P-05

CHARACTERIZATION OF THE BIOLOGIC THERAPY USED BY PATIENTS WITH PSORIASIS AND PSORIATIC ARTHRITIS TREATED IN HDS

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INTRODUCTION

Psoriasis is chronic, immune-mediated, inflammatory, multi-system disease, which manifests predominantly in the skin and at the joint. The most common and severe form is plaque-type psoriasis (PP) (1).Psoriatic arthritis (PsA) is a negative spondyloarthropathy associated with psoriasis (2). PsA can occur in 6% to 42% patients with PP (2).In both subtypes, there is a prominent lymphocytic infiltrate due the action of interleukin 12 (IL-12) and interleukin 23, but populations of lymphocytes T that migrate to the inflammatory area are different. IL-12 stimulates the synthesis of tumor necrosis factor-alfa (TNFα), which exerts a pro-inflammatory action by stimulating the synthesis of other cytokines such as interleukin 6 or adhesion molecules (3), and a proliferative action by stimulating the proliferation of keratinocytes in PP, or hyperplasia of synovial cells in PsA. In the both diseases, stimulates angiogenesis, which also allows a more recruitment of inflammatory cells into the affected areas (4).In the PsA, occurs an activation of osteoclast precursor cells, which leads to bone deformation, contributing to decreased functionality of the joint (2, 4).

Scientific studies such as clinical trials have demonstrated that treatment with antagonists of TNFα reduces the progression of inflammation in those diseases (1,2). There are three TNFα antagonists: adalimumab (ADA) (monoclonal antibody), infliximab (INF) (chimeric monoclonal antibody) and etanercept (ETA)(tumor necrosis factor-receptor Fc-fusion protein), and these molecules bind this cytokine, that allows to block all action in cascade inflammatory.

Our objective wasto describe a biologic therapeutic of the patients with PsA and PP that are treated in the Hospital Distrital de Santarém.

MATERIAL AND METHODS

In this project, patients were selected from a sample of patients which achieved biologic therapeutic in October 2010 at the Pharmacy of the HDS. The data base was elaborated at SPSS (*Statistical Package for the Social Sciences*) for windows (V 17.0), which was used for descriptive and statistical analysis.

RESULTS AND DISCUSSION

The sample studied (n=68) were mostly female (58,8%) and older than fifty years (52,94%). Diagnose is described in figure 1, where the most frequent disease were Rheumatoid Arthritis, PsA and PP. In this study, only biological therapy was considered for PsA and PP therapeutic treatment.

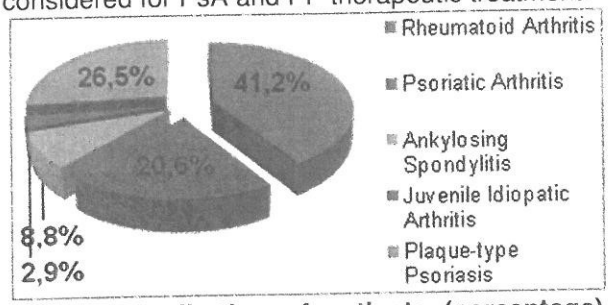

Figure1 Distribution of patients (percentage) for diagnose.

The total amount for the patients with PsA or PP was 32, and they were treated with ADA 40 mg, ETA 50 mg and INF 100 mg, mostly since 2008, when it was approved to be released in Hospital´s Pharmacy. These patients have been mainly treated with a biological agent (84, 38%) or two (15, 62%). The current biological therapeutic is described in figure 2, patients with PP are mostly treated with ADA and patients with PsA are treated both with ADA (18,8%) e ETA (25%).

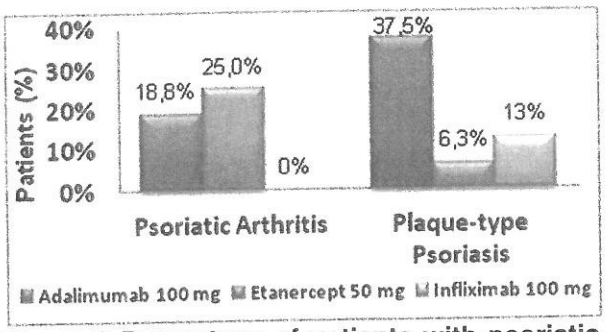

Figure 2 Percentage of patients with psoriatic arthritis and psoriasis which achieved biological therapy. %: Percentage.

In this sample there are no data regarding skin lesions on patients with PsA, but in some clinical studiesfor PsA it has been considered.

