POS0922

RECOMBINANT HUMAN HYALURONIDASE-FACILITATED SUBCUTANEOUS IMMUNOGLOBULIN FOR IDIOPATHIC INFLAMMATORY MYOSITIS: A MULTICENTER OBSERVATIONAL STUDY

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Background: The spectrum of idiopathic inflammatory myositis (IIM) includes a heterogeneous group of diseases characterized by chronic inflammation of skeletal muscle, often associated with skin, joints, lungs, esophageal, gastrointestinal and cardiac involvement. Conventional treatment for IIM is based on glucocorticoids and immunosuppressants. Moreover, intravenous immunoglobulin (IVIg) has emerged as a promising steroid- and DMARD-sparing treatment for myositis [1]. However, the long-term use of IVIg is complicated by the fact that the intravenous route requires in-hospital drug administration, which not only influences patients' quality of life, but is also associated with an increased risk of systemic adverse effects, difficulties in venous access over time, and high costs [2]. On these bases, administration of subcutaneous Ig (SCIg) by a programmable pump has been considered as a possible alternative to IVIg. Recombinant human hyaluronidase-facilitated (hf)-SCIg is currently approved for the use in patients with primary immunodeficiency disorders, while its efficacy and safety in myositis disorders is limited [3].
Objectives: This multicenter retrospective observational study is sought to evaluate the effectiveness and safety of recombinant human hf-SCIg in patients with IIM treated at different referral centers.
Methods: A multicenter, retrospective, cohort study was conducted on adult patients diagnosed with IIM according to the EULAR/ACR classification criteria [4] treated with recombinant human hf-SCIg according to routine clinical practice. The effectiveness of this treatment was assessed in terms of variations in the Medical Research Council (MRC) score, creatine kinase values, inflammatory parameters, and daily prednisolone dosage. Safety data were also collected.
Results: Twenty-three patients with IIM treated with hf-SCIg were included (16/23 females, 70%; median age at diagnosis of 61 years (IQR 43-65)).
In most patients (22/23, 96%), IIM had been initially treated with high-dose corticosteroids (+/- synthetic or biologic DMARDs), and 20/23 patients (87%) had received previous IVIg treatment (in 12 for remission induction and in 8 for maintenance).
Hf-SCIg were introduced after a median time of 2 years (1-4) from the diagnosis of IIM, mostly for remission maintenance (18/23). Hf-SCIg was started in combination with oral corticosteroids in 19/23 [83%, at a median dose of 5 mg/day (4-12.5)] and/or with traditional or biologic DMARDs (18/23, 78%).
At time of hf-SCIg introduction, the median MRC score was 4 (3-4) and the median creatine kinase level was of 134 U/L (44-243). After 6 months of treatment, the median MRC score was 4 (3-5); no patient discontinued hf-SCIg, and only one experience a mild adverse event.
Conclusion: Hf-SCIg seems effective to maintain remission in a high proportion of IIM patients, while showing a good safety profile in the first 6 months of treatment.
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Table 1. Effectiveness and safety of hf-ScIG treatment in a cohort of patients with IIM

	hf-Sclg beginning	3 months	6 months
N patients with available follow-up data	23	20 *	19*
MRC score §	4 (3-4)	4 (4-5)	4 (3-5)
Creatine kinase, U/L §	134 (44-243)	118 (77-308)	130 (84-222)
ESR, mm/h §	21 (15-28)	30 (25-43)	31 (23-39)
CRP, mg/dl §	0.2 (0.1-0.5)	0.3 (0.1-0.5)	0.3 (0.1-0.3)
Prednisolone dosage, mg/day §	5 (4-12.5)	7.5 (5-10)	5 (5-7.5)
Adverse events	-	NA	1 **

*none discontinued**One infusion site reaction§ median value (IQR)CRP=C reactive protein; ESR=erythrocyte sedimentation rate

