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ABOUT COVER

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AIM AND SCOPE

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ORIGINAL ARTICLE

Observational Study

Outcomes assessment of hepatitis C virus-positive psoriatic patients treated using pegylated interferon in combination with ribavirin compared to new Direct-Acting Antiviral agents

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Author contributions: Damiani G and Pigatto P designed the research; Franchi C, Pigatto P and Pacifico A performed the research; Damiani G analyzed the data; Altomare A and Pace MC supervised the manuscript; Petrou S revised the manuscript in order to improve and polish language; Damiani G, Leone S and Fiore M wrote the paper.

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Abstract

AIM

To evaluate the outcomes in biological treatment and quality of life of psoriatic patients with chronic hepatitis C (CHC) treated with new Direct-Acting Antiviral agents (DAAs) compared to pegylated interferon-2α plus ribavirin (P/R) therapy.

METHODS

This is a retrospective study involving psoriatic patients in biological therapy who underwent anti-hepatitis C virus (HCV) treatment at the Department of Dermatology Galeazzi Orthopaedic Institute Milan, Italy from January 2010 to November 2017. The patients were divided into two groups: patients that underwent therapy with DAAs and patients that underwent HCV treatment with P/R. Patients were assessed by a dermatologist for psoriasis symptoms, collecting Psoriasis Area Severity Index (PASI) scores and the Dermatology Quality of Life Index (DLQI). PASI and DLQI scores were evaluated 24 wk after the end of HCV treatment and were assumed as an outcome of the progression of psoriasis. Switching to a different bDMARD was considered as an inadequate response to biological therapy. The dropout of HCV therapy and sustained virological response (SVR) were considered as outcomes of HCV therapy.

RESULTS

Fifty-nine psoriatic patients in biological therapy underwent antiviral therapy for CHC. Of this, 27 patients were treated with DAAs and 32 with P/R. After 24 wk post treatment, the DLQI and the PASI scores were significantly lower ($P < 0.001$ and $P < 0.005$, respectively) in the DAAs group compared with P/R group. None of the patients in the DAAs group (0/27) compared to 8 patients of the P/R group (8/32) needed a shift in biological treatment.

CONCLUSION

DAAs seem to be more effective and safe than P/R in HCV-positive psoriatic patients on biological treatment. Fewer dermatological adverse events may be due to interferon-free therapy.

Key words: Hepatitis C virus; New Direct-Acting Antiviral agents; Psoriasis; Biological disease modifying drugs

Core tip: Psoriasis is a chronic inflammatory disease affecting approximately the 2% of population in Europe and North America. The hepatitis C virus (HCV) infection affects approximately the 3% of the world population with an estimated prevalence of 5 million people in the United States. Up to 0.06% of people in the United States suffer from both psoriasis and HCV. Psoriatic patients with HCV are excluded by randomized controlled clinical trials. Therefore, no data is currently available concerning the concomitant administration of biological disease modifying drugs and the new Direct-Acting Antiviral agents (DAAs) medications approved for the treatment of HCV infection. The aim of this study is to evaluate the outcomes in biological treatment and quality of life of psoriatic patients with HCV infection treated with DAAs compared to the previous standard therapy of Pegylated Interferon plus Ribavirin.

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INTRODUCTION

Psoriasis is a chronic systemic inflammatory disease affecting approximately 2% of the population in Europe and North America with approximately 7.5 million people in the United States[1,2]. Hepatitis C virus (HCV) is an infection affecting approximately 71 million people worldwide; the most affected regions being WHO Eastern Mediterranean and European Regions with a prevalence of 2.3% and 1.5%[3]. Prevalence of HCV infection in other WHO regions varies from 0.5% to 1.0%[3]. According to the Centers for Disease Control and Prevention, there are currently about 3.3 (2.7-3.9) million people with chronic hepatitis C (CHC) in the United States[4]. The estimated prevalence of both psoriasis and HCV in the United States is 0.02%-0.06% (55000-150000 persons)[5].

