


Patient preferences for systemic sclerosis treatment: A descriptive study within an Italian cohort

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Abstract

Objectives: The aim of this study is to ascertain systemic sclerosis patients' preferences regarding the formulations of the medications they use.

Methods: We undertook questionnaires and interviews aimed at understanding systemic sclerosis patients' preferences with respect to the medications they used.

Results: Among 160 systemic sclerosis patients, we found that the majority does not have difficulty taking their medication. However, preferences were identified (81.25% – 65/80 – preferred oral meds and 47.50% – 38/80 – disliked rectal/vaginal meds), as well as some systemic sclerosis patients have significant difficulties using their medications. In fact, factors such as swallowing and fine finger motion difficulties were frequent, while intravenous/intramuscular/subcutaneous medicines were usually not preferred because they are felt as inconvenient (intravenous = 33.4% and subcutaneous/intramuscular = 10%) or painful (intravenous = 37.50% and subcutaneous/intramuscular = 10%)

Conclusion: Most systemic sclerosis patients are able to take their medication despite having some difficulties. However, as there were clear preferences, we could improve patients' adherence to drug therapy if taking these preferences into account.

Keywords

Scleroderma, patient preferences, medication, systemic sclerosis, drug administration

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Introduction

Systemic sclerosis (SSc) is a complex disease involving multiple organ systems and multiple molecular mechanisms.^{1,2} Thus, it requires multiple medications and therapies, and adherence to this complex regimen may depend, at least to some degree, on patients' preferences.³

Patient adherence in rheumatoid arthritis and systemic lupus erythematosus is only 20%–70%,^{4–6} while little has been written about adherence in SSc.⁷ The factors governing adherence are multiple, including prior experience, comorbidities, education, social economic status, insurance, depression, life stresses and complex medication regimens.^{8,9}

Among these factors, patients' preference to taking their medications could be of interest, including the route of administration of the prescribed medication and little is

known about preferences for medication formulations in SSc. Moreover, in SSc, significant musculoskeletal, mobility and hand disabilities may contribute to adherence and preference problems. We designed a study to describe SSc patients' preferences regarding medication use and to qualitatively examine some of the reasons for these preferences.

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Table 1. Reasons for SSc patients' difficulty with medication use (see Appendix A).

	Difficulty with fine finger motion ^a	Difficulty with wrist/forearm ^a	Problems for gastrointestinal tract ^a	Difficulty for flexibility ^a
Topical	Question 3.3 squeeze the container (1 ± 0.86 M ± SD – 6 points: no difficulty, 9: mild, 4: moderate and 1: severe difficulty)	Question 3.4 get topical out of the container (0.58 ± 1 M ± SD – 8 points: no difficulty, 2: mild, 1: moderate and 1: severe difficulty)		
Pills	Question 5.4 open the blister packs (1.13 ± 0.83 M ± SD – 13 points: no difficulty, 30: mild, 13: moderate and 4: severe difficulty)		Question 5.5 swallow the pill/capsule because it is too large (0.82 ± 0.87 M ± SD – 27 points: no difficulty, 19: mild, 12: moderate and 2: severe difficulty)	
Liquids			Question 6.5 swallow the liquid (0.45 ± 0.9 M ± SD – 17 points: no difficulty, 1: mild, 3: moderate and 1: severe difficulty)	
Rectal				Question 13.3 insert the rectal/vaginal medication (1.20 ± 0.45 M ± SD – 0 points: no difficulty, 4: mild, 1: moderate and 0: severe difficulty)

^aBased on a four-point Likert-type scale (no, mild, moderate or severe difficulty), displayed as mean ± standard deviation.

Methods

We examined 160 Italian patients with SSc, classified according to 2013 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria.¹⁰ In all cases, data were collected immediately following a routine clinical visit and all questions were asked in the patient's native language (Italian).

