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Effectiveness of Aprepitant in Patients with Refractory Pruritus Secondary to Sézary Syndrome

Iolanda Conde Fernandes[1,4]*, Tiago Torres[1,4], Manuela Selores[1,4], Rosário Alves[1,2,4] and Margarida Lima[2,3,4]

[1]*Department of Dermatology, Centro Hospitalar do Porto, Portugal*
[2]*Multidisciplinary Consultation for Cutaneous Lymphomas, Centro Hospitalar do Porto, Portugal*
[3]*Hematology Department, Centro Hospitalar do Porto, Portugal*
[4]*Centro Hospitalar do Porto, EPE – Hospital de Santo António, Portugal*

Abstract

Background: In advanced stages, patients with Sézary Syndrome (SS) commonly report an ill-defined, severe and diffuse pruritus. Recently, it has been reported that Aprepitant, an oral neurokinin-1-receptor (NK1) antagonist, may have an important role in relief of refractory pruritus in patients with SS.

Material and methods: A prospective study which included four patients with SS, in whom pruritus is the main symptom, was performed. Our purpose was to assess efficacy of Aprepitant for treatment of refractory pruritus, secondary to SS. Patients were treated with Aprepitant 80 mg/d during 10 days and then the dosage was reduced to alternate days. The length of treatment ranged between 4 and 23 weeks. Improvement was assessed by the Dermatology Life Quality Index (DLQI) questionnaire, which ranges from 0 to 30, with high scores indicating worse outcome and by Visual Analogue Scale (VAS) which varies from 0 to 10, with higher scores meaning severe pruritus.

Results: Prior to treatment, subjects had severe pruritus with mean DLQI score of 21.5 (SD ± 2.4) and mean VAS score of 9.0 (SD ± 0.8). At the end of the treatment, a statistically significant reduction in both indexes ($p<0.05$) was evident. In all patients, an improvement of pruritus was rapidly observed after the first week of therapy. No side effects were reported.

Conclusion: The study confirms the effectiveness and safety of Aprepitant as an antipruritic agent in patients with refractory pruritus secondary to SS.

Keywords: Aprepitant; Pruritus; Sézary syndrome

Introduction

In advanced stages, patients with Sézary Syndrome (SS) commonly report an ill-defined, severe and diffuse pruritus that may turn into "burning pain". This is responsible for significant morbidity and adversely affects patients' quality of life. It is known that pruritus, insomnia and depression impair significantly the quality of life and may even lead to suicide [1]. Multiple options are available for pruritus treatment, including topical and oral corticosteroids, anti-histamines, phototherapy, gabapentin, mirtazapine, amitriptyline or naltrexone, each with varying efficacy and side effects profiles. Recently, it has been reported that Aprepitant, an oral neurokinin-1-receptor (NK1) antagonist, may have an important role in relief of refractory pruritus in patients with SS [2,3].

Aprepitant was approved in 2003 to prevent both acute and delayed chemotherapy-induced nausea and vomiting [4]. The dominant ligand for NK1, substance P, has been found to be an important mediator in the induction and maintenance of pruritus [5]. Moreover, an increase of NK1 has been described on keratinocytes in patients with chronic pruritus. Thus, it seems reasonable for its use in the treatment of this important symptom.

Material and Methods

A prospective study which included four patients with SS, in whom pruritus was the main symptom, was performed. Our purpose was to assess efficacy of Aprepitant for treatment of refractory pruritus, secondary to SS. In all patients, pruritus could not be controlled with conventional treatments (Table 1). Patients were treated with Aprepitant 80 mg/d during 10 days and then the dosage was reduced to alternate days. The length of treatment ranged between 4 and 23 weeks. Improvement was assessed by the Dermatology Life Quality Index (DLQI) questionnaire, which ranges from 0 to 30, with high scores indicating worse outcome and by Visual Analogue Scale (VAS) which varies from 0 to 10, with higher scores meaning severe pruritus. When Aprepitant was introduced, the patients were not on other drugs. All patients have signed an informed consent. Statistically, T test was used to compare data.

Results

Three patients were women (75%). The mean age was 68 years. The time between the diagnosis of SS and the initiation of Aprepitant ranged from 5 to 18 months. All patients have been treated with other antipruritic agents, which included topical and oral corticosteroids, antihistamines, antidepressants, thalidomide and phototherapy (Table 1).

