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PSORIASIS, PHYSICAL ACTIVITY AND BRODALUMAB TREATMENT

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ABSTRACT

Purpose: The Environmental and genetic factors seem to have a crucial role in the psoriasis treatment. The objective is to investigate the improvement and fast response of moderate-to-severe psoriasis under brodalumab treatment, in patients who exercise more intensely compared to those with reduced physical activity. **Design/Setting:** Patients divided into 3 groups depending on their physical activity intensity (high-moderate-low) by International Physical Activity Questionnaire (IPAQ). **Subjects:** Adult, moderate-to-severe plaque psoriasis patients treated with brodalumab were involved. **Measures:** Psoriasis was evaluated with Psoriasis Area Severity Index (PASI), quality of life was estimated with Dermatology Life Quality Index (DLQI) and inflammation was measured with C-Reactive Protein (CRP) at 0, 12 and 52 weeks. **Results:** At baseline, patients (N=40) had mean age 51 years and mean PASI [Standard Deviation-(SD)] score 20.35 (6.16). The relevant results were: mean (SD) PASI score: 1.67 (1.21), p-value<0.001; mean (SD) DLQI scores: baseline, 15.72 (5.25); week 52, 0.47 (1.41), p-value<0.001; mean (SD) CRP values: baseline, 3.03 (2.82); week 52, 1.86 (1.84), p-value=0.003; mean overall physical activity (SD): baseline, 1237.59 min/week (1780.43); week 52, 2046.19 min/week (2006.93), p-value<0.001. **Conclusions:** The statistically significant results confirm the initial aim of the study, indicating that the rapid improvement and maintenance of the outcome in the long-term treatment with brodalumab is enhanced in patients with increased physical activity. The real-world treatment effectiveness and physical activity relation, alongside the pathophysiological mechanism of the potential physical activity impact on the therapeutic outcome, is an interesting field to be further explored.

INTRODUCTION

Autoimmune diseases (ADs) affect 5–10% of the globe and have detrimental effects on patients' quality of life, life expectancy, and healthcare costs. Psoriasis is one of those ADs. Accumulating evidence shows that changes in diet, lifestyle, and socioeconomic status have resulted in a substantial metabolic shift associated with the rapid increase of ADs. As such, there is a growing pressure from patients' increasing demand and substantial healthcare costs for tailor-made solutions that combine effective drugs with lifestyle interventions such as physical activity.[1]

Moderate-to-severe psoriasis is a chronic inflammatory disease usually treated with biological agents including brodalumab, which selectively targets the interleukin (IL) 17 receptor A.[2] Environmental, along with the genetic factors seem to have a crucial role in the pathophysiology pathway.[3] Physical activity as a lifestyle factor, actis on both the pathogenetic background of psoriasis along with the co-morbidities such as the metabolic syndrome.[4-5] A possible reasonable explanation would be the increased function of T-regulatory cells (T-regs) that are anti-inflammatory and atherosclerotic lymphocytes which not only release cytokines such as IL-10, IL-13, Transforming Growth Factor beta (TGF-β) but also reduce the production of pro-inflammatory cytokines such as Interferon gamma (IFN-γ).[6-7] A study in athletes showed that in this category of individuals there is an increase in T-reg cells and especially in those who exercise particularly intensely.[8-9] In more detail, T-regs lead to an alteration in the Type 1 T helper/Type 2 T helper (Th1/Th2) balance, reducing Th1 cell production and increasing Th-2 population that produce IL-4, IL-5, IL-6 and IL-10. Exercise promotes the release of IL-6 from the muscles. IL-6 acts as myosin and has been shown to induce anti-inflammatory activity through IL-10 secretion and IL-1β inhibition.[10]

Psoriasis is inextricably linked to metabolic syndrome and exercise/physical activity, which is also prominent in the treatment of metabolic syndrome. Exercise has benefits: 1. Reduces obesity 2. Reduces the risk of cardiovascular events 3. Improves diabetes 4. Reduces inflammatory markers [eg. C-Reactive Protein (CRP)] 5. Improves healing 6. Improves mental health by reducing depressive symptoms and anxiety. Outdoor exercise also improves psoriasis through the mechanism of vitamin D due to patient exposure to Ultra Violet (UV) radiation.[11-16]

The aim of the study is to investigate the improvement and rapid response of patients with moderate-to-severe psoriasis under brodalumab, who exercise more intensely compared to those who have reduced physical activity.

