CANNABINOIDS IN THE TREATMENT OF PAIN RELATED TO SYSTEMIC SCLEROSIS SKIN ULCERS: OUR EXPERIENCE

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Background: Skin ulcers (SU) represent one of the most frequent complications of Systemic Sclerosis (SSc), characterized by severe chronic pain and frequent complications. Pain related to SSc SU(SSU) remains yet an area of significant unmet need. Moreover, pain control is fundamental for the wound care procedures in SSc patients (pt), increasing treatment adherence and compliance to skin ulcers dressing changes. The pain relief obtained by standard therapy (NSAIDs) is often inadequate or dose limited by side effects. Opioids currently are the mainstay of SSc pain treatment but burdened by side effect profile and/or inefficacy. Thus, novel analgesic strategies need to be investigated. Cannabidiol (CBD), one of many constituents of the Cannabis sativa, has received interest in the treatment of numerous pathological conditions.

Objectives: Evaluate our experience to define the efficacy of CBD preparation in patients with SSc.

Methods: 25 SSc pt (F/M 22/3, mean age 52.3 ± 12.9 SD-years), referred to our Sclerodema Unit during 2018, were consecutively included. In all pt the disease was complicated by long-standing, painful SU resistant to opioids. Pain was classified as severe, according to WHO guidelines in all subjects. 25/25 pt carried out systemic (calcitonin gene-related peptide, prostanoids and/or anti-ET receptors) and local (debride-ment and dressing) therapies. The CBD (10% oral administration oil) was used daily for the treatment of SSSU-related pain. We performed both an oral (five drops bid) as local treatment (two drops in the site of SSSU) during surgical debridement of SSSU for a period of 5.9 ± 3.2 SD months. Patients have been provided with a diary to record the following symptoms daily: self-evaluation of pain at the same time in the evening, using a visual analog scale (VAS), use of other analgesics, eventual side effects. Health Assessment Questionnaire-Disability Index (HAQ-DI) was administrated baseline and at the end of treatment. Safety of CBD was evaluated by patient’s records of side effects, while vital signs and laboratory parameters were monitored at each weekly medication.

Results: The local treatment with CBD produced a significant reduction of SSSU-related pain. After 1 month of therapy, pain VAS decreased from 94.8 ± 8.72 SD to 54.7 ± 9.4 SD (p<0.0001), total hours of sleep increased from 2.56 ± 1.28 SD to 5.67 ± 0.85 SD (p<0.0001). Additional analgesic therapy was necessary in 12/25 (48%). After 2 months, further clinical improvement was observed: the HAQ-DI decreased from 5.18 (1.8) to 3.18 (1.3) (p=0.03), the total number of hours of sleep per night was 6.10 ± 0.85 SD and the HAQ-DI decreased from 1.1 ± 0.67 SD (baseline) to 0.46 ± 0.46 SD at the last patient’s evaluation, when complete healing of SSSU and pain relief were obtained and CBD was discontinued. 20/25 (80%) pt registered a better compliance to the local wound management.

Conclusion: Our study suggests that the use of CBD as a local therapy is effective and safe in maintaining analgesia in patients with SSSU; not secondarily it could be essential for an adequate healing of a local wound with consequent improvement of SSc patients’ quality of life and compliance on local SSSU management. Further larger-scale studies will be needed to finally demonstrate CBD efficacy and to monitor long-term effects.

Disclosure of Interests: None declared


HEALTHCARE UTILIZATION AMONG INCIDENT CASES OF SYSTEMIC SCLEROSIS: RESULTS FROM A POPULATION-BASED COHORT (1988–2016)

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Background: Systemic sclerosis (SSc) is an autoimmune disorder associated with multi-organ dysfunction including but not limited to vascular, cardiac and pulmonary involvement. Few studies have estimated the healthcare resource usage of patients with SSc.

Objectives: To compare healthcare utilization among incident cases of SSc vs age- and sex-matched comparators.

Methods: This study utilized a retrospective, population-based cohort of physician-diagnosed patients with SSc in a geographically well-defined area from Jan 1, 1988 to Dec 31, 2016. A 2:1 cohort of age- and sex-matched non-SSc subjects from the same population base was randomly selected for comparison. Inpatient and outpatient utilization data were obtained from the Rochester Epidemiology Project beginning 12 months prior to the SSc incidence/index date. Patients were followed until death, migration from Olmsted County, or December 31, 2017. A maximum of 5 years following the incidence/index date was used for analysis and the follow-up of each matched triple was further truncated at the shortest length of follow-up for any member, to ensure similar periods of observation for SSc cases and non-SSc comparators. Services were summarized as visit-days (number of days at least one service in the category was billed) to avoid overestimation of services provided. Utilization was compared between SSc and non-SSc cohorts using negative binomial models.

Results: The cohort included 69 incident SSc cases and 138 non-SSc comparators (mean age of 57 ± 16 years at diagnosis/index, 90% female for both cohorts; 87% [SSc] and 95% [non-SSc] Caucasian). Patients with SSc had the highest utilization of outpatient physician, laboratory and combined radiology visit-days during the year of the SSc diagnosis compared with the year prior to diagnosis or years 1-4 after diagnosis of SSc (Table). Patients with SSc had higher utilization of outpatient physician, laboratory and combined radiology visit-days annually for the year prior to diagnosis of SSc and for each of the first 5 years after diagnosis of SSc compared to patients without SSc. Rate ratios comparing utilization in patients with and without SSc ranged from 1.8 to 3.0 for all comparisons.

