HOW TO DEAL WITH THE CHALLENGES ABOUT THE PHARMACOLOGICAL THERAPY IN PKU

ALVARO HERMIDA$^{1,2}$; MIGUEL A. MARTINEZ-OLMOS$^{1,2}$; HELENA ESTEBAN-CARTELLE$^2$, PILAR BOLAÑO$^2$; Mª LUZ COUCE PICO$^2$

$^1$ University of Santiago de Compostela (USC)
$^2$ CSUR - National unit of expertise for congenital metabolic diseases. MetabERN Santiago de Compostela

INTRODUCTION

In Spain, 41.4% of the patients are ≥18 years and >20% are not early-diagnosed. Many adults with PKU are lost to follow-up or if they are followed, it is most likely in pediatric units. Another major problem in the management of adults patients with PKU is the poor adherence to the treatment. Bad metabolic control occurs in 61.5% of adult patients compared to the 25.5% of patients in childhood and adolescence.

With pegvaliase, 79% of patients reached therapeutic targets of ≤600 μmol/L within 48 months of treatment. However, the introduction of pegvaliase into dietary management is challenging.

**CASE REPORT**

56y woman, late-diagnosed with PKU at 26y, poorly controlled DM type II, osteoporosis, obesity and hyperlipidemia. Blood Phe levels > 1200 μ mol/L repeatedly, despite being adherent with dietary treatment. She discontinued Phe-free formula due to GI intolerance.

PAH mutations (p. R261Q and IVS10nt-11g) were consistent with classical PKU and null response to BH4. Cerebral MRI scan showed mild generalized cortical atrophy. And several neurocognitive domains (attention, processing speed, inhibitory control) and mood disorder (anxiety) were observed.

Accordingly to our center’s protocol, she started 2.5 mgrs of pegvaliase on April, 15th. In order to mitigate risk of hypersensitivity adverse events, we agreed with the general practitioner and she goes to the primary care center to be observed after each dose. She receive s 20 mgrs daily and her plasma Phe levels decreased to 664.6 μ mol/L.

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**Fig.1** Performing Trail-making test B took 378 sec (NR: p50 < 74) and lot of mistakes were observed (black arrows).

**Fig.2** MRI brain scan (T2-weighted). Cortical atrophy and no white matter lesions were observed.
CONCLUSIONS
Low adherence and the need to maintain optimal Phe levels, especially in the most severe cases of PAH inactivity, highlight the call for therapeutic alternatives such as sapropterin and/or pegvaliase. The increase of Phe tolerance as a result of the new therapies may allow more permissive diets that improve the quality of life of adult patients with PKU.