The pathogenesis of psoriasis remains unclear, however Th1/Th17 autoimmune involvement has been hypothesized[6]. Its association with HCV is still a matter of debate. Some evidence suggests that psoriasis may be initiated and maintained by both HCV and interferon-α[7]. In a large case-control study, including 12502 psoriatic patients and 24287 controls, the prevalence of HCV in psoriatic patients was increased compared to controls (1.03% *vs* 0.56%; $P < 0.001$)[8].

The therapeutic armamentarium available for psoriasis encompasses the conventional disease modifying drugs (cDMARDs) and biological DMARDs (bDMARDs). cDMARDS represent the first line therapy in high-need psoriatic patients, while bDMARDs are for those subjects in whom cDMARDs have either failed, were not tolerated, or were contraindicated[9]. While bDMARDs are generally safer than cDMARDs, there is one concern emerging from registries or long-term studies which is an increased risk of infection. When patients lose an adequate response to bDMARDs the possible options include increasing the dose, shortening the dosing interval, combination therapy with a topical or another systemic treatment, or switching to a different drug[10].

Recently, the standard of care for CHC has changed. The new Direct-Acting Antiviral agents (DAAs) such as Sofosbuvir, Daclatasvir and the Sofosbuvir/Ledipasvir

combination are now part of the preferred regimens in the WHO guidelines and can achieve cure rates above 95%[3]. These agents are much more effective, safer and better-tolerated than older therapies involving pegylated interferon and ribavirin (P/R) which nowadays play a very limited role for specific scenarios[3]. Of the 71 million persons living with CHC globally in 2015, 20% (14 million) knew their diagnosis and 7.4% of those diagnosed (1.1 million) were started on treatment[3].

Psoriatic patients with CHC are excluded by randomized controlled clinical trials. Data on psoriatic patients with HCV infection treated with bDMARDs is available solely on the reports of single cases or analyses of small groups of patients. Therefore, no data is currently available concerning the concomitant administration of bDMARDs for psoriasis and the new DAAs approved for the treatment of CHC[9].

The aim of this study is to evaluate the disease progression and outcomes in biological treatment and quality of life of HCV psoriatic patients on bDMARDs also treated with new DAAs compared to P/R therapy.

MATERIALS AND METHODS

Study population

This is an observational analysis performed by checking all psoriatic patients admitted to the Department of Dermatology and Venereology of I.R.C.C.S. Istituto Ortopedico Galeazzi (Milan, Italy) after 2007. Furthermore, in the present study we collected only HCV positive psoriatic patients admitted in our department from 2010 until now undergoing biological therapy. The study complies with the Declaration of Helsinki and all patients signed a standard consent regarding sensitive personal data treatment.

Study design

The present study is a spin-off observational retrospective study on HCV psoriatic patients, resulted as re-analysis of a previous study towards the re-circulation of CD4+ memory T-cells in psoriatic patients, approved by the Institutional Review Board (Comitato Etico dell'Ospedale San Raffaele, Milano)[11]. This previous study had as exclusion criterion the absence of acute and chronic systemic or cutaneous infections during sample collections[11], conversely we enrolled the previously discarded HCV psoriatic patients, focusing on their HCV eradication management. The subjects were divided into two groups: (1) Patients that underwent therapy with DAAs (DAA-group) (2) patients that underwent HCV treatment with P/R (P/R-group). Patients were assessed by a dermatologist for psoriasis symptoms, collecting Psoriasis Area Severity Index (PASI) and Dermatology Quality of Life Index (DLQI). They were also assessed by a hepatologist to determine liver function while collecting biochemical and clinical data in two times: Baseline (before HCV treatment) (T0) and 24 wk after the end of HCV treatment (T1). The data was extracted to monitor psoriasis biological therapy and HCV therapy[12,13].

Inclusion criteria

Inclusion criteria were age > 18 years old, signed consent forms, no previous transplantation, no pregnancy, no hereditary hepatic diseases, no drug addiction, and no alcohol abusers [Alcohol Use Disorders Identification Test (AUDIT) score < 7], negative results at screening tuberculosis, absence of acute and chronic systemic or cutaneous infections during sample collection. Psoriasis diagnosis was performed by a Dermatologist following the Psoriasis Italian Guidelines[10], and the diagnosis of CHC according the WHO guidelines[14].

