How the COVID-19 pandemic affected the treatment of phenylketonuria? An observational study based on two Brazilian Reference Centers

Gama L1,2; Nunes AJB1,2; Poloni S2,3; Refosco LF2,3; Moura de Souza CF2; Poswar F2; Pinheiro VRP4; Gabetta S4; Fornazim MC4; Schwartz IVD2

1 Federal University of Rio Grande do Sul
2 Medical Genetics Service – Hospital de Clínicas de Porto Alegre
3 Nutrition and Diet Service
4 UNICAMP

Introduction: The COVID-19 pandemic demanded the need for measures to reduce contamination through social isolation, changing people's routine. Some referral centers located in Europe, Asia and Africa reported a 60-80% decline in services related to inborn errors of metabolism from March 1, 2020 to May 31, 2020 compared to the same period in 20191. In Poland, the comparison of the median levels of phenylalanine (Phe) in the periods without and with isolation showed no difference. However, more patients were unable to perform Phe tests in the isolation period (32.7%) than in the non-isolation periods 15.6%, 15.1%, 17.2% (p<0.001)2. The investigation of the effects of the COVID-19 pandemic in the treatment of inborn errors of metabolism is essential for greater preparation for similar future situations.

Objective: To investigate whether the adherence to PKU treatment was affected by the COVID-19 pandemic in Brazil.
Methods: Retrospective study including two Brazilian reference centers for treatment of PKU (center A at Southeast Brazil, center B at South Brazil – figure 1). Patients with at least three Phe dosages in each year (2018, 2019 and 2020) and at least one dosage from January to April 2021 were included; 2018 and 2019 were considered as the pre-pandemic (preP) and 2020 and 2021 as the pandemic period (PP). In center 2, the BMI Z-score for age (BMI/A) was also retrieved. Statistical analysis was performed using the Wilcoxon test for paired samples with asymmetric distribution. The significance level considered was a p<5%.

Figure 1. Map of Brazil with the location of reference centers
Results: Center A: 26/84 (31%) patients were included (54% female), median age: 15.96 yrs. As shown in Figure 2, the median of Phe was 387.2 μmol/L in the preP and 425.92 μmol/L in the PP (p=0.195), with a median of 4 exams in the preP and 4.51 exams in the PP (p = 0.731). Center B: 15/91 (16.5%) patients were included (60% female), median age: 6 yrs. As shown in Figure 3, the median of pre and post Phe levels were 381.75 μmol/L and 379.94 (p = 0.156), respectively; the number of tests/yr ranged from 9.5 in the PreP to 6.01 in the PP (p = 0.027). The BMI/A Z score increased from 1.16 in the PreP to 1.74 in the PP (p= 0.016). All results are shown in table 1.

Table 1. Results

<table>
<thead>
<tr>
<th></th>
<th>Center A</th>
<th>Center B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients included</td>
<td>26/84 (31%)</td>
<td>15/91 (16.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>54%</td>
<td>60%</td>
</tr>
<tr>
<td>Mean age</td>
<td>15.96 yrs</td>
<td>6 yrs</td>
</tr>
<tr>
<td>Median of Phe in the preP and in the PP</td>
<td>387.2 μmol/L - 425.92 μmol/L (p = 0.195)</td>
<td>381.75 μmol/L - 379.94 μmol/L (p = 0.156)</td>
</tr>
<tr>
<td>Median of exams in the preP and in the PP</td>
<td>4 - 4.51 (p = 0.731)</td>
<td>9.5 - 6.01 (p = 0.027)</td>
</tr>
<tr>
<td>BMI/A Z score in the PreP and in the PP</td>
<td>1.16 - 1.74 (p = 0.016)</td>
<td></td>
</tr>
</tbody>
</table>

Phe (phenylalanine); preP (pre-pandemic); PP (post-pandemic); BMI/A Z score (Body mass index z-score for age).

Figure 2. Comparison of Phe levels in the preP period and in the PP period for Center A

Phe preP (median pre-pandemic phenylalanine).
Phe PP (median post-pandemic phenylalanine).

Figure 3. Comparison of Phe levels in the preP period and in the PP period for Center B

Phe preP (median pre-pandemic phenylalanine).
Phe PP (median post-pandemic phenylalanine).
Conclusion: Our results for center B were similar to those for Poland, demonstrating a drop in the number of Phe tests in the PP period. Although we were not able to demonstrate a significant increase in the Phe levels in the PP, the rate of patients included in each center probably reflects a decrease in the number of Phe measurements during the PP. Pandemic is associated with an increased sedentary lifestyle, raising the BMI/A Z score.

Acknowledgements: We thank the organization of the event that provided the exposure of this study, as well as the Research and Events Incentive Fund (FIPE) of the Hospital de Clínicas de Porto Alegre (HCPA), the State University of Campinas (UNICAMP) and the Coordination for the Improvement of Higher Education Personnel (CAPES).

References
