Screening, Diagnosis, Treatment and Genotype of the Children of Primary Carnitine Deficiency

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- **Objective** To investigate the clinical diagnose, treatment and genetic features of infant and maternal primary carnitine deficiency (PCD) in newborn screening.

- **Method** Heel prick blood samples of newborns were collected after 3 days of their birth for the genetic metabolic diseases screening by tandem mass spectrometry (MS/MS) in Zhejiang province. The infants with lower free carnitine (C0<10 mmol/L) and their mothers were recalled for diagnosis.

- **Result** During 01/01/2009 to 12/31/2018, 4459 infants were detected with C0 lower than the cut-off value (10 mmol/L), and finally 121 subjects were diagnosed with PCD (55 males and 66 females) in 3 040 815 newborns screening program. The prevalence rate was 1/25 131 and the positive expected value was 2.71%. The results of 111 infant PCD with complete follow-up data after diagnosis showed that the initial screening time was 3.99±1.81 days, the diagnosis time was 27.02±9.23 days, the initial screening C0 value was 5.94±1.89 mmol/L, the recalled C0 value was 4.99±1.93 mmol/L, and the difference between them was not significant (t=0.29, p>0.05). After 1-3 months of treatment with L-carnitine, the C0 level at maintenance dose was 24.94±10.26 mmol/L, which was significantly higher than that of pre-treatment (t = 4.51, P < 0.01). A total of 64 maternal PCD patients were identified with a prevalence of 1/47 513 and an average C0 of 3.31±1.79 mol/L. The average value of C0 in initial screening of their infants was 5.24±1.96 mmol/L; the average value of C0 in recall was 28.72±15.54 mmol/L. Furthermore, mutational analysis of SLC22A5 gene were performed in 94.59% (105/111) infant cases with PCD. The most common mutation was c.1400C>G (p.S467C), accounting for 39.05% (41/105); followed by c.51C>G (p.F17L) mutation, accounting for 14.73%. There were 93.75% maternal cases of PCD patients under genic testing(60/64), and the SLC22A5 c.1400C>G (p.S467C) mutation accounted for 36.67% (22/60). Except for 2 deaths due to unknown reasons, other PCD patients and their mothers were avoided starvation, and given long-term standardized treatment with different doses of L-carnitine. Then blood sugar, blood ammonia, liver function, electrocardiogram, cardiac ultrasound, growth and development were evaluated regularly.

- **Conclusion** PCD can be detected early by newborn screening and confirmed by genetic analysis, however maternal carnitine deficiency should be excluded. SLC22A5 c.1400C>G (p.S467C) is the most common mutation identified in PCD patients in our province. The treatment of L-carnitine is effective.

- **Key words** Primary carnitine deficiency; Maternal carnitine deficiency; Newborn genetic metabolic disease screening; Tandem mass spectrometry; Mutation