Exclusion criteria

Exclusion criteria were age < 18 years old, pregnancy, drug addiction, alcohol abusers [Alcohol Use Disorders Identification Test (AUDIT) score > 7], HIV infection.

Outcomes of the study

PASI, DLQI were evaluated 24 wk after the end of HCV treatment (T1) and were assumed as an outcome of the progression of psoriasis. Switching to a different bDMARD was considered as inadequate responses to biological therapy. The dropout of HCV therapy, and sustained virological response (SVR) were considered as outcomes of HCV therapy.

Data collection and variables definitions

Baseline clinical characteristics, medical history, biochemical variables, and pharmacologic treatments employed during hospitalization were retrospectively collected and recorded on a computer database. SVR was defined as a confirmed undetectable serum HCV-RNA level 24 wk after the discontinuation of HCV therapy. Patients not fulfilling the SVR definition criteria were classified as non-SVR.

Statistical analysis

Continuous variables are presented as mean ± SD and categorical variables are presented as absolute values and percentages. Comparisons between continuous variables were performed using Mann–Whitney or Kruskall–Wallis tests and comparisons between categorical variables were performed using the χ^2 or Fisher's exact test. Statistical significance was defined as $P < 0.05$. Data analysis was performed using statistical software R-version 3.2.4.

RESULTS

A total of 59 psoriatic patients met the inclusion criteria (27 in the DAA-group and 32 in the P/R-group) and were included in this analysis. The patients' main characteristics are summarized in Table 1. All the patients in the P/R-group were treated with pegylated interferon-2α plus ribavirin; in the DAA-group 25 patients (92.6%) were treated with Sofosbuvir plus Daclatasvir, 1 patient was treated with Sofosbuvir + ribavirin: 1 (3.7%) and 1 patient (3.7%) was treated with Sofosbuvir plus simeprevir plus ribavirin. The median age was 56.7 ±

Table 1 Levels of sIL-2R, ALT, and HBV DNA in the sera of patients with chronic hepatitis B virus infection (mean ± SD)

	DAA-group	P/R-group
Age, yr, mean ± SD	56.7 ± 8.9	58.2 ± 6.7
Male/female, *n* (%)	18/9 (66.7/33.3)	24/8 (75/25)
BMI, mean ± SD, kg/m^2	24.3 ± 2.41	25 ± 1.86
Psoriasis duration, yr, mean ± SD	21.5 ± 8.6	18 ± 6.7
Current biological therapy, *n* (%)		
Etanercept	12 (44.4)	15 (46.9)
Adalimumab	9 (33.3)	10 (31.3)
Infliximab	-	-
Ustekinumab	5 (18.5)	7 (21.9)
Secukinumab	1(3.7)	-
Shifted biological drugs, mean ± SD	1.2 ± 0.3	1.5 ± 0.5
Psoriatic arthritis, *n* (%)	2 (7.4)	3 (9.4)
HCV		
Genotype, *n* (%)		
1	21 (77.8)	29 (90.6)
2	5 (18.5)	1 (3.1)
3	-	2 (6.3)
4	1 (3.7)	-
5/6	-	-
MELD score	9.3 ± 2.5	6,5 ± 0.8
HCV viral load (T0), IU/mL, mean ± SD	6.2 log10 ± 5.7 log10	6.1 log10 ± 6.0 log10
SVR, *n* (%)	27/27 (100)	12/32 (37.5)
Autoimmune comorbidities, *n* (%)		
Rheumatic arthritis	1 (3.7)	-
Ankylosing spondylitis	-	1 (3.1)
Systemic erythematosus lupus	1 (3.7)	-
Other comorbidities, *n* (%)		
Cardiovascular disease	6 (22.2)	3 (9.4)
Metabolic syndrome	2 (7.4)	1 (3.1)
COPD	5 (18.5)	2 (6.3)
Renal insufficiency	0 (0)	0 (0)
HBV	1 (3.7)	1 (3.1)
	0 (0)	0 (0)

Categorical variables are expressed as *n* (%). Numeric variables are expressed as median and SD. BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; DAA: New Direct-Acting Antiviral agent; HBV: Hepatitis B virus; HCV: Hepatitis C virus; P/R: Pegylated interferon-2α plus ribavirin; MELD: Model for end-stage liver disease; SVR: Sustained virological response.