MATERIALS AND METHODS

Patients and study design

This study was conducted from June 2019 to December 2020. Patients with moderate-to-severe psoriasis treated with brodalumab were included and their physical activity was assessed. Exclusion criteria were age <18 years, pregnancy and mild psoriasis [Psoriasis Area Severity Index (PASI) <10]. All participants were monitored at the outpatient clinic of Dermatological Department of Tzaneio General Hospital in Attica, Greece and written informed consent was obtained from all of them. The study was approved by the Institutional Ethics Committee of Tzaneio General Hospital of Piraeus and was in accordance to the Declaration of Helsinki and Good Clinical Practice guidelines. Patient's physical activity, which is defined as any type of activity, including the daily (walking, cycling, housekeeping or gardening) and leisure activities and sedentary behavior was evaluated by using the International Physical Activity Questionnaire (IPAQ).[17] It has to be noted that the patient's physical activity is part of the patient's daily routine, regardless of their inclusion in the study. Detailed medical history including all patient's previous treatments was reported and except physical examination, psoriasis evaluation was calculated with PASI score, patient's quality of life

was estimated with Dermatology Life Quality Index (DLQI) and inflammation was measured with CPR value at 0, 12, 52 weeks as per standard clinical practice.

Statistical analysis

Continuous variables were summarized with the use of descriptive statistical measures (mean value, standard deviation [SD]). Categorical/distinct variables are displayed as frequency tables (n, %). Post-hoc power calculation revealed that 32 patients were enough to estimate a mean change in PASI between baseline and visit 2 (52 weeks) with a type I error of <0.05 and a power of >90%, however, 40 patients were planned to be enrolled initially. The statistical comparisons of continuous variables between groups were conducted with the Kruskal Wallis or the Mann-Whitney non-parametric tests as applicable. The chi-square test was used to evaluate the statistical relationship between categorical variables. Paired samples tests were applied for the comparisons continuous variables between different timepoints. All analyses were carried out with IBM SPSS 22.

RESULTS

In total, 40 patients with severe psoriasis (mean PASI score 20, 35 at baseline visit) and mean age 51 years old were included (Table 1). The preliminary results of 12 weeks follow-up are presented, with all available information in both time points (baseline and visit 1): mean (SD) PASI scores: baseline, 20.35 (6.16); week 12, 9.68 (4.29), p-value <0.001; mean (SD) DLQI scores: baseline, 15.38 (5.62); week 12, 5.59 (2.62), p-value <0.001 and mean overall physical activity (SD): baseline, 1263.67 min/week (1733.59); week 12, 1647.18 min/week (1869.20), p-value =0.004 (Fig. 1). The final results of 52 weeks follow-up are presented comparatively between baseline visit and final visit (visit 2) in Fig. 2: mean (SD) PASI scores: baseline, 20.04 (6.04); week 52, 1.67 (1.21), p-value <0.001; mean (SD) DLQI scores: baseline, 15.72 (5.25); week 52, 0.47 (1.41), p-value <0.001; mean (SD) CRP values: baseline, 3.03 (2.82); week 52, 1.86 (1.84), p-value = 0.003 and mean overall physical activity (SD): baseline, 1237.59 min/week (1780.43); week 52, 2046.19 min/week (2006.93), p-value <0.001.

Table 1: Demographic characteristics of patients, previous treatments and physical activity at baseline.

Gender	Frequency	Percent	Cumulative Percent
Female	16	40	40
Male	24	60	100
Total	40	100	
Previous Treatment			
Biologics	8	20	20
Conventional systemics	3	7.5	27.5
Apremilast	9	22.5	50
Biologics + conventional systemics	5	12.5	62.5
Biologics + apremilast	2	5	67.5
Conventional systemics + apremilast	1	2.5	70
Biologics + conventional systemics + apremilast	2	5	75
Naïve	10	25	100
Total	40	100	
Sedentary category			
Home	27	67.5	67.5
Work	13	32.5	100
Total	40	100	
Physical activity			
High	6	15	15
Moderate	11	27.5	42.5
Low	23	57.5	100
Total	40	100	