For the first 80 patients (January–February 2017), a uniform case report form was used (see Appendix A). The formulations of medications were grouped as follows: topical (skin and eye/nose/eardrops), oral (tablets/capsules and liquids), injected medications (intravenous, intramuscular and subcutaneous) and intra-vaginal/rectal administration. Preferences for the formulation of medications used were ascertained and degrees of difficulty were requested using categories (e.g. the most difficult and the least difficult). Furthermore, the specific reasons for the difficulty were asked (see Appendix A). We examined questions which specifically addressed a form of administration and difficulties related to its use (e.g. for topical, there was a question which asked about 'difficulty squeezing a container; for pills/liquids, there were questions regarding difficulty swallowing. . .' (see Appendix A and Table 1). Difficulties were classified

into 'difficulties with finger motion' (i.e. squeezing the container or opening the blister pack), 'difficulties with wrist/forearm' (i.e. getting the topical out of the container), 'difficulty for flexibility' (i.e. inserting the rectal/vaginal medication) and problems for gastrointestinal (GI) tract (i.e. difficulty in swallowing the medication).

In a separate non-overlapping 80 patients (January–February 2019), we obtained data immediately following a routine visit, in the same Italian centre, solely about their preferences for medication administration and their reasons for their preference. Questions were open-ended and were as follows: 'Which way that you take medication is most preferred? Why did you prefer "xx" medication? Which way that you take medication is least preferred? Why did you not prefer "xx" medication?' (see Appendix B). After completion of these latter 80 interviews, the interviewer (K.E.A.) examined the notes and summarized the common words and concepts for both most and least preferred reasons for medications use (see Table 2).

No clinical data were recorded, no changes or interventions occurred and anonymity was preserved. As such, no consent forms were required.

Data analysis was descriptive, including means and standard deviations, medians and ranges and percentages.

Table 2. Qualitative interviews for SSc patients’ difficulty with medication use, displayed as positive and negative comments.

Use	Positive comments – most preferred (examples)	Negative comments – least preferred (examples)
Oral	I can be more consistent in taking the drug Feasibility, easier, faster, self-management, no pain, non-invasive, I like it, easier, it is self-manageable	I have acidity, omeprazole is carcinogenic, gastric problems (2pts), they are big pills to take, dysphagia
IM-SC	Self-management Faster	Pain, lots of organizational issues, I travel often so it’s (transporting syringes ^a) problematic, I can’t control (the injection ^a), I have difficulty (giving the injection ^a) by myself
IV	Presence of oesophageal reflux feel comfortable faster, no pain, immediate effect	Problems finding my veins, annoying, more invasive, fear of needles, adverse effects, seems complex, need of an expert
Topical	Easy, self-care, less invasive procedure, less adverse effects	
Drops and spray	Easy and feasible	
Inhalation	I just prefer it	Hand pain to do it, aerosol therapy lasts too long
Rectal and vaginal		Annoying, I don’t like it, painful, invasive procedure, I have a prolapse, I can’t stand it, it’s not pleasant, I don’t want to, I have haemorrhoids, not feasible or pleasant, privacy reasons

^aInvestigator extrapolated the unspoken aspect of the sentences.