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POS0923

EXTRACELLULAR VESICLES AS POTENTIAL BIOMARKERS OF EARLY DISEASE STAGE IN SYSTEMIC SCLEROSIS

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Background: Extracellular vesicles (EVs) are membrane-coated vesicles most often generated from the vasculature and circulating blood cells upon cell activation and during the early phase of apoptosis (1).
Objectives: To evaluate the concentration of different subpopulations of EVs in plasma from patients with SSc in relation to the disease duration and to the markers of endothelial injury.
Methods: Our study included 59 SSc patients (36 limited (lSSc) and 23 diffuse cutaneous subset (dSSc)) and 46 healthy age and gender matched controls subjects. Disease duration less than 3 years in patients with dSSc and less than 5 years in those with lSSc was considered as early disease stage. Clinical evaluation of patients was performed. EVs were analysed with flow cytometry after staining platelet poor plasma with fluorescent cell-specific monoclonal antibodies. The concentration of following phosphatidylserine-positive EVs (PS+ EVs) were analyzed: total EVs, endothelial EVs (EEVs; CD144+), platelet EVs (PEVs; CD42b+), monocytes EVs (LEVs; CD14+), EVs expressing ICAM1 (CD54+), VCAM1 (CD106+) and P selectin (CD62p+). Serum levels of ICAM1, VCAM1 and P selectin were determined with ELISA.
Results: Median disease duration of our cohort was 4 (0-29) years (early lSSc [20/36]: 2.5 (0-4.5) years; early dSSc [11/23]: 10 (1-30) months). All types of investigated EVs were significantly elevated in SSc patients compared to controls ($p<0.05$). Patients with early disease stage had significantly increased levels of all PS+EVs compared to HC ($p<0.05$). Moreover, the levels of EVs expressing ICAM1 and VCAM1 showed good validity in identifying patients with early disease stage (AUC 0.7, $p<0.01$). PEVs were increased in early dSSc compared to early lSSc, but the difference did not reach statistical significance ($p=0.07$). There was a correlation between serum levels and the levels of EVs expressing specific adhesion molecules (ICAM1: $r=0.7$, $p<0.01$; VCAM1: $r=0.7$, $p<0.01$; P selectin: $r=-0.7$, $p<0.01$), only within the group with early dSSc subtype of the disease. Further correlations were detected between ICAM1+EVs with either mRSS ($r=0.07$, $p< 0.01$) or EUSTAR activity index ($r=0.07$, $p= 0.02$) among patients with early dSSc.
Conclusion: Increased levels of circulating EVs of different cell origin were present in patients with early SSc. EVs expressing either ICAM1 or VCAM1 could be novel biomarkers of early disease. EVs expressing ICAM1 showed association with severity of skin involvement and disease activity in patients with early dSSc giving insight into their role in the pathogenesis of SSc.
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POS0924

THE ROLE OF RAYNAUD'S PHENOMENON ON MATERNAL AND FETAL OBSTETRICAL OUTCOMES

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Background: It is established that Raynaud's phenomenon (RP) may influence pregnancy outcomes when secondary to rheumatic conditions (1,2). Data on the impact of primary RP (pRP) on pregnancy are very limited.
Objectives: To retrospectively evaluate the impact of pRP on pregnancy outcomes.
Methods: Women with pRP were included in the study. They were compared with a group of women affected by UCTD with RP, and by UCTD without RP. These women were assessed and followed at our outpatient clinic from January 2011 to October 2020 and they did not exhibit an evolution to a UCTD or to a definite CTD during at least one-year follow-up. Antiphospholipid antibody positivity, twin pregnancies and voluntary termination of pregnancy were exclusion criteria. Women with pRP were also compared with a group of healthy pregnant women

enrolled by our gynaecologist during the first trimester of pregnancy. Maternal and foetal outcomes were retrospectively recorded. ANOVA or the Kruskal-Wallis test for continuous variables, and the Chi2 test or the Fischer exact test for categorical were performed (level of significance. P<0.050). In the post-hoc analysis we used the Mann-Whitney test (quantitative variables) or with the Chi2 test/ Fischer exact test (qualitative variables), applying the Bonferroni correction with pRP women as a reference group (level of significance: p<0.0167).