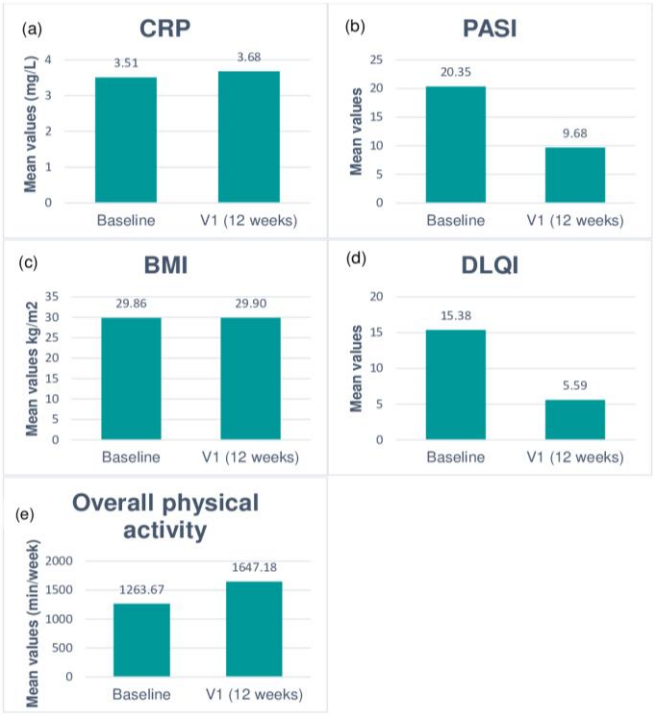

Figure 1: Preliminary results of 12 weeks follow-up [comparison between baseline (BL) visit and visit 1 (V1)]; (a) CRP, change in mean values: 0.17, p-value =0.783; (b) PASI, change in mean values: -10.67, p-value <0.001; (c) BMI, change in mean values: 0.04, p-value =0.882 (d) DLQI, change in mean values: -9.79, p-value <0.001; (e) Overall physical activity, change in mean values: 383.51, p-value =0.004. N=39.

Figure 2: Final results of 52 weeks follow-up [comparison between baseline visit and visit 2 (V2)]; (a) CRP, change in mean value: -1.17, p-value =0.003; (b) PASI, change in mean value: -18.37, p-value <0.001; (c) BMI, change in mean value: -0.27, p-value =0.358; (d) DLQI, change in mean value: -15.25, p-value <0.001; (e) Overall physical activity, change in mean value: 808.60, p-value <0.001. N=32.

Figure 3: Changes in physical activity profile of patients in baseline (BL) and visit 2 (V2) [52 weeks follow-up].

DISCUSSION

Lifestyle interventions such as physical activity seem to improve the therapeutic effect of biologic psoriasis treatment even more. The preliminary and the final results confirm the initial purpose of the study, indicating with statistically significant results that the remarkable, rapid improvement of psoriasis and the maintenance of the outcome in the long-term treatment with brodalumab is enhanced in patients with increased physical activity and also affects the lifestyle habits as a therapeutic add-on, maintaining the good clinical result even more. Although at 12 weeks of treatment the improvement in PASI, DLQI, IPAQ and exercise hours were remarkably noticeable, at one year of treatment the result was even more impressive with a statistically significant improvement also in the inflammatory index as measured by CRP, showing maintenance of the long-term effectiveness of the drug but also the progressive and cumulative effect of physical activity on psoriasis and the general health of patients. One year after initiating treatment with brodalumab, patients maintained the improvement in psoriasis, in quality of life, in inflammatory index, in physical activity, keeping their Body Mass Index (BMI) unchanged (small decrease but not statistically significant) as reflected by statistical analysis and the clinical picture of them. It is also very interesting that in the period of 52 weeks, the patients' physical activity was improved both visibly and statistical significantly, and a "movement" of patients from the level of mild exercise to moderate was observed, while those who exercised intensely remained in the same category (Fig. 3).

One of the study key limitations is the relatively low sample size, which did not allow for more complex comparisons or fitting of regression models, along with the factors that could condition the variations according to the physical activity index, such as age, weight or toxic habits. However, the site is considered one of the reference hospitals for plaque psoriasis in Greece and every effort was made to minimize the amount of missing data, despite the non-interventional nature of the study.

The association between real-world treatment effectiveness and physical activity along with the pathophysiological mechanism of the potential impact of physical activity on the therapeutic effect is an interesting field to be explored. The study results indicate the need for the conduct of larger-scale, multicenter studies to evaluate the potential relationship between physical activity and clinical outcomes for patients with plaque psoriasis, possibly using other lifestyle interventions as well that affect psoriasis and patients' daily lives.