8.9 years in the DAA-group and 58.2 ± 6.7 years in the P/R-group, respectively; 66.7% patients were men in the DAA-group and 75% patients were men in the P/R-group, respectively. The median body mass index (BMI) was 24.3 ± 2.41 in the DAA-group and 25 ± 1.86 in the P/R-group, respectively. The median psoriasis duration was 21.5 ± 8.6 years in the DAA-group and 18 ± 6.7 years in the P/R-group, respectively. In the DAA-group the bDMARD used, was Etanercept, Adalimumab, Ustekinumab and Secukinumab in 12 (44.4%), 9 (33.3%), 5 (18.5%), and 1 (0.04%) patients, respectively; in the P/R-group the bDMARD used, was Etanercept, Adalimumab and Ustekinumab in 15 (46.9%), 10 (31.3%) and 7 (21.9%) patients, respectively. Switching among biologic therapies, before hepatitis C treatment, was 1.2 ± 0.3 in DAA-group and 1.5 ± 0.5 in P/R-group. Two patients (7.4%) of the DAA-group and 3 patients (9.4%) of the P/R-group presented psoriatic arthritis, respectively. In the DAA-group the HCV genotypes were 1, 2 and 4 in 21 (77.8%), 5 (33.3%) and 1 (3.7%) patients, respectively; in the P/R-group the HCV genotypes were 1, 2 and 3 in 29 (90.6%), 1 (3.1%) and 2 (6.3%) patients, respectively. The MELD score was 9.3 ± 2.5 in DAA-group and 6.5 ± 0.8 in the P/R-group, respectively. The viral load at the baseline was 6.2 $\log_{10}$ ± 5.7 $\log_{10}$ UI/mL in the DAA-group and 6,1 $\log_{10}$ ± 6.0 $\log_{10}$ UI/mL in the P/R-group, respectively. All the 27 patients (100%) in the DAA-group obtained SVR, whereas only 37.5% (12/32) of patients in the P/R-group achieved a SVR. Two out of 27 patients of DAA-group had autoimmune comorbidities: 1 (3.7%) rheumatic arthritis and 1 (3.7%) systemic erythematosus lupus; 1 (3.1%) out of 32 patients of P/R-group had autoimmune comorbidity: ankylosing spondylitis. In the DAA-group other comorbidities were cardiovascular diseases, metabolic syndrome, chronic obstructive disease, and HBV in 6 (22.2%), 2 (7.4%), 5 (18.5), 1 (3.7%) patients, respectively. In the P/R-group other comorbidities were cardiovascular diseases, metabolic syndrome, chronic obstructive disease, and HBV in 3 (9.4%), 1 (3.1%), 2 (6.3%), 1 (3.1%) patients, respectively. None of the 59 psoriatic patients enrolled in the study had renal insufficiency.

The comparison between the patient scores and laboratories findings according to HCV eradication treatment is shown in Table 2: There were no differences in PASI scores between the 2 HCV treatment groups; after 24 wk to the end of the HCV treatment there

Table 2 Levels of sIL-2R, ALT, and HBV DNA in the sera of patients with chronic hepatitis B virus infection (mean ± SD)

