

Letter to the Editor (Other)

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Use of subcutaneous immunoglobulin in inflammatory myositis

Key message

- s.c. immunoglobulin could be effective and safe in the treatment of inflammatory myositis.

DEAR EDITOR, IVIG is used to treat primary immunodeficiency, neurological, haematological and rheumatic conditions; s.c. immunoglobulin (SCIG) is an alternative route of administering immunoglobulin (Supplementary Table S1, available at *Rheumatology Advances in Practice* online). Studies have demonstrated that home-based SCIG therapies are cost effective, with similar outcomes, fewer adverse events and improved patient satisfaction compared with IVIG [1, 2]. SCIG has been reported in rheumatic disease, but there have been no randomized controlled trials. Our objective was to summarize published data on the effectiveness and safety of SCIG in CTD.

We searched Medline, EMBASE and the Cochrane Central Register of Controlled Trials for clinical studies on SCIG in adults (age ≥ 18 years) with CTD. Case reports were excluded. Two reviewers (A.L.Z. and C.I.) screened abstracts and full texts independently. Disagreements were resolved through consultation with a third reviewer (N.M.). Reviewers independently extracted data including demographics, diagnosis, prior treatments, effectiveness (defined by disease remission) and safety (defined by mortality and adverse events). We contacted study authors for additional information not reported. Given significant heterogeneity among studies, meta-analysis was not possible, and data were summarized descriptively. Methodological quality was assessed using the National Institutes of Health (NIH) quality assessment tool.

We identified 614 articles in our search. Fifty full texts were reviewed, of which 47 were excluded (15 duplicate patient cohorts; 12 case reports; 12 inclusion criteria not met; 5 protocols; 1 corrigendum; 2 insufficient data). Three case series were included for analysis, with a total of 61 patients, all with inflammatory myositis [3–5]. The mean NIH Quality Assessment score was 7.7 of 9.

Patient characteristics are summarized in Table 1. Diagnoses included PM (25 of 61, 41%), DM (16 of 61, 26.2%), inclusion body myositis (7 of 61, 11.5%), mixed CTD (6 of 61, 9.8%), necrotizing autoimmune myositis (2 of 61, 3.3%), cancer-associated myositis (2 of 61, 3.3%) and ocular myositis (3 of 61, 4.9%). Two studies used

European Neuromuscular Centre diagnostic criteria. Danieli *et al.* [3] did not report diagnostic criteria, but prior publications by the same group used Bohan and Peter criteria. Previous IVIG was common (45 of 61, 74%); other treatments were insufficiently reported. There was significant variability in SCIG dose (between 0.1 g/kg/week and 60 g/week) and mean duration (between 190 days and 18.8 months). Reasons for initiating SCIG included patient preference, difficult venous access, intolerance or other constraints.

Clinical improvement or stability in muscle strength was reported in 49 of 56 (87.5%) patients; 2 of 2 necrotizing autoimmune myositis patients developed worsening muscle strength in the study by Danieli *et al.* [3]. Muscle enzymes decreased in all cases except necrotizing autoimmune myositis and cancer-associated myositis patients in the study by Danieli *et al.* [3], decreased (not statistically significant) in the study by Cherin *et al.* [4] and remained unchanged in the study by Hachulla *et al.* [5]. Functional scores improved (statistically significant) in the study by Cherin *et al.* [4], did not change in the study by Hachulla *et al.* [5] and were not reported by Danieli *et al.* [3].

SCIG was well tolerated. Danieli *et al.* [3] noted mild injection site reactions but did not quantify them, although a previous publication by the same group reported injection site reactions in two of eight patients [6]. The remaining two studies reported injection site reactions (12 of 31), rash (2 of 31), headache (3 of 31), myalgia (4 of 31), fatigue (1 of 31), hot flushes (2 of 31) and diarrhoea (1 of 31). There were no cases of serious infections. One death was reported, unrelated to SCIG use [4].

Our review demonstrates that SCIG is effective in the short-term treatment of myositis as defined by improvement in muscle strength, muscle enzymes and functional scores, both in patients transitioned from IVIG and in those initially treated with SCIG. There might be a lesser effect in necrotizing autoimmune myositis, although sample sizes were too small to draw conclusions. SCIG was well tolerated; the most common adverse event was self-limiting injection site reactions.

