Impact of COVID-19 on outpatient therapy with iloprost for Systemic Sclerosis digital ulcers

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Short Report

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Abstract

Introduction and objectives

The outbreak of COVID-19 epidemic imposed temporary changes in the management of patients with chronic diseases. We analyzed the impact of COVID-19 epidemic in patients with Systemic Sclerosis (SSc) receiving intravenous iloprost infusions for digital ulcers (DU) treatment.

Methods

During the epidemic, iloprost infusion therapy in our Hospital was guaranteed; patients were regularly contacted by telephone before the scheduled infusions. DU were evaluated with DUCAS (DU Clinical Assessment Score).

Results

Between 20th February and 31st May 2020, 47/64 SSc patients did not receive at least one of the scheduled infusions, for patients fear and/or logistical difficulties (43 cases), COVID-19 (2), or other intercurrent diseases (2). At the last evaluation before 20th February DUCAS was not different between patients who stopped the therapy and those who continued it. The 2 groups had similar rate of new DU during the emergency period, but DUCAS slightly increased during therapy discontinuation, decreasing after resuming it. After COVID-19, one patient underwent a fingertip sub-amputation, and an 85-year-old male with multiple comorbidities died for complications related to the infection.

Conclusions

Most SSc patients briefly discontinued iloprost therapy, without increase of new DU number, but with a slight increase of their severity. The regular telephonic contact helped the management that, although not optimal, was adapted to the needs of the individual patient during this emergency period. DUCAS proved to be a useful tool for rheumatologists. COVID-19 had serious consequences in the two patients who contracted it.

Main Text

After the epidemic of Coronavirus associated disease (COVID-19) sustained by SARS-CoV-2 in Wuhan (China), the first case of COVID-19 in Lombardy, a region in Northern Italy, was reported on 20th February 2020. In the following weeks this region rapidly became the most affected area in the world [1], causing great difficulty in the management of patients with chronic illnesses, including rheumatic diseases such as Systemic Sclerosis (SSc). The number of new COVID-19 cases in Lombardy peaked on 15th March and slowly decreased thereafter [2].

Immediately after the first report of a COVID-19 case, therapies for rheumatic outpatients in our University Hospital (ASST Spedali Civili of Brescia, Lombardy), serving an area of nearly one million people, were

centralized in a Clinic having a separate entry. Patients were allowed to access this area only after having undergone a triage and received personal protective equipment.

Here we report the follow-up of patients with SSc who were receiving periodic intravenous iloprost infusions (or, in 3 patients with iloprost intolerance, alprostadil infusions) in our outpatient clinic in February 2020. Iloprost is recommended used for treatment of digital ulcers (DU) in patients with SSc [3]. Main demographic and clinical characteristics of these patients are reported in Table 1. All patients were regularly contacted by telephone before the scheduled access, to assess their health status, particularly focusing on the presence of flu-like symptoms and on DU, which were assessed with the DU Clinical Assessment Score (DUCAS) [4]. When necessary, photos and other files were received from the patients, and diagnostic and therapeutic prescriptions were sent electronically.

Even if infusive therapies with iloprost were never interrupted at our Hospital, between 20th February and 31st May, 47 of 64 SSc patients (73%) did not receive at least one of the scheduled infusions. The main cause of therapy discontinuation was patients concern related to Hospital access and/or logistical difficulties (43/64, 91%), while in 2 cases therapy was interrupted because of COVID-19, and in other 2 cases for other concomitant diseases. The mean length of time of therapy discontinuation was 2.4 months.

Baseline DUCAS (at the last infusion before 20th February) was not different between patients who discontinued prostanoid infusion (group 1) and never discontinued it (group 2; p= 0.09 Mann-Whitney test). During the period considered, 12 of 63 evaluable patients (19%) had new DU (observed directly or via images sent by e-mail); this was similar in group 1 (9/46; 20%) and group 2 (3/17; 18%). However, in group 1 DUCAS score slightly increased during therapy discontinuation, and then decreased once therapy was resumed (Table 2). In one patient with multiple DU at baseline, despite therapy with iloprost and bosentan, after COVID-19, sub-amputation of the 2nd right fingertip was necessary. An 85-year-old patient with severe neoplastic and cardiovascular comorbidities died of complications related to COVID-19.

In summary, although the iloprost infusion activity was never suspended by our Hospital during the COVID-19 emergency, the majority of SSc patients briefly discontinued the therapy. The regular telephonic contact with them allowed a good control of the symptoms. Although not optimal, this management was tailored on individual needs, thereby optimizing the timing of iloprost therapy restart. In fact, patients who discontinued the therapy did not experience an increase in the number of new DU, but a slight increase of their severity. While this observation reflects the importance of therapeutic continuity, it should be noted that the optimal regimen (dosage, duration and frequency) of iloprost infusions is not yet fully defined [5]. DUCAS proved to be a useful tool for the rheumatologist in evaluating DU.

COVID-19 had serious consequences in the two SSc patients of this cohort who suffer it. The impact of COVID-19 on SSc patients is still not defined [6-8] and strategies to improve their management have been suggested [6, 9-10].

Declarations

Funding: nothing to declare

Conflicts of interest/Competing interests: nothing to declare

Ethics approval: the study was approved by local ethics committee

Consent to participate: the study was performed according to the principles of the Declaration of Helsinki. All patients signed a written informed consent to their data treatment.

Consent for publication: the study was performed according to the principles of the Declaration of Helsinki. All patients signed a written informed consent to their data treatment.

Availability of data and material: Francesca Crisafulli is the responsible for the data collection

Code availability: not applicable

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Ethical Standards

The study was performed according to the principles of the Declaration of Helsinki. All patients signed a written informed consent to their data treatment.

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Tables

Table 1

Demographic and clinical features of 64 patients with SSc referred to our Hospital for periodic infusions with prostanoids. Continuous variables are reported as median [25^{th}-75^{th} percentile] and categorical variable as number (%).

Gender	Female 59 (92%) Male 5 (8%)
Age	64 years [56-73]
Disease duration	12 years [7-22]
Disease subset	Diffuse cutaneous involvement 30 (46%) Limited cutaneous involvement 34 (54%)
Autoantibodies	Anti-Topoisomerase I: 30 (46%) Anti-Centromere: 21 (33%) Anti-RNA Polymerase III: 4 (6%) Other autoantibodies: 6 (9%)
Prostanoid therapy	Iloprost: 61 (95%) Alprostadil: 3 (5%)
Concomitant therapy with bosentan	15 (23%)

Table 2

DUCAS at the last evaluation before 20th February (T1), at the first visit after the period of suspension of treatment (T2), and at last evaluation (T3).

Data are reported as median [10°-90° percentile].

	T1	T2	T3	*p T1-T2**	*p T2-T3**	*p T1-T3**
Patients who have suspended prostanoid treatment (group 1)	0 [0-1]	0 [0-3.7]	0 [0-1]	*0.012*	*0.004*	*0.75*
Patients who have not suspended prostanoid treatment (group 2)	0 [0-3.8]	*n.e.*	0 [0-2]	*n.e.*	*n.e.*	*0.07*
Total SSc patients	0 [0-2]	*n.e.*	0 [0-1]	*n.e.*	*n.e.*	*0.48*

n.e.: not evaluable; *paired sign test