	DAA-group	P/R-group	*P* value
PASI (T0), mean ± SD	11.6 ± 5.2	9.4 ± 3.5	-
PASI (T1), mean ± SD	5.2 ± 1.6	8.3 ± 4.5	< 0.005
Biological treatment shifts, *n* (%)	-	8 (25)	< 0.001
Topical treatments (T0), *n* (%)	27 (100)	32 (100)	-
Topical treatments (T1), *n* (%)	27 (100)	32 (100)	-
DLQI (T0), mean ± SD	13 ± 2.3	12 ± 3.1	-
DLQI (T1), mean ± SD	4.2 ± 2.3	11 ± 2.3	< 0.001
HCV treatment details, *n* (%)	Sofosbuvir + daclatasvir: 25 (92.6) Sofosbuvir + simeprevir + ribavirin: 1 (3.7) Sofosbuvir + ribavirin: 1 (3.7)	Pegylated interferon-2α + ribavirin 32 (100)	-
Laboratory tests, mean ± SD			
T0			
ALT	45.6 ± 16.5	43 ± 9.2	-
AST	54.6 ± 5.51	52.4 ± 12.5	-
GGT	42.0 ± 13.59	43.3 ± 14.6	-
T1			
ALT	42.21 ± 12.4	43 ± 8.5	-
AST	51.3 ± 4.2	51.9 ± 8.9	-
GGT	40.8 ± 12.2	42.9 ± 14.1	-
Dropout HCV-treatment, *n* (%)	0/27 (0)	9/32 (28.1)	< 0.005
SVR, *n* (%)	27/27 (100)	12/32 (37.5)	< 0.005

Categorical variables are expressed as *n* (%), and compared by χ^2 or Fisher's exact test. Numeric variables are expressed as median and SD, and compared by Mann–Whitney or Kruskall–Wallis tests. Statistical significance was considered as a *P*-value of < 0.05. DAA: New Direct-Acting Antiviral Agent; P/R: Pegylated interferon-2α plus ribavirin; PASI: Psoriasis Area Severity Index; T0: Baseline time (before starting the hepatitis C eradication treatment); T1: Six months after the end of hepatitis C eradication treatment; DLQI: Dermatology Quality of Life Index; HCV: Hepatitis C virus; SVR: Sustained virological response; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyl transferase.

was a significant reduction of PASI score in DAA-group when compared to P/R-group patients ($P < 0.005$). Patients in the P/R-group (8 patients, 25%) need a significantly ($P < 0.001$) frequent change of biological treatment compared to DAA-group (no patients). There was no difference in the use of topical treatments in the 2 groups at baseline (100% in both groups) and after 24 wk to the end of the HCV treatment (100% in both groups). Although there was no difference in the DLQI at the beginning of the treatment in the 2 groups, after 24 wk the DLQI was significantly improved in the DAA-group when compared to P/R-group patients ($P < 0.001$). HCV treatment was significantly better tolerated ($P < 0.005$) by DAA-group patients with no dropout; 9 out of 32 P/R-group patients (28.1%) dropped out of HCV treatment. HCV eradication was significantly higher ($P < 0.005$) in DAA-group compared to P/R-group: SVR was obtained in 100% (27/27) of patients treated with DAAs and in 37.5% (12/32) of patients treated with P/R. Three Adverse Drug Events (ADEs) were observed in DAA-group patients during HCV treatment. Two of the patients experienced fatigue and one experienced insomnia. Fifteen of the thirty-two patients of the P/R-group experienced ADEs during HCV treatment. Ten experienced fatigue with nausea, three diarrhea and two cefalea.

DISCUSSION

In our study, psoriatic patients of the DAA-group had a better prognosis compared to the P/R-group, both in progression of psoriasis (and consequent worsening of quality of life) and in eradication of HCV. Patients with a worse prognosis treated with P/R could be attributed to two possible causes: (1) Interferon "itself" has dermatological side effects[15], worsening psoriasis and (2) DAAs are more effective than interferon-based therapy increasing the rates of SVR (even up to 100%)[16], suggesting that HCV could promote psoriatic disease.

Eradication treatment of HCV with interferon has been described as the drug that can induce *de novo* psoriasis or flares in psoriatic patients[17-19]. The flare usually occurs one to 6 wk after starting interferon-α and may lead to its discontinuation[20].

