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SHORT COMMUNICATION

A Retrospective Study of Patients with Psoriasis Treated with Biologics: Relation to Body Mass Index and Gender

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Several biologic agents have been used for the treatment of moderate-to-severe plaque psoriasis in which the Psoriasis Area Severity Index (PASI) and/or Dermatology Life Quality Index (DLQI) and/or body surface area (BSA) are ≥ 10. At the time of this study, there were 4 licensed biologics in use in Europe, of which, 3 were tumour necrosis factor (TNF) inhibitors (etanercept, adalimumab and infliximab). The adult dosage for etanercept and adalimumab are fixed, whereas infliximab and ustekinumab are adjusted according to weight (1). Direct and indirect comparative efficacies were assessed by random effects meta-analysis of risk differences (RDs) of 48 randomized controlled trials. Infliximab showed the highest efficacy (RD 76%), followed by ustekinumab 90 mg (RD 67%), ustekinumab 45 mg (RD 63%) and adalimumab (RD 61%). Etanercept (RD 44%) was less efficacious than the previously mentioned treatments (2).

The relationship between obesity and psoriasis has also been the subject of discussion for many decades. It was noted first in a Swedish study of 159,200 citizens over 10 years that obese patients had a higher risk of developing psoriasis (3). Subsequent studies suggested an association between higher body mass index (BMI) and increased severity of psoriasis (4). In addition, patients with higher body weight may also show compromised effect of some systemic and biological treatments in comparison with their normal weight counterparts (5). Naldi et al. even suggested that weight loss through diet and exercise might help improve psoriasis in systemically treated overweight patients (6, 7). Furthermore, anti-TNF-α may increase appetite and induce weight gain, which might be persistent (8, 9). No similar association has been found between gender and treatment outcome in psoriasis patients receiving biologics (10).

The aim of the present study was to investigate these factors in the response to biologics in our cohort of Swedish psoriasis patients.

MATERIALS AND METHODS

A register study was initiated on psoriasis patients receiving biologics who were attending dermatology clinics at Sahlgrenska University Hospital, Gothenburg, Sweden. The data were extracted from PsoReg (a web-based national register for psoriasis patients on systemic treatment, founded in 2007) of all enrolled patients from our clinic who were currently taking, or had previously received, biologics in any time period since biologics were introduced at our department until the beginning of 2014 (11). In case of missing values from PsoReg we used patients' records to check and complete the data. Patients lacking any registered PASI value were then excluded. The values of concern were age, gender, type of treatment, treatment dose in each visit, type of psoriasis, PASI, BMI, DLQI and, if applicable, concurrent methotrexate (MTX) treatment for each patient. The studied period was then narrowed down to the first 2 years in each treatment round in order to focus on the main objective of the study. A treatment round consists of a baseline (–3 months) and several consecutive values at 3 months (± 1 month), 6 months (± 2 months), 12 months (± 2 months), 18 months (± 2 months) and 24 months (± 3 months). Any interruption of treatment longer than 4 months was considered a new treatment round, as patients on biologics, even those with a long half-life, such as ustekinumab, were noted to have a mean relapse time of 16 weeks (12). A single patient could have several treatment rounds in different periods with different biologics. If a treatment round was the first in which the patient had a biological medication, then the treatment round was referred to as "naïve". PASI values were transformed with the logarithmic transformation log(1+PASI) in order to make them more normally distributed.

The study was approved by the ethics committee at the University of Gothenburg, Sweden.

Mixed effects multiple linear regression models were used with $\log(1+PASI_{baseline})$ and the differences $\log(1+PASI_T) - \log(1+PASI_{baseline})$, where T is, 3, 6 and 24 months as the dependent variables. The unit of analysis is the treatment round and a random intercept for each patient was used. The independent variables were "type of biologic" (etanercept, adalimumab, infliximab or ustekinumab), "sex" (male/female), "age" (in years), "BMI" (body mass index in kg/m^2) and whether the patient had had biological treatment before (naïve or non-naïve treatment round).

All tests were 2-sided and $p < 0.05$ was considered statistically significant. All data were analysed using R version 3.0.3.

