Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Molecular Genetics and Metabolism 130 (2020) 170–171

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

journal homepage: www.elsevier.com/locate/ymgme

Commentary

Impact of COVID-19 related healthcare crisis on treatments for patients with lysosomal storage disorders, the first Italian experience

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ARTICLE INFO

Keywords:
COVID-19
Lysosomal storage disorders
Enzyme replacement therapy

ABSTRACT

The direct and indirect effects of Coronavirus Disease-19 (COVID-19) pandemic, on Italian patients with lysosomal storage disorders receiving therapy, were analyzed by a phone questionnaire. No proved COVID-19 emerged among 102 interviewed. No problems were reported by patients receiving oral treatments. Forty-nine% of patients receiving enzyme replacement therapy in hospitals experienced disruptions, versus 6% of those home-treated. The main reasons of missed infusions were fear of infection (62.9%) and re-organization of the infusion centers (37%).

The Coronavirus Disease-19 (COVID-19), caused by the SARS-CoV-2 virus was labeled as a global pandemic by the World Health Organization in March 2020. Italy was one of the first seriously affected countries after China, facing a healthcare crisis of unprecedented magnitude. From the beginning of the emergency until 20th April 2020, the Italian Ministry of Health have reported 178.972 positive cases and 23.660 deaths [www.salute.gov.it]. The consequences of the pandemic infection are both direct and indirect, secondary to the forced re-organization of the healthcare system. Lysosomal storage disorders (LSDs) are a group of inherited metabolic diseases characterized by accumulation of toxic material inside lysosomes, mainly due to the lack of enzymes involved in substrate degradation. In many cases this accumulation affects various organs leading to a severe multisystem disease and premature death [1]. For many LDSs specific treatments, consisting of infusions of enzyme replacement therapy (ERT), or oral drugs (substrate reduction therapy, chaperones) are available, and require regular administration to be effective [2,3] The Regional Coordinating Center for Rare Diseases (RCCRD) of Udine (North East Italy), is one of the main referral centers for LSDs in Italy, with more than 150 patients coming from all the national territory. The aim of this study was to assess the impact of COVID-19 emergency on patients with LSDs receiving specific treatments.

A questionnaire, including 55 questions, was developed by the authors. Patients were contacted by phone by physicians and nurses of the RCCRD. Data were collected between April 6th and 17th 2020. Percentages were used to describe the frequency of different responses to each question. All participants gave their consent for data collection and publication.

A total of 102 patients (pt) from 16 different Italian Regions were included, 53 male (51%) and 49 female (49%), mean age 38.8 ± 18.6 years. Participants were affected by the following diseases: Gaucher (44 pt.; 39 type I, 5 type III), Pompe (16 pt), Fabry (15 pt), mucopolysaccharidosis (12 pt.: 3 type I, 5 type II, 1 type IV, 3 type VI), Niemann Pick type C (10 pt), cystinosis (5 pt). No proved infection by the SARS-Cov-2 virus was recorded. More precisely, no one was specifically tested for COVID-19 since no typical symptoms (fever over 37.5 °C, caugh or pneumonia), or direct contact with a known positive case were reported. At the beginning of the emergency, 71 pt. (69.6%) were receiving i.v. ERT (imiglucerasi, velaglucerase, iaronidase, galsulphase, idursulfase, elosulphase alpha, alglucosidase alpha, alpha and beta galactosidase), and 26 (25.5%) were on oral treatments (miglustat, eliglustat, migalastat, mercaptamine). Five pt. (4.9%) were not treated, since they were supposed to start ERT when COVID-19 began and it was postponed. Regular drug supply or delivery were ensured all over Italy. No interruption or modification occurred for patients receiving only oral therapy. Considering patients on ERT, before COVID-19 outbreak 55 pt. (77.5%) were receiving infusions in the hospital and 16 pt. (22.5%) were on home-therapy. All patients who were already on home-therapy continued their infusions regularly except one, who missed one infusion due to problems in nurses' planning.

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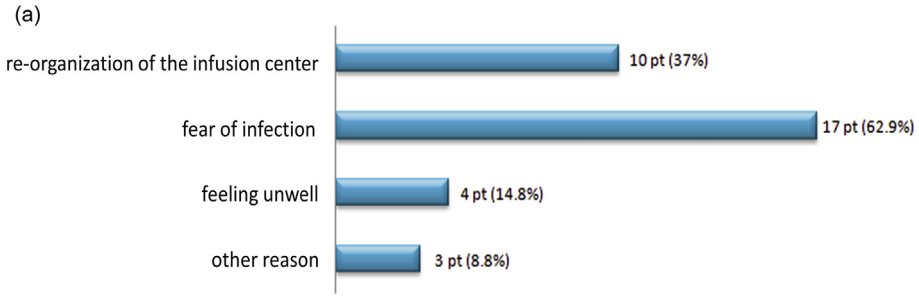
https://doi.org/10.1016/j.ymgme.2020.04.002
Received 24 April 2020; Received in revised form 27 April 2020
Available online 29 April 2020