Our study was limited by paucity of data because the existing literature consisted of small case series. There was significant heterogeneity in SCIG dosing, duration and outcome measures reported, making statistical analysis impossible. Additionally, several studies reported on the same cohort of patients. We contacted authors for clarification, but no responses were received. Best judgement was therefore used to include the most inclusive studies. Although this resulted in omission of some data, this was deemed necessary to avoid multiple publication bias. Review of the excluded publications revealed similar effectiveness and tolerability, with some caveats. For instance, Danieli *et al.* [7] subsequently reported on cardiac involvement in 11

TABLE 1 Patient demographics and outcomes of selected studies [3–5]

Parameter		Danieli <i>et al.</i> (2018) [3]	Cherin <i>et al.</i> (2016) [4]	Hachulla <i>et al.</i> (2017) [5]
Follow-up		1 year	18 months (median)	6 months
Female/total, <i>n</i> (%)		23/30 (76.7)	15/19 (78.9)	11/12 (91.7)
Mean age, years		Not reported	56.8	53
Prior immunosuppression		GC, MTX, AZA, HCQ, CSA, MMF, CYC, IVIG	GC, MTX, AZA, RTX, PLEX, IVIG	GC, immunosuppressants, IVIG
Prior IVIG, <i>n</i> (%)		19 (63)	14 (74)	12 (100)
Dose and formulation of SCIG		0.1–0.2 g/kg/week of SCIG 20%	1.9 g/kg/month (median) of SCIG 16.5%	9.6–60 g weekly of SCIG 16%
Duration of SCIG, mean		12–18 months	18.8 months	190.75 days
Muscle strength	PM	11/11 improvement in mMRC	5/6 improvement in mMRC 1/6 worsening	12/12 maintenance of remission as defined by Kendall score
	DM	8/9 improvement in mMRC 1/9 worsening	1/2 improvement in mMRC 1/2 worsening	
	NAM	2/2 worsening of symptoms	–	
	OM	3/3 improvement of symptoms	–	
	CAM	2/2 improvement in symptoms	–	
	MCTD	3/3 improvement in mMRC	1/1 improvement in mMRC	
	IBM	–	3/5 improvement in mMRC 2/5 worsening	
Muscle enzymes	PM	Median CK improved (<i>n</i> = 11)	CPK normal in 8 patients, significantly improved in 4 patients, unchanged in 4 patients	No clinically relevant change in CK from baseline
	DM	Median CK improved (<i>n</i> = 9)		
	NAM	Median CK worsened (<i>n</i> = 2)		
	CAM	Median CK unchanged (<i>n</i> = 2)		
	MCTD	Median CK improved (<i>n</i> = 3)		
Function	PM	Not reported	3/6 improvement in MDS 2/6 no change 1/6 worsening	12/12 no change in functional scores
	DM		1/2 improvement in MDS 1/2 no change	
	IBM		2/2 improvement in MDS	
	MCTD		1/1 improvement in MDS	

CAM: cancer-associated myositis; CK: creatine kinase; CPK: creatine phosphokinase; GC: glucocorticoids; IBM: inclusion body myositis; MCTD: mixed CTD; MDS: muscle disability scale; mMRC: modified Medical Research Council; NAM: necrotizing autoimmune myositis; OM: ocular myositis; PLEX: plasma exchange; RTX: rituximab.

patients, 6 of whom progressed and 2 died despite SCIG; other non-muscular manifestations improved; that study was excluded because it omitted several patients

in comparison to our chosen study. Finally, it has been theorized that SCIG might be less effective in severe manifestations of immune-mediated diseases owing to

lower peak serum concentrations [8], but our data were not granular enough to demonstrate this, and head-to-head trials with IVIG in myositis do not exist.

This review provides evidence to support SCIG in myositis. Although limited data exist, SCIG appears effective, with a good safety profile. Larger controlled studies are needed to validate the utility of SCIG compared with IVIG across the spectrum of manifestations in myositis.

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Data availability statement

No new data were generated or analysed in support of this research.

Supplementary data

Supplementary data are available at *Rheumatology Advances in Practice* online.

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