Conclusion: A higher utilization of outpatient physician, laboratory and radiology visits was observed among patients with SSc compared to non-SSc subjects throughout 5 years of disease duration, indicating high and continued care needs in this patient population.

Table. Comparison of outpatient visits, labs and imaging visit-days in patients with and without incident SSc.

<table>
<thead>
<tr>
<th>Services</th>
<th>Time Interval (years)</th>
<th>Number of patients</th>
<th>SSc</th>
<th>Non-SSc</th>
<th>Rate Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient visits</td>
<td>-1 to 0</td>
<td>68/138</td>
<td>4 (1–9)</td>
<td>2 (0–6)</td>
<td>1.8 (1.2–2.7)</td>
</tr>
<tr>
<td>Labs</td>
<td>-1</td>
<td>69/138</td>
<td>3 (0–8)</td>
<td>1 (0–3)</td>
<td>2.1 (1.4–3.3)</td>
</tr>
<tr>
<td>Radiology</td>
<td>-1</td>
<td>69/138</td>
<td>2 (0–5)</td>
<td>0 (0–2)</td>
<td>2.1 (1.6–4.2)</td>
</tr>
</tbody>
</table>
ASSOCIATION OF VASCULAR BIOMARKERS WITH SYSTEMIC SCLEROSIS CLINICAL FEATURES AND NAILFOLD VIDEOMICROCAPILLAROSCOPY ALTERATIONS - CROSS-SECTIONAL STUDY


Background: The most reliable markers reflecting endothelial activation and injury in Systemic sclerosis (SSc), are intercellular adhesion molecule (ICAM1), vascular cell adhesion molecule (VCAM1), E selectin (Es) and P selectin (Ps) (1).

Objectives: To assess concentrations of these vascular biomarkers in SSc patients (pts) in comparison to healthy controls (HC) and in relation to disease manifestations.

Methods: Patients who fulfilled the 2013 ACR/EULAR SSc classification criteria and have never been treated with endothelin receptor antagonists, phosphodiesterase 5 inhibitors or prostanoids were eligible. Exclusion criteria were overlap syndromes, other autoimmune and cardiovascular diseases, diabetes mellitus, thrombosis, pregnancy, active infection or neoplastic diseases. Our study included 53 SSc pts [34 limited (lcSSc) and 19 diffuse cutaneous SSc (dcSSc)] and 31 age- and sex matched HC. Serum concentration of ICAM1, VCAM1, Es and Ps were measured using a commercial ELISA kit (Quintikine; R&D Systems), expressed as ng/mL. Clinical evaluation of patients was obtained, including nailfold videomicrocapillaroscopy (NVC). Disease activity was assessed by the revised EUSTAR activity index. Statistical analysis was done in R. Student’s t-test or Spearman correlation were done depends on nature of data. ICAM1 cut off value were assessed with ROC analysis. Association were performed with univariate logistic regression for NVC alterations and multivariate for Anti-Topol/ScI70 antibodies (aTSas).

Results: Concentration of all markers were elevated in SSc pts compared to HC (ICAM1 p<0.01, VCAM1 p<0.01, Es p<0.05, Ps p>0.05). Different disease subsets exhibited higher values of ICAM1 and VCAM1 respect to HC (lSSc p<0.05, dSSc p<0.001). Concentration of ICAM1 was higher in dcSSc compared to lcSSc (p<0.05). ICAM1 level were independently associated with positive aTSa (OR 1.2, 95% CI 1.02–1.35, p=0.031) with distinguishing cut off value of 34.94 (Sn 0.90%, Sp 0.60%, AUC 0.85). ICAM 1 was positively correlated with the erythrocyte sedimentation rate (r 0.3, p<0.05) especially within disease duration > 3 years group (r 0.4, p<0.05). Higher levels of ICAM1 was found in diffuse capacity of the lungs for carbon monoxide>70% (p<0.05), modified Rodnan skin score >14 (p<0.05) and active disease (p<0.05) group. Calcinosis group had decreased level of Es (p<0.05) and increased Ps (p<0.05). Es was lower in group with acroosteolysis (p<0.05). Trends towards increasing markers concentration from early to late NVC pattern were observed for all biomarkers except Es which showed the highest concentration in active group, but without significant differences (p>0.05). Few megacapillaries were associated with ICAM1 (OR 1.2, 95% CI 1.06–1.34, p<0.05) and Ps (OR 1.2, 95% CI 1.08–1.39, p<0.05), while presence of bushy capillaries were associated with ICAM1 (OR 1.3, 95% CI 1.06–1.36, p<0.05) level.

Conclusion: Our results support the role of vascular biomarkers in SSc pathogenesis. Besides anti-Topol/ScI70 antibodies, ICAM-1 could be used as an additional marker of dSSc. Elevation of ICAM1 and Ps concentration might be associated with late NVC alterations.

REFERENCES


Disclosure of Interests: None declared.