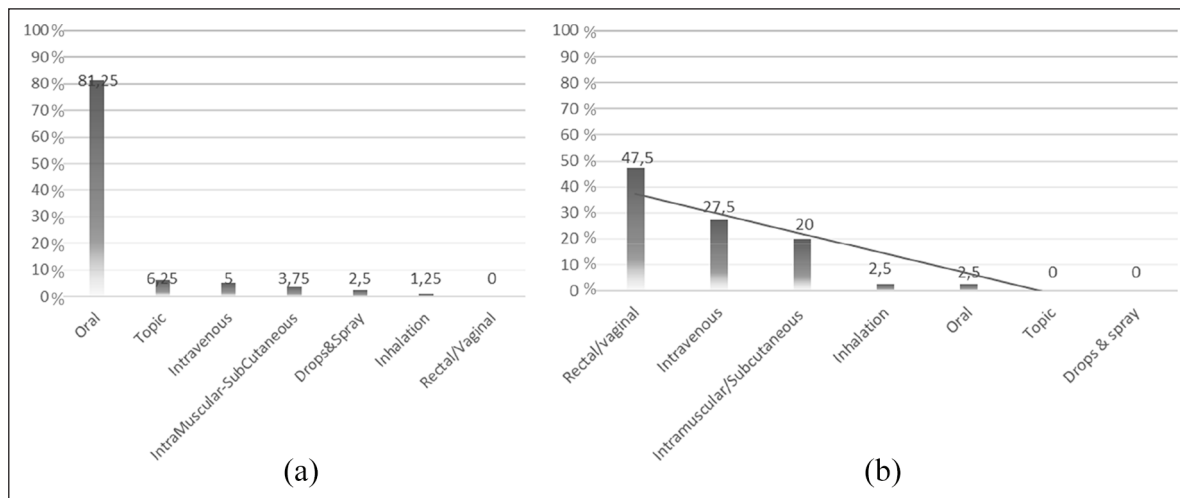


Figure 1. (a) The percentages are based on the answers to the following question ‘What do you prefer most?’ among the second group of 80 patients and (b) the percentages are based on the answers to the following question ‘What do you prefer least?’ among the second group of 80 patients.

Results

All 80 patients interviewed in 2017 took oral medications (100%). Other routes were used less frequently – topical preparations (33.8%) and intramuscular/subcutaneous injections (28.7%) – or were used uncommonly to rarely – eyes/nose/ear drops (16.3%), rectal/vaginal (6.25%) or inhalation (5%).

Although there was generally no or little difficulty with any of these routes of use, there were some patients who had significant or great difficulty including oral, rectal/vaginal or intramuscular/subcutaneous medications (great

difficulty (4+) on the level of difficulty scale). Among the most frequently reported, 41.25% (33/80) of those using pills had difficulty swallowing, while 42.5% (34/80) had difficulty with fine finger motion (e.g. pinching – see Table 1). Average difficulty was mild to moderate when finger motion and flexibility were required, while none to mild for difficulty with forearm of problem with GI tract (see Table 1).

Among the second group of 80 patients, 81.25% (65/80) preferred oral medications mostly, while other preferences were much less frequent (see Figure 1(a)).

The least preferred medications were rectal/vaginal 47.5% (38/80); intravenous 27.5% (22/80) and subcutaneous/intramuscular 20% (16/80); other methods of administration were mentioned by only two patients or were not mentioned at all (see Figure 1(b)).

Common concepts derived from open questions showed that oral medication, despite being the favourite route of administration, were still associated with negative concerns: GI adverse events and issues with swallowing remained a problem in at least 6 and 18 patients, respectively (see Table 2).

Four patients preferred the IV route of drug administration most. They preferred IV for the 'immediacy of the therapy'; they also felt that having a health professional who took care of them was comforting. Conversely, IV was least preferred by 24/80 (30%). Nine of those 24 (37.5%) listed difficulty in finding veins as the main reason of not preferring this particular route of drug administration, while 4/24 (16.7%) listed duration of infusion and 3/24 (12.5%) listed having to come in for their medical care; only 1 patient (4.2%) feared adverse events.

SC/IM were preferred by only 3/80 (3.8%) patients, mostly because of the autonomy and ability to self-manage their treatment. When SC/IM was least preferred (16/80, 20%), the pain of injection was mentioned as the reason by eight patients (10% of 80% and 50% of those 16 who preferred SC/IM least), difficulty in hand function by three (3.8% of 80% and 19% of those 16 preferring SC/IM least), fear of adverse events in one (1.3% of 80% and 6% of the 16 above), and the other four (25% of the 16) spoke about miscellaneous overlapping issues which could not be separated (hard skin, problematic and invasive procedure).

Rectal and vaginal medications were least preferred by 38/80 (46.25%) patients. Among those, 30 of 38 (78.9%) felt the application distasteful, unpleasant, objectionable or disgusting, while only 2/38 (5.3%) patients had an anatomic reason or because they lacked flexibility (i.e. haemorrhoids and prolapse).

Discussion

Our data are unique in documenting SSc patients' preferences for a given medication formulation and their difficulties taking their medications and also in probing the reasons patients preferred or avoided medications.