The *Adalimumab Effectiviness in Psoriatic Arthritis Trial* (ADEPT) (6) demonstrated that significantly improves in skin and joint manifestations in patient's whit PsA. This study reported that ADA

allowed establishing of the disease, with radiographic data proved an inhibition of structural progression that could significantly improve physical functions(5).
A phase III study for patients with PsA, during 12 months, showed that ETA allowed a significant improvement in symptoms of PsA, with inhibition of structural progression of the disease(2).
In a phase III, double-blind study, it was verified that ETA was effective and safe in PP after two years of treatment (6).
A phase III study confirmed the efficacy of INF in moderate a severe PP treatment (3).
In this sample, it is notorious that patients with PP are mostly treated with ADA, probably due to ETA lower efficacy for the treatment of this disease (7). The reduced efficiency can be explained by his mechanism of action, in which crosslink between ETA and transmembrane TNFα(tmTNF) is less stable that other biological agents, and has a lower able to cause a reverse of the signal. ETA is able to suppress the cytokine synthesis, such as interleukin 1-beta, but not IL-12 (4, 8), which has an important function in PP (3) and has ability to suppress lymphocyte T proliferation (4). An important point can be associated on some individuals, that is the ability for ETA to induce the apoptosis of inflammatory cells (4,9). In PsA patients has been observed an increase in neutrophil infiltration compared to PP(2), and in this case ETA is more efficient, due to the property of drug to allow rapid reduction of cell infiltrate in synovial tissue, decreased angiogenesis, and consequently reduce the whole process of inflammatory cells recruitment (5).
In this sample, for a patient with PP, a switch was reported from ETA to ADA. The need for this switch can be achieved when patients does not positively respond to treatment. (12). A phase III study demonstrated that ADA is effective and safe for patients with PP after poor response with ETA, after adjustment in posology, 50 mg once a week was switched for 50 mg twice a week (8).

The tumor necrosis factor-alfa by intervening in the inflammatory process in PP and PsA, is used as a therapeutic target. These biological agents are effective and safe for these diseases, and we notice that ADA is preferred for the PP treatment and can also be used in patients where ETA 50 mg once a week does not leads to an adequate response.

CONCLUSIONS

REFERENCE

(1) Papoutsaki M, Chimenti M-S, Costanzo A, Talamonti M, Zangrilli A, Giunta A, *etal.*Adalimumab for severe psoriasis and psoriatic arthritis: An open-label study in 30 patients previously treated with other biologics. J Am AcadDermatol 2007; 57: 269-75;

(2) Gottlieb A, Korman N, Gordon K, Feldman S, Lebwohl M, Koo J, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: Overview and guidelines of care for treatment with an emphasis on the biologics. J Am AcadDermatol 2008; 58: 851-64;

(3) Pietrzak A, Zalewska A, Chodorowska G, Krasowska D, Michalak-Stoma A, Nockowski P *et al.*. Cytokines and anticytokines in psoriasis. ClinChimActa 2008; 394: 7–21;

(4) Tracey D, Klareskog L, Sasso E, SalfeldJ,Tak P. Tumor necrosis factor antagonist mechanisms of action: A comprehensive review. PharmacolTher 2008;117:244–279;

(5) Mease, P, Ory P, Sharp J, Ritchlin C, Bosh F, Wellborne F *et al.*Adalimumab for long-term treatment of psoriatic arthritis: 2-year data from the Adalimumab Effectiveness in Psoriatic Arthritis Trial (ADEPT). Ann Rheum Dis 2008;68: 702–709;

(6) Zaragoza V, Pérez A, Sánchez J, Oliver V, Martínez L, Alegre V. Long-term Safety and Efficacy of Etanercept in the Treatment of Psoriasis. ActasDermosifiliogr. 2010; 101(1): 47-53;

(7) Bissonnette R, Bolduc C, Poulin Y, Guenther L, Lynde C, Maari C.Efficacy and safety of Adalimumab in patients with Plaque Psoriasis who have shown an unsatisfactory response to Etanercept. J Am AcadDermatol 2010; 63: 228-34;

(8) Wong M, Ziring D, Korin Y, Desai S, Kim S, Lin J, et al. TNFα blockade in human diseases: Mechanisms and future directions. ClinImmunol 2008; 126(2): 121–136;

(9) Taylor P. Pharmacology of TNF blockade in rheumatoid arthritis and other chronic inflammatory diseases. Current Opinion in Pharmacology 2010; 10:308–315;

(10) Switching between anti-TNF alfa agents: what is the evidence?. Joint Bone Spine 2004; 71: 169–171