Results: The analysis included 188 women with a total of 375 pregnancies divided in 4 groups:

-Group "pRP": 46 women with RP without secondary causes, and a total of 106 pregnancies (reference group),

-Group "RP-UCTD": 48 UCTD women with RP and a total of 88 pregnancies,

-Group "UCTD": 37 UCTD women without RP and a total of 88 pregnancies,

-Group "HC": 57 healthy women with a total of 93 pregnancies.

The reference group did not differ from the others regarding age at conception. Prophylactic acetylsalicylic acid was administered during pregnancy to 9% of patients with pRP compared to 1% in HC (p=0.010). In contrast, in the RP-UCTD this percentage was significantly higher (32%, p<0,001) than in pRP.

pRP group showed an increased rate of 1st trimester miscarriages (33% vs 16%, p=0.006, OR 2.05 and 95%CI 1.05-3.98), a lower median birth weights (3038 g vs 3358 g, p=0.002), a higher rate of infants with a birth weight <10th percentile (21% vs 3%, p=<0.001, OR 8.36 and 95% CI 1.85 - 37.84) with respect to HC. There was no statistically significant difference between the reference and the UCTD groups.

No statistically significant differences were observed when considering obstetrical outcomes (eg: mode of delivery, median gestation duration, gestational diabetes mellitus, hypertensive disorder of pregnancy, premature rupture of membranes, oligo-anhydramnios).

Conclusion: Our study shows that pRP in a retrospective cohort has an impact on pregnancy outcomes, with significantly more miscarriages and lower birth weight infants compared to HC. Importantly, pregnancy outcome in pRP women did not differ with respect to UCTD with and without RP, conditions generally associated to maternal morbidity, but in the RP-UCTD group prophylactic acetylsalicylic acid was more commonly prescribed. Further prospective studies aiming at evaluating these differences and at identifying the appropriate follow-up and the possible benefit from the use of prophylactic acetylsalicylic acid during pregnancy in RP are necessary.

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Table 1. Analysis of obstetrical outcomes

	Primary RP (pRP)	RP-UCTD	UCTD	HC	p-value
Miscarriages *N. (%)*	35 (33%)	17 (19%)	30 (31%)	15 (16%)	**p=0,017**
vs pRP	*reference*	p=0,051	p=0,750	**p=0,006**	
Median weight at birth *(IQR), gr*	3038 (2710-3500)	3180 (2935 - 3465)	3157 (2910 - 3610)	3358 (3195 - 3583)	**p=0,02**
vs pRP	*reference*	p=0,3473	p=0,1542	**p=0,0002**	
Birthweight < 10th percentile *N. (%)*	15 (21%)	7 (10%)	5 (8%)	2 (3%)	**p=0,002**
vs pRP	*reference*	p=0,087	p=0,03	**p=<0,001**	

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POS0925 HIGH LEVELS OF BOTH CCL2 AND CCL17 WERE ASSOCIATED WITH MORE SEVERE SSC-ILD

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Background: Systemic sclerosis (SSc) carries a high risk for progressive interstitial lung disease (ILD). Several anti-inflammatory therapies have been used to treat SSc-ILD and recently the first antifibrotic therapy has been approved. Personalized treatment strategies are largely missing to date. The two chemokines, CCL2 (MCP-1) and CCL17 (TARC), have been shown to be markers of inflammation and fibrosis, respectively.

Objectives: To examine associations between ILD severity and serum levels of CCL2 and CCL17 in two different but complementary sources of biomaterial.

