Gene Mutations and Steroid-Resistant Nephrotic Syndrome

Mitra Mahdavi-Mazdeh

Iranian Tissue Bank Research and Preparation Center, Tehran University of Medical Sciences, Tehran, Iran

See articles on pages 357 and 399

IJKD 2013;7:335-9
www.ijkd.org

Glomerulopathies are the known cause of end-stage renal disease in 10% of cases in Iran. Furthermore, 8.6% to 11.4% of the end-stage renal disease population from 1996 till 2006 has been younger than 25 years.[1] Idiopathic nephrotic syndrome is the most common cause of nephrotic syndrome in children, and it is estimated that 20% of them are steroid resistant and half of this population develop ESRD in 6 to 8 years. It leads clinicians to look for different treatment options to prevent such an outcome.[2-4]

It has been well documented that nephrotic syndrome is related to different mutations in podocyte proteins. The *NPHS2* gene, which encodes podocin (a main constituent of the slit diaphragm), has drawn so much attention. Many studies have shown a strong correlation between the *NPHS2* gene mutations and steroid-resistant nephrotic syndrome (SRNS) in children.[5-7] In 2009, Otukesh and colleagues did not find *NPHS2* mutations in exons 5 and 7 in 20 Iranian children with SRNS. Therefore, they did not recommend *NPHS2* (exons 5 and 7) mutation screening in Iranian children with SRNS.[8] Abid and colleagues looked for mutations in the *NPHS1* and *NPHS2* genes in 145 patients with nephrotic syndrome. All mutations in the *NPHS1* gene were found in the early-onset cases and homozygous p.R229Q mutation in the *NPHS2* gene was found in 2 children with childhood-onset nephrotic syndrome. They concluded a low frequency of mutation of these two genes in children with nephrotic syndrome in Pakistan.[9] Similarly, Vasudevan and coworkers who examined *NPHS2* mutations in 25 Indian children with sporadic SRNS found only 4% pathogenic mutation.[10] As it was expected, no mutation of the *NPHS2* gene was found in 50 Czech adult patients with focal and segmental glomerulosclerosis/minimal change disease, either.[11]

However, there is a wide spectrum of the *NPHS2* mutations and Lipska and coworkers showed a 14% detection rate of *NPHS2* mutations in Polish patients, and it was advocated to test the whole gene coding sequence.[12] Carrasco-Miranda and colleagues analyzed a third exon of *NPHS2* and found missense mutation of *L142P* in SRNS patients.[5]

The different results may be due to varieties in design of studies: enrolled patients with different features, severity or familial background, and the mutations which were looked for. On the other hand, genetic variations in populations should not be overlooked, which shows the importance of genetic testing in different races.

It seems that testing for *NPHS2* mutations may help clinicians to make the decision to administer drugs with a high rate of side effects or not.[5] However, the first necessity is to know the prevalence of different mutations in each race and region.

In this issue of the Iranian Journal of Kidney Diseases, two articles have addressed gene mutations in SRNS. Basiratnia and colleagues,[13] in their study on 49 SRNS and 50 steroid-sensitive nephrotic syndrome in southwest of Iran, found a higher frequency of *NPHS2* gene mutation in SRNS cases in comparison with steroid-sensitive nephrotic syndrome (31% versus 4%) and also in familial forms, which is totally different from findings neighborhood countries like Pakistan and India.[9,10] Their study emphasized the fact that the histologic features and clinical finding are not helpful to differentiate between those with or without mutation.[13] Additionally, another study by Fotouhi and coworkers paid attention to this topic from northwest of Iran.[14] They studies on 25 adult patients with focal and segmental

Archive of SID

www.SID.ir

glomerulosclerosis, and similar to Reiterova and colleagues,[11] found no R229Q polymorphism.[14] It would seem that we still need such studies to have a better scheme for our practice.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Aghighi M, Mahdavi-Mazdeh M, Zamyadi M, Heidary RA, Rajolani H, Nourozi S. Changing epidemiology of end-stage renal disease in last 10 years in Iran. Iran J Kidney Dis. 2009;3:192-6.
2. Nickavar A, Safarzadeh AE, Sotoudeh K, Otukesh H, Hooman N. Mycophenolate mofetil for treatment of idiopathic nephrotic syndrome in children. Iran J Kidney Dis. 2012;6:346-9.
3. Moriconi L. [Therapeutic apheresis in idiopathic nephrotic syndrome]. G Ital Nefrol. 2012;29 Suppl 54:S67-S72.
4. Otukesh H, Otukesh S, Mojtahedzadeh M, et al. Management and outcome of steroid-resistant nephrotic syndrome in children. Iran J Kidney Dis. 2009;3:210-7.
5. Carrasco-Miranda JS, Garcia-Alvarez R, Sotelo-Mundo RR, Valenzuela O, Islas-Osuna MA, Sotelo-Cruz N. Short Communication Mutations in NPHS2 (podocin) in Mexican children with nephrotic syndrome who respond to standard steroid treatment. Genet Mol Res. 2013;12:2102-7.
6. Relle M, Cash H, Brochhausen C, et al. New perspectives on the renal slit diaphragm protein podocin. Mod Pathol. 2011;24:1101-10.
7. Santin S, Bullich G, Tazon-Vega B, et al. Clinical utility of genetic testing in children and adults with steroid-resistant nephrotic syndrome. Clin J Am Soc Nephrol. 2011;6:
8. Otukesh H, Ghazanfari B, Fereshtehnejad SM, et al. NPHS2 mutations in children with steroid-resistant nephrotic syndrome. Iran J Kidney Dis. 2009;3:99-102.
9. Abid A, Khaliq S, Shahid S, et al. A spectrum of novel NPHS1 and NPHS2 gene mutations in pediatric nephrotic syndrome patients from Pakistan. Gene. 2012;502:133-7.
10. Vasudevan A, Siji A, Raghavendra A, Sridhar TS, Phadke KD. NPHS2 mutations in Indian children with sporadic early steroid resistant nephrotic syndrome. Indian Pediatr. 2012;49:231-3.
11. Reiterova J, Safrankova H, Obeidova L, et al. Mutational analysis of the NPHS2 gene in Czech patients with idiopathic nephrotic syndrome. Folia Biol (Praha). 2012;58:64-8.
12. Lipska BS, Balasz-Chmielewska I, Morzuch L, et al. Mutational analysis in podocin-associated hereditary nephrotic syndrome in Polish patients: founder effect in the Kashubian population. J Appl Genet. 2013;54:327-33.
13. Basiratnia M, Yavarian M, Torabinezhad S, Erjaee A. NPHS2 gene in steroid-resistant nephrotic syndrome: prevalence, clinical course, and mutational spectrum in South-West Iranian children. Iran J Kidney Dis. 2013;7:357-62.
14. Fotouhi N, Ardalan M, Jabbarpour Bonyadi M, et al. R229Q polymorphism of NPHS2 gene in patients with late-onset steroid-resistance nephrotic syndrome: a preliminary study. Iran J Kidney Dis. 2013;7:399-403.

Correspondence to:
Mitra Mahdavi-Mazdeh, MD
Iranian Tissue Bank Research and Preparation Center, Tehran University of Medical Sciences, Tehran, Iran
E-mail: mmahdavi@tums.ac.ir

Archive of SID

www.SID.ir