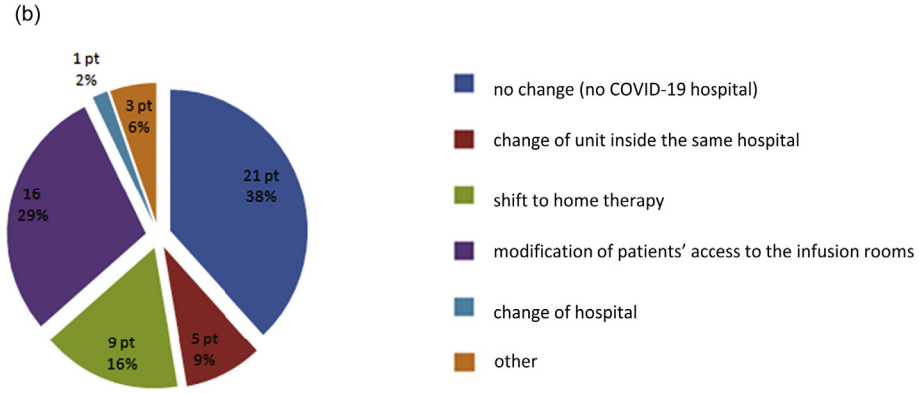


Fig. 1. A Reasons for infusion disruptions for patients receiving ERT in hospitals. Answers from 27 patients who experienced treatment disruptions during COVID-19 emergency, more than one answer possible.
Fig. 1B. Changes in the infusion organization secondary to the COVID-19 pandemic for patients receiving ERT in hospitals.

Among patients receiving ERT in the hospital, 27 pt. (49%) experienced treatment disruptions: 12 pt. (44.4%) missed one infusion, 9 pt. (33.3%) missed two infusions, 6 pt. (22.2%) missed 3 or more infusions. Three pt. who were not receiving therapy for 2 months (2 with Pompe disease and 1 with mucopolysaccharidosis type II) reported increased fatigue and walking difficulties. The main reasons of disruptions are summarized in Fig. 1A. Thirty-four pt. (61.8%) received therapy in hospitals in which COVID-19 patients were admitted. In all cases separated paths and areas for COVID and non-COVID patients were organized. All interviewed patients treated in those centers reported changes in the infusion organization, which are summarized in Fig. 1B. Among patients receiving ERT in the hospital: 26 pt. (47.2%) were in favor of changing from hospital to home-therapy, of whom 7 pt. (26.9%) only during the time of COVID-19 emergency, 19 pt. (73%) even after. Psychological support services were proposed to 66 pt. (65.3%), 6 pt. (9%) contacted the psychologist.

The emergency for pandemic COVID-19 has challenged the world healthcare systems. The direct and un-direct impact of this unprecedented event on patients with rare diseases is still unknown. Particularly, patients with LSDs can be considered at high risk of developing severe complication in case of SARS-CoV-2 infection, since they often suffer from a multisystem disease [4]. From our survey data, among 102 interviewed patients, no one was infected. The reason could be the particular attention of this category of patients in respecting measures of hygiene and infection prevention. A further explanation could be the re-organization of the infusion centers and management units. Indeed 61.8% of the interviewed on ERT received treatment in hospitals having COVID-19 patients admitted, but all of them adopted strict measures of containment, and preferred to suspend one or more infusions until conditions were considered safe, or shifted to home-therapy. However, since no specific tests (oropharyngeal swab or serum antibodies) were performed, asymptomatic or pre-symptomatic cases cannot be excluded among our cohort. When specific validated antibodies tests will be internationally available, it will be interesting to assess the real impact of COVID-19 infection in LSDs population and its consequences. No problems with the chain of drug supply were reported in our country, even in the most affected regions. Thus all oral treatments continued to be administered regularly. Considering patients on ERT, only one patient on home-therapy experienced a missed infusion, while among those treated in hospitals 49% had disruptions. Interestingly the main reason for disruption was patients' personal feeling (fear of infection). In general, patients were in favor of changing from hospital to home-therapy, not only during the emergency, but even after.

In conclusion, from our data, home-therapy seems to be the most efficient way to maintain therapy access during pandemic; however, the personnel involved should be monitored and the correct use of personal protective equipment should be guaranteed. At present, no official indication exist on the management of LDSs patients during emergency and post-emergency period. Therefore, the analysis of the COVID-19 pandemic effects on medical care and health status of patients with LSDs will be useful to delineate consensus guidance.

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