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POS1326 LONG TERM TREATMENT WITH RITUXIMAB IN PROGRESSIVE SYSTEMIC SCLEROSIS: A MONOCENTRIC RETROSPECTIVE STUDY

Keywords: Systemic sclerosis, Safety

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Background: Treatment of Systemic Sclerosis (SSc) remains challenging and some clinical studies reported the efficacy of Rituximab (RTX) in skin disease and in stabilizing lung involvement. Recently 2 randomized clinical trial demonstrated the efficacy of RTX in SSc and in lung involvement in connective tissue diseases (1,2), however current data are limited by the small number of samples examined and the short duration of follow-up.
Objectives: We aimed at retrospectively evaluate the efficacy, safety, and long-term persistence of RTX therapy in a monocentric SSc cohort.
Methods: All clinical records of SSc patients (pts) treated with RTX in our center were retrospectively analyzed. Demographic, clinical and disease characteristics, treatment approach, combination therapies, and adverse events during RTX were considered. Every 6 months, skin score, pulmonary function test and swollen joint count (SJC) modifications as well as digital ulcer occurrence were recorded.
Results: Fifty-two SSc pts (pts) have been treated with RTX in our center since 2005. The mean age of the pts was 55.3±24.3 years and 21.5% were male. The disease duration at the time of the first treatment with RTX was 4.4±2.8 years and the mean reached follow-up was 6.6±2.2 years (range 2-17 years). Forty pts (77.0%) had a diffuse cutaneous involvement, 33 pts (63.6%) had anti-topoisomerase positivity, 45 (88.2%) an interstitial lung disease on high resolution chest CT, 30 pts (59.2%) arthritis or tenosynovitis, and finally 38 pts (73.1%) presented any history of digital ulcers. Twenty-three (44.2%) pts had been previously treated with cyclophosphamide. During RTX treatment, 39 pts (75.0%) received an immunosuppressive combination therapy, most with mycophenolate mofetil (53.8%). Concomitant glucocorticoids treatment was assumed by the 53.8% of pts. Twenty-five pts (48.1%) were treated with Rituximab for only one clinical involvement, 27 pts (51.9%) received treatment for more than one organ involvement including skin, lung or joint. Overall, 82.7% were treated for progression of skin disease, 50.0% for lung involvement deterioration and 23.1% for active arthritis. Treatment showed improvement in the skin score, arthritis, and/or stabilization of the pulmonary functional status in 44 pts (84.6%), while in the remaining 8 pts, therapy was stopped because of worsening of the disease over the 6 months of follow-up. Among responders, skin score improved from 17.3±8.9 to 10.3±8.6 (p=0.04), while FVC and DLco remained stable (87.4±3.5% to 86.2±20.5% and 66.3±23.9% to 64.3±22.1%, respectively). As expected, there was an improvement in DAS28 (4.9±0.8 to 1.9±0.5, p<0.01). Finally, there was a reduction in the rate of ulcer occurrence (46.15% to 21.70%, p=0.04). Twenty-two pts (42.3%) were treated with one single cycle of therapy (1 gr two weeks apart), while the remaining 30 pts were treated with repeated cycles of RTX, with a mean number of cycles of 4.3±2.0. Among the re-treated pts, 50% were treated every year and 50.0% at the time of new clinical worsening, and retreatment was done every 60.5±31.4 months. All pts re-treated with RTX on demand responded to the therapy. Nineteen percent of pts developed adverse events (5.7% leukopenia, 7.7% infusion reactions, 1.9% sepsis, 3.8% pneumonia). Ten pts (19.2%) died during follow-up: 8 deaths were related to organ complication of SSc and 2 to cancer.
Conclusion: Our data suggest long-term efficacy and safety of RTX in pts SSc. Further real world studies will be necessary to evaluate the best therapeutic approach with RTX (regular cycles or retreatment when clinical worsening occurs) and/or the combination with other immunosuppressant drugs.
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POS1327 HORMONE REPLACEMENT THERAPY INCREASES THE RISK OF SYSTEMIC SCLEROSIS: RESULTS FROM LARGE POPULATION-BASED CASE-CONTROL STUDY

Keywords: Epidemiology

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Background: Systemic sclerosis (SSc) exhibits, similarly to other autoimmune diseases, a strong female preponderance. Estrogen has been found to activate signaling pathways involved in immune response and promote autoimmunity [1]. Several studies on cultured SSc skin fibroblasts have reported fibrinogenic role of female sex steroids, but the hormonal impact on the risk of SSc remains underexplored. In a recently published pharmacovigilance report, hormone replacement therapy (HRT) was highlighted as potentially implicated in SSc development [2].
Objectives: In this case-control study, we aimed to assess the relationship between HRT and risk of SSc in a population-based cohort of SSc patients and matched controls.
Methods: Participants with newly diagnosed SSc and their matched controls were identified from nationwide registers. Definition of SSc required a first-time diagnosis of SSc (ICD10 codes: M34.0, M34.1, M34.9, M34.8, as a primary diagnosis) in specialist care, with a second visit listing SSc within 12 months We included visits between Jan 1, 2009 and December 31, 2017 with the first visit representing the index date. Controls were sex, age and region-matched to SSc cases in 1:5 ratio. Study sample was restricted to women aged 40 or older at index date. Participants on progestogen in monotherapy and those with history of thromboembolism, stroke, ischemic heart disease, endometrial and breast cancer before index date, were excluded. Dispensations of HRT were extracted from Prescription register, using The Anatomical Therapeutic Chemical classification system codes. Study participants with a history of ever taking HRT (estrogen, estrogen and progestogen combination and tibolone) at least three years before the index date were considered exposed. The relationship between HRT and SSc was assessed using conditional logistic regression models adjusted for socioeconomic factors and polypharmacy. The impact of underlying comorbidities was evaluated by identifying the most common ICD-10 codes among the users of HRT and sequentially excluding cases and controls with a history of these comorbidities from the analyses.
Results: In total, 553 SSc cases and 2,696 controls were included. Twelve percent of cases and 9% of controls were taking HRT at any time ≥3 years before the index date was associated with a 42% increased risk of SSc (95% CI: 1.1,1.9; p=0.02, Figure 1 a). Combination of estrogen and progestogen showed statistically significant associations with SSc (OR=1.5; 95% CI: 1.0,2.05; p=0.03) (Figure 1 a). Subsequent sensitivity analyses indicated that underlying comorbidities did not influence the observed relationship between HRT and SSc (Figure 1 b).
Conclusion: The findings of this study implicate HRT in the development of SSc and add to a growing body of evidence pointing to the proinflammatory role of female sex steroids in the pathogenesis of immune-mediated disorders.
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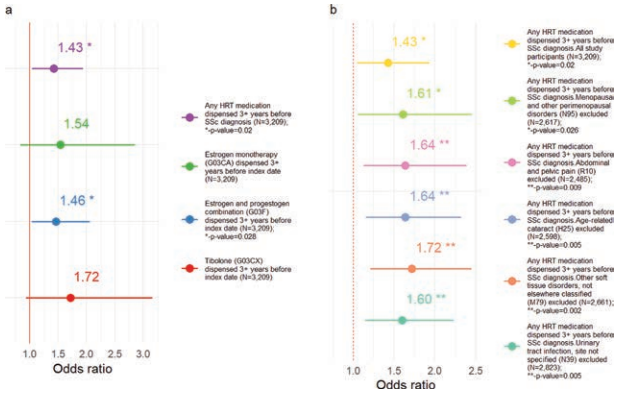

Figure 1 Associations between SSc and HRT. Panel a) and b) show associations with different HRT medications and results of sensitivity analyses, accordingly