Methods: Sera from the prospective Oslo University Hospital SSc cohort (n=371) and healthy blood donor controls (HC; n=100) and lung tissue at the time of lung transplantation from UCLA SSc-ILD patients (n = 12) and healthy donors (n = 12) were analyzed for CCL2 and CCL17 by multiplex assays. CCL2 and CCL17 levels were defined in serum as high or low using 95% CI in HC sera as cut-off values. Paired pulmonary function tests and HRCT images were obtained at baseline and follow-up. ILD was diagnosed on HRCT and categorized by the extent of lung fibrosis as limited (<10%) or extensive (>10%) ILD. Cellular sources of CCL-2 and CCL-17 in lung tissues were determined by immunohistochemistry. Descriptive statistics were applied.

Results: CCL2 and CCL17 were increased in SSc in sera and in lung tissue compared to HC (Figure 1). High levels of CCL17 (>700 pg/ml) and CCL2 (>1000pg/ml) in sera were identified in 43/254 (17%) and 84/471(18%) of the SSc patients (Table 1 and Figure 1). High levels of both CCL17 and CCL2 were associated with lower FVC at baseline and higher extent of lung fibrosis on HRCT (Table 1). Of those with high CCL2 and CCL17, 67% had extensive lung fibrosis. Categorization of ILD into no ILD, limited or extensive ILD showed an association between high CCL17 levels and the extent of fibrosis (Table 1). Reactive epithelium and macrophages and plasma cells expressed TARC, while more AM and infiltrating mononuclear cells expressed CCL-2.

Conclusion: High levels of both CCL17 and CCL2 were associated with more severe ILD and expressed in end-stage kung tissue and may reflect an ongoing inflammatory and fibrotic processes in SSc-ILD. This may have an implication on treatment choices for SSc-ILD.

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POS0926 HOW GOOD ARE WE AT CAPTURING THE GI SYMPTOMS IN OUR PATIENTS WITH SCLERODERMA?

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Background: Scleroderma is a rare autoimmune condition affecting around 1 in 10,000 individuals causing multisystem inflammation and fibrosis. The gastrointestinal (GI) system is the most commonly affected system, with nearly 90% of patients experiencing GI manifestations. The disease can affect any part of the GI tract with symptoms ranging in severity. Complications include oesophagitis and oesophageal strictures, vascular lesions in the stomach, reduced movement and absorption within the intestines and anorectal involvement. Recent guidance by the BSR highlight the importance of GI complications.

Objectives: To conduct a quality improvement project to improve the care provided to our scleroderma patients, focusing on GI symptom burden and identifying any unmet need when comparing local care to BSR guidelines and consensus best practice guidelines.

Methods: A proforma was developed for assessing and treating GI symptoms based on BSR and consensus best practice guidelines. This proforma was trialled on an initial cohort of 32 scleroderma patients from the Royal Glamorgan Hospital in Wales. The last clinical assessment was assessed for the following - regurgitation, nausea, vomiting, heartburn, dysphagia, abdominal pain, bloating, diarrhoea, faecal incontinence, constipation and weight loss. The symptoms were recorded as present, not present or not documented. The management of symptoms were evaluated against the guidelines. The cohort were then contacted regarding their last clinical assessment and asked if they were experiencing these symptoms at the time of their last assessment. The results from the documented assessment were compared to the additional patient information to address unmet needs.

Results: The results show that there is limited documentation of the presence of GI symptoms amongst scleroderma patients at clinic appointments. The initial assessment results were compared with the subsequent patient telephone reported symptoms in order to identify unmet need. The following refer to unidentified symptoms at assessment - regurgitation 9%, nausea 6%, vomiting 3%, heartburn 31%, dysphagia 31%, abdominal pain 9%, bloating 25%, diarrhoea 6%, faecal incontinence 9%, constipation 15% and weight loss 19%. Many patients stated they were unaware that their condition could cause GI symptoms and would not routinely mention these symptoms in a rheumatology assessment. The proforma proves to be an effective way to document and guide management of these patients. The clinical proforma that has now been created will help us improve patient care which can be reassessed in the future.