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REFERENCES

1. Tsoukalas D, Sarandi E, Thanasoula M. Non communicable diseases in the era of precision medicine: an overview of the causing factors and prospects. In: Koukios E, Sacio-Szymanska A (eds) Bio # Future Springer, Cham, 2021; 275-299 http://doi.org/10.007/978-3-030-64969-2_13.
2. Foulkes AC, Warren RB. Brodalumab in psoriasis evidence to date and clinical potential. *Drugs Context*, 2019; 8: 212570.
3. Zheng J, Luo S, Huang Y, Lu Q. Critical role of environmental factors in the pathogenesis of psoriasis. *J Dermatol*, 2017; 44(8): 863-872.
4. Schmitt-Egenolf M. Physical activity and lifestyle improvement in the management of psoriasis. *Br J Dermatol*, 2016; 175(3): 452-453.
5. Wilson PB, Bohjanen KA, Ingraham SJ, Leon AS. Psoriasis and physical activity: a review. *J Eur Acad Dermatol Venereol*, 2012; 26(11): 1345-1353.
6. Mallat Z, Gojova A, Brun V, Esposito B, Fournier N, Cottrez F, Tedgui A, Groux H. Induction of a regulatory T cell type 1 response reduces the development of atherosclerosis in apolipoprotein E knockout mice. *Circulation*, 2003; 108(10): 1232-1237.
7. Qu HX, Guo BB, Liu Q. Regulatory T cells as a new therapeutic target for atherosclerosis. *Acta Pharmacol Sin*, 2018; 39(8): 1249-1258.
8. Foks AC, Lichtman AH, Kuiper J. Treating atherosclerosis with regulatory T-cells. *Artenoscler Thromb Vasc Biol*, 2015; 35(2): 280-287.
9. Weinhold M, Shimadoukuro-Vornhagen A, Franke A, Theurich S, Wahl P, Hallek M, Schmidt A, Schinkothe T, Mester J, von Bergwelt-Baildon M, Bloch W. Physical exercise modulates the homeostasis of human regulatory T cells. *J Allergy Clin Immunol*, 2016; 137(5): 1607-1610.

10. Sharif K, Watad A, Bragazzi NL, Lichtbroun M, Amital H, Shoenfeld Y. Physical activity and autoimmune diseases: get moving and manage the disease. *Autoimmunity Reviews*, 2018; 17(1): 53-72.
11. Lrincz K, Haluszka D, Kiss N, Gyongyosi N, Banvolgyi A, Szipocs R, Wikonkal NM. Voluntary exercise improves murine dermal connective tissue status in high-fat diet induced obesity. *Arch Dermatol Res*, 2017; 309(3): 209-215.
12. Edwards MK, Blaha MJ, Loprinzi PD. Influence of sedentary behavior, physical activity and cardiorespiratory fitness on the atherogenic index of plasma. *J Clin Lipidol*, 2017; 11(1): 119-125.
13. Flood A, Waddington G, Cathcart S. Examining the relationship between endogenous pain modulation capacity and endurance exercise performance. *Res Sports Med*, 2017; 25(3): 300-312.
14. Pence BD, Woods JA. Exercise, obesity and cutaneous wound healing: evidence from rodent and human studies. *Adv Wound Care*, 2014; 3(1): 71-79.
15. Zheng G, Qiu P, Xia R, Lin H, Ye B, Tao J, Chen L. Effect of aerobic exercise on inflammatory markers in healthy middle aged and older adults: a systematic review and meta-analysis of randomized controlled trials. *Front Aging Neurosci*, 2019; 11: 98.
16. Soyland E, Heier I, Rodriguez-Gallego C, Mollnes TE, Johansen F-E, Holven KB, Halvorsen B, Aukrust P, Jahnsen FL, de la Rosa Carrillo D, Krogstad A-L, Nenseter MS. Sun exposure induces rapid immunological changes in skin and peripheral blood in patients with psoriasis. *Br J Dermatol*, 2011; 164(2): 344-355.
17. Papathanasiou G, Georgoudis G, Papandreou M, Spyropoulos P, Georgakopoulos D, Kalfakakou V, Evangelou A. Reliability measures of the short International Physical Activity Questionnaire (IPAQ) in Greek young adults. *Hellenic J Cardiol*, 2009; 50(4): 283-294.