In general, there was little difficulty in taking any medication. Patients who had difficulties noted that small motor function of the hands caused problems opening blister packs and giving intramuscular or subcutaneous injections (11.5% and 17.4%, respectively). Thus, for SSc, blister packaging should be avoided, in our view.

There were single instances of other significant difficulties among patients and these all supported the idea that, for some patients, small hand function is a real challenge when using medications.

One patient had numerous difficulties with small muscle function, large muscle function, swallowing and

understanding directions and this single patient contributed to multiple areas of difficulty. Because she represented only one patient among 80 (1.3%), her data do not significantly change the conclusions that may be derived from our data. In fact, her data support the concept that the major difficulties in taking medications for some SSc patients relate to the use of their hands.

When questioned about why patients did not like a particular route of administration, they looked at different methods differently. For example, for oral medication, if difficulty occurred, GI issues were prominent, in particular, swallowing pills (i.e. big pills). In contrast, patients avoided IV medications most frequently because there was difficulty accessing their veins or because they feared the pain.

In the 50% who avoided IM/SC administration, pain was the greatest issue. However, 50% of those using IM/SC preferred it because it allowed them to be independent.

Most of the 80 of the second cohort of SSc patients preferred avoiding rectal/vaginal administration principally because it was distasteful to them to use this route of administration. However, all patients came from a single centre in Italy and more than half of the patients used rectal suppositories, despite their statements. Other centres and other continents may yield a somewhat different percentage of patients using specific formulations.

Our results are supported by a recent study which showed that SSc patients experience difficulties in swallowing oral medication due to laryngeal and/or oesophageal problems.¹¹ In fact, organ failure in SSc can include the GI tract¹² and GI issues may affect the patient's quality of life and lead to self-management strategies (such as splitting or crushing pills), thus reducing patient's adherence to medication.¹³

Awareness of this issue for specific SSc patients might be useful when prescribing medications, as actually being able to take the medications will probably contribute to better adherence among SSc patients.

Strengths of this study

A strength of our data is its relative uniqueness and that it may point the way to improving patient adherence. In addition, this study included a relatively large sample. Finally, combining both qualitative and quantitative data is a useful attribute.

Limitations of this study

There are, however, some limitations. The main issue is that we do not have detailed clinical data on these patients, although they come from a centre caring for more than 1000 SSc patients and they were consecutive patients who consented to the questionnaires.

It is important to point out that no correlation between patients' preferences and clinical characteristics were examined in this study (as they were not obtained), and other non-SSc factors may play a role in the results.

Clinical data should be included in future studies, as should psychosocial factors which might contribute to difficulties. While uniform case report forms were used and uniform questions were asked, the interviewer did not have a transcription of the notes and summarized the data from the interview per se.

Conclusion

In this Italian SSc cohort, oral medications were most preferred, followed by topical medications, while rectal-vaginal formulations were by far the least preferred. Reasons for these patients' preferences and avoidances were medication administration specific. Thus, for oral medications, GI issues and difficulties with fine finger function (e.g. inability to open blister packs) were paramount. For IV medication, venous access and the pain associated with inserting the IV was an issue; pain was an issue also for IM-SC medications. Distaste regarding rectal/vaginal administration dominated this formulation.

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Author contributions

E.A.K. substantially contributed to the acquisition; M.-C.M. and F.D.E. substantially contributed to the conception and design of the work; B.C. substantially contributed to the design of the work; R.L. substantially contributed to the conception; E.A.K. and F.D.E. were involved in interpretation of data, analysis of data and drafting the work; all authors contributed to final approval of the version to be published and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of conflicting interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: B.C.: Eli Lilly and Actelion; M.-C.M.: Actelion, Bayer, BMS, Chemomab, J&J, Janssen, Lilly, MSD, and Pfizer, F.D.E.: Amgen, BMS, Boerinher-Ingelheim, Corbus, Galapagos, Genentech, Gilead, NIH, Novartis, Pfizer, Sanofi and Roche.

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