There appears to be an intricate relationship between psoriasis and HCV infection as seen in previous reports. HCV in predisposed individuals upregulates cathelecidin, Toll like receptor 9 (TLR-9) and interferon (IFN)-γ which are all involved in the development of psoriasis plaques. Pegylated interferon may also initiate and maintain psoriasis inflammation by activating Th1 and Th17 *via* myeloid DCs[7,21]. Cathelecidin bonds self-DNA. It is released after various injury stimuli *via* TLR-9 plasmacytoid and DCs to produce type I interferons (α/β), which drives T-cell polarization towards Th1 and Th17 *via* myeloid DCs. This initiates the trigger and further maintenance of psoriasis[7]. Likewise, pegylated interferon may act directly *via* myeloid resident DCs on Th1 cells and also on Th17 cells at the same time by increasing their activation and release of IL-17. IL-17 is a chemo-attractant for neutrophils to the skin and IL-22 causes keratinocyte hyperproliferation[21]. Despite these preliminary hypotheses, data regarding the association of HCV and psoriasis remain unclear and a matter of

debate. Some studies show no association[22] while others show an increased prevalence of psoriasis among HCV-patients as reported by Cohen[8]. Furthermore, limited data is present in literature regarding psoriasis induction and exacerbation due to interferon in HCV-psoriatic patients[21].

Experimental studies have shown that an intradermal injection of IFN-γ, both on the non-lesional psoriatic and healthy skin, causes an elevation of inflammatory products such as TNF, IL-23 and inducible nitric oxide synthase which are characteristic of psoriatic plaques[23]. An association between HCV infection and psoriasis has been suggested. The prevalence of HCV in psoriatic patients was increased compared to controls (1.03% *vs* 0.56%; $P < 0.001$)[8]. In a single center cross-sectional study conducted in a Japanese university hospital, the frequency of HCV infection was significantly higher in psoriatic (7.5%) than in non psoriatic patients (3.3%) in overall ages[24]. Interestingly, when stratified by age at the first visit, HCV infection frequency was significantly higher in patients with psoriasis than in controls aged over 60 years (11.8% *vs* 6.6%, respectively, $P = 0.0215$) and 70 s (19.5% *vs* 7.3%, $P < 0.0001$)[24]. Psoriatic patients with CHC were significantly older at onset than non psoriatic CHC patients (median, 54 *vs* 39 years)[24]. There was also a stronger male predominance (male/female ratio, 4.4:1), similar family history of psoriasis, higher association of diabetes mellitus and hypertension, and significantly lower body mass index, in an age-stratified (≥ 40 years) analysis[24]. Psoriatic patients with CHC were less obese, but still had a higher frequency of diabetes mellitus and hypertension[24]. The authors hypothesized that psoriasis and HCV have pathophysiological factors in common with both mediated by proinflammatory cytokine tumor necrosis factor (TNF-α)[24]. In HCV infection, continuous inflammation mediated by TNF-α leads to liver cirrhosis and diabetes mellitus[24]. The link between psoriasis and HCV infection has been shown experimentally in a recent study of Chun *et al*[7]; the authors performed two 2 mm punch biopsies of lesional and nonlesional skin in 10 patients who were HCV-negative psoriatic and 7 HCV-positive psoriatic patients. The biopsies were used to measure cathelicidin, TLR9 and IFNc mRNA expression by quantitative reverse-transcriptase polymerase chain reaction (qRT-PCR)[7]. The mRNA expression was calculated relative to the housekeeping gene glyceraldehyde-3-phosphate dehydrogenase (GAPDH) and demonstrated that the cutaneous levels of inflammatory genes in HCV positive psoriatic patients are higher than the levels in patients with only psoriasis[7]. The increased cutaneous levels of cathelicidin, TLR9 and IFNc of HCV-positive psoriatic patients as compared to HCV-negative psoriatics suggest that HCV infection may predispose patients to developing psoriasis[7]. These findings seem to be confirmed clinically due to the worse prognosis of psoriasis in HCV-positive patients[7,25]. The mean PASI score is significantly higher in cohorts of patients affected with hepatitis C than those with psoriasis alone[7,25].