RESULTS

A total of 98 patients were included in the study, with 138 treatment rounds with registered PASI at baseline. The male:female ratio was 4:1. The mean PASI baseline values for women vs. men and for naïve vs. non-naïve treatment rounds are shown in Fig. S1[1].

A mixed effects multiple linear regression model with $\log(1+PASI_{baseline})$ as the dependent variable showed a significant dependence on sex ($p = 0.005$) and type of treatment round (naïve/not naïve) ($p = 0.0002$), but no significant dependence on the type of biologic, concurrent MTX, age or BMI (Table SI[1]).

Mixed effects multiple linear regression models with $\log(1+PASI_T)$–$\log(1+PASI_{baseline})$ for T = 3, 6 and 24 months as the dependent variable showed a significant dependence on type of treatment round (naïve/not naïve) ($p = 0.005$ for T = 3 months, $p = 0.004$ for T = 6 months and $p = 0.024$ for T = 24 months), but no significant dependence on sex, type

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of biologic, age or BMI (Table SI[1]). Change of PASI score (%) during treatment in both naïve and non-naïve group for each medication is shown in Table SII[1] and Fig. 1.

DISCUSSION

In our biologics-receiving patient group, there was a clear male dominance. Similar male dominance was also noted in a Danish nationwide database DERMBIO study, where male sex was associated with longer drug survival (13). The possibility of pregnancy in women of child-bearing age might be a reason for reduced usage of biologics in women. With regards to response to biologics, gender was not a predicting factor to response, either in our study or in other larger meta-analysis (10). On the other hand, naïvety to biologics was an important factor, as our naïve patients did not only have worse psoriasis at baseline, but even showed better PASI improvement at 3 and 6 months in comparison with non-naïve patients. However, since the patients with naïve treatment rounds had higher baseline PASI values compared with the non-naïve patients, it is possible for their PASI to decrease more during the treatment. This fact could have introduced a bias when comparing the reduction in PASI scores between naïve and non-naïve treatment rounds. A superior response to TNF-α was also noted in naïve rheumatoid arthritis patients in comparison with their non-naïve counterparts (14). Nevertheless, similar findings were inconsistently published in the literature and the reports of conflicting results gave rise to the need for more studies investigating that aspect (10).

No significant correlation was found between PASI, BMI or age, on the one hand, and type of biologics, on the other hand. Interestingly, MTX-treated patients who in addition received biologics did not show any better PASI improvement than patients treated with biologics alone. A probable explanation might be the low number of patients concomitantly treated with MTX in this study.

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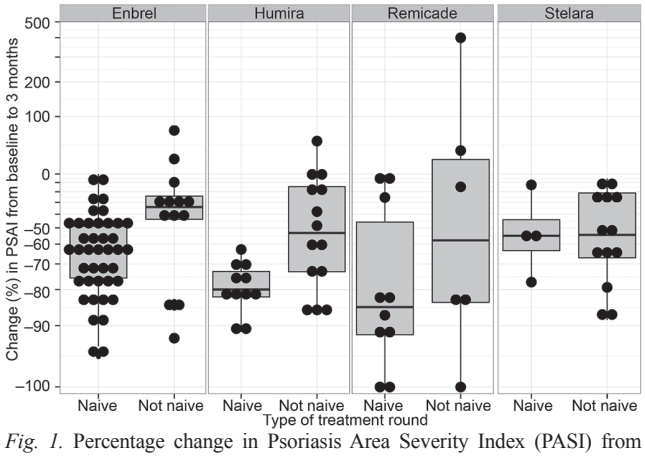

Fig. 1. Percentage change in Psoriasis Area Severity Index (PASI) from baseline to 3 months in each biologic type divided further by naïvety. Enbrel: etanercept; Humira: adalimumab; Remicade: infliximab; Stelara: ustekinumab.

A major limitation of this study was its retrospective nature, as all data had been collected from a national quality register and patients' records. Exclusion of patients with no baseline PASI subsequently led to an overall relatively smaller number of patients.

In conclusion, naïvety to biologics could influence treatment outcome. On the other hand, obesity did not change the outcome for our group of patients. In relation to female patients, male patients tend to show more severe psoriasis, specifically, at presentation. More studies are needed to illuminate these findings.

The authors declare no conflicts of interest.

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