially incriminated drug for 7 of the 15 patients included (46.7%) (Table 1). Nine patients were women (60%) and six were men (40%), for an overall mean age of 60.5 years (range [21–89]). We retrieved eight patients presenting with isolated arthralgia, two with isolated myalgia, two with arthralgia and myalgia, one with arthralgia and thrombocytopenia, one with myalgia and nausea, and one with arthralgia associated with myalgia and abdominal pain. The localization of these adverse effects was specified for 7/15 patients: lower limbs ($n = 2$), lower limbs and back ($n = 1$), all lower and upper limbs and back ($n = 1$), metacarpophalangeal joints, hips, knee, and feet ($n = 1$), right wrist, then right ankle, left and right elbow, and then left knee ($n = 1$), and non-specific generalized clinical manifestations ($n = 1$). The adverse effects were considered "severe" in 7 of 15 patients (46.7%), including four patients who had to be hospitalized or whose hospital stay had to be prolonged, and three patients presenting with "another medical condition".

Time to symptom onset following pristinamycin initiation ranged from 1 to 9 days for 14 patients and was 11 weeks for one patient.

Seven patients had to discontinue treatment (including one following unsuccessful tapering of pristinamycin) and three kept on receiving it. The evolution of symptom was favorable in 11 patients (73.3%), unfavorable in two (13.3%), and unknown in two (13.3%).

Time to regression was specified for 8/15 patients: the symptoms of two patients rapidly disappeared at treatment discontinuation, symptoms disappeared within one day for two patients, within five days for another patient, six days after pristinamycin discontinuation for another one, following symptomatic treatment with paracetamol for one patient, and

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