In line with previous studies, our study confirmed that bDMARDs are safe in psoriatic patients with HCV infection[26-29]. In literature bDMARDs are safe either in psoriatic patients with HCV infection and past HBV infection[30]. Patients in the DAA-group had a significantly better response to bDMARDs compared to P/R-group, requiring a smaller transition to different bDMARDs[10]. This may be due to a more favorable outcome in psoriasis (due to interferon-free therapy and greater HCV eradication), but also due to intrinsic DAAs action[31]; Immune reconstitution occurs in patients with whom HCV was successfully eradicated *via* DAAs therapy[31]. Restoration of the CD4+ T-cell compartment in the peripheral blood and a re-differentiation of the T lymphocyte memory compartment resulted in a more effector memory T cell population and a reduction in expression of the co-inhibitory molecule TIGIT in bulk T lymphocytes[31]. Burchill *et al*[31] observed a partial reversal of the exhausted phenotype in HCV-specific CD8+ T cells and a dampening of the activation state in peripheral NK cells. Spaan *et al*[32] showed that viral load decline, as a consequence of DAAs therapy in patients with chronic hepatitis C infection, reduces serum levels of NK cell-stimulating cytokines and causes correction of the altered NK cell phenotype observed in chronic HCV patients. CHC is characterised by innate immune activation with increased interferon-stimulated gene expression and by an altered phenotype of interferon-responsive natural NK cells[33]. DAAs treatment could improve the pro-inflammatory status due both to psoriasis and to the HCV infection making bDMARDs actions more effective.

The current study contains some limitations that need to be taken into account. This is a retrospective observational study conducted in a single Italian centre, thus our conclusions should be interpreted with caution and cannot be generalized to all HCV-positive psoriatic patients. In particular, a general under-reporting of toxicity, as with all observational studies, is possible. Another limitation is the small sample size and the relatively short follow-up. This is the first study to compare DAAs to P/R for the management of HCV-positive psoriatic patients and unmeasured confounding variables could influence our findings. Thus, larger series with long-term follow-up are required to confirm this preliminary data.

In conclusion, new DAAs are more effective than P/R in the eradication of HCV and the control of symptoms in psoriatic patients with CHC. Future studies are needed to evaluate the effects of DAAs in this clinical setting, which may further aid in elucidating the etiologic and pathogenetic mechanism of psoriasis.

ARTICLE HIGHLIGHTS

Research background

Up to 0.06% of people suffer from both psoriasis and hepatitis C virus (HCV). Psoriatic patients with HCV are excluded by randomized controlled clinical trials.

Research motivation
No data is currently available concerning the concomitant administration of biological drugs and the medications approved for the treatment of HCV infection, as new Direct-Acting Antiviral agents (DAAs).

Research objectives
Evaluate the outcomes in biological treatment and quality of life of psoriatic patients with chronic hepatitis C (CHC) treated with new DAAs compared to pegylated interferon-2α plus ribavirin (P/R) therapy.

Research methods
Psoriatic patients, in biological therapy, who underwent anti-HCV treatment were retrospectively reviewed. The patients were divided into two groups: patients that underwent therapy with DAAs and patients that underwent HCV treatment with P/R. Patients were assessed for Psoriasis Area Severity Index (PASI) scores and the Dermatology Quality of Life Index (DLQI) switching to a different bDMARD, dropout of HCV therapy and sustained virological response (SVR).

Research results
Twenty-seven patients were treated with DAAs and thirty-two with P/R. At three months, after completion of antiviral therapy, the DLQI and the PASI scores were significantly lower ($P < 0.001$ and $P < 0.005$, respectively) in DAAs group compared with P/R group. None of the patients in the DAAs group compared to the eight patients of the P/R group needed a change in biological treatment.

Research conclusions
DAAs seem to be more effective and safe than P/R in HCV-positive psoriatic patients on biological treatment.

Research perspectives
This is the first study which evaluated the HCV treatment of psoriatic patients on biological agents. Future studies are needed to evaluate the effects of DAAs in this clinical setting, which may further aid in elucidating the etiologic and pathogenetic mechanism of psoriasis.

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