Prior to treatment, subjects had severe pruritus with mean DLQI score of 21.5 (SD ± 2.4) and mean VAS score of 9.0 (SD ± 0.8). At the end of the treatment, a statistically significant reduction in both

***Corresponding author:** Iolanda Conde Fernandes, Department of Dermatology, Centro Hospitalar do Porto, EPE – Hospital de Santo António, Building the External Consultations - Former CICAP, Rua D. Manuel II, s / n, 4099-001 Porto, Portugal, Tel/Fax: 00351 22 6097429l, E-mail: iolanda.c.fernandes@iol.pt

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Patients	Gender/Age/ Clinical outcome	Diagnosis of SS	Initiation and length of treatment with Aprepitant	Previous antipruritic therapy	Previous therapy for SS	DLQI and VAS scores before and after treatment with Aprepitant
Patient 1 †	F/68 Initial good response	11/2010	11/03/11 4 weeks	TCS Antihistamines Antidepressant Thalidomide PUVA	Alemtuzumab	**Before treatment:** DLQI: 23 VAS: 10 **After treatment:** DLQI: 21 VAS: 8
Patient 2	M/65 Response	01/2010	10/02/2011 4 weeks	TCS Antihistamines Antidepressant	CVP Alemtuzumab	**Before treatment:** DLQI: 18 VAS: 9 **After treatment:** DLQI: 3 VAS: 0
Patient 3	F/70 Response	07/2009	05/11/2010 ‡ 21 weeks	TCS Antihistamines PUVA	Bexarotene INF-α CHOP Alemtuzumab	**Before treatment:** DLQI: 22 VAS: 9 **After treatment:** DLQI: 4 VAS: 1
Patient 4	F/67 Response	04/2009	20/10/20 ‡ 23 weeks	TCS Antihistamines Antidepressant	Bexarotene INF-α CHOP	**Before treatment:** DLQI: 23 VAS: 8 **After treatment:** DLQI: 4 VAS: 1

†This patient showed a good initial response, but by the 12th day he stopped responding to Aprepitant
‡The treatment was interrupted for two weeks
Abbreviations: F: Female; M: Male; TCS: Topical Corticosteroids; PUVA: Phototherapy UVA; CVP: Cyclophosphamide, Vincristine, and Prednisone; INF-α: Interferon α; CHOP: Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone

Table 1: Representative table of patients treated with Aprepitant.

indexes ($p<0.05$) was evident (Table 1). One patient (Table 1, patient 1) showed a good initial response but by the 12th day of treatment a substantial worsening of pruritus was noted. Therefore, after 4 weeks of treatment the drug was discontinued. The treatment failure was probably related with disease progression, confirmed by an increase of blood Sézary cells (SC) quantified by flow cytometry. The 2nd patient (Table 1, patient 2) received Aprepitant over 4 weeks with an excellent response. By the 4th week of treatment, Aprepitant was stopped in the other two patients (Table 1, patient 3 and 4), because they have achieved pruritus control. However, after the discontinuation, relapse of pruritus was observed. In these patients, after two weeks without treatment, Aprepitant was reintroduced with the same good response. In all patients, an improvement of pruritus was rapidly observed after the first week of therapy. No side effects were reported.

Conclusion

The study confirms the effectiveness and safety of Aprepitant as an antipruritic agent in patients with refractory pruritus secondary to SS. However, it would be still important to determine the optimal dosage and ideal period of time for the treatment of this condition in view of its elevated cost.

References

1. Sampogna F, Frontani M, Baliva G, Lombardo GA, Alvetreti G, et al. (2009) Quality of life and psychological distress in patients with cutaneous lymphoma. Br J dermatol 160: 815-822

2. Torres T, Fernandes I, Selores M, Alves R, Lima M (2012) Aprepitant: Evidence of its effectiveness in patients with refractory pruritus continues. J Am Acad Dermatol 66: e14-e15.

3. Booken N, Heck M, Nicolay JP, Klemke CD, Goerdt S, et al. (2011) Oral aprepitant in the therapy of refractory pruritus in erythrodermic cutaneous T-cell lymphoma. Br J Dermatol 164: 665-657.

4. Poli-Bigelli S, Rodrigues-Pereira J, Carides AD, Julie Ma G, Eldridge K, et al. (2003) Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting. Results from a randomized, double-blind, placebo-controlled trial in Latin America. Cancer 97: 3090-3098

5. Wallengren J (2005) Neuroanatomy and neurophysiology of itch. Dermatol Ther 18: 292-303.