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LETTER TO THE EDITOR

Polymorphisms in Pediatric Idiopathic Nephrotic Syndrome

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TO THE EDITOR

Moussa et al. reported an interesting observation on "Polymorphisms in Pediatric Idiopathic Nephrotic Syndrome" [1]. Moussa et al. concluded that "*Here we report that only the G2677A polymorphism was associated to NS susceptibility and steroid resistance. The TAT haplotype was associated with NS susceptibility especially at an early age and with steroid resistance*" [1]. In fact, the effect of the genetic polymorphism has been widely reported for several years. The result in different reports might be different due to the limitation of the number of studied subjects to reproduce the statistically significant observation on the population genetic polymorphism effect. Based on the consideration on molecular charge, the change in molecular weight due to G2677A polymorphism can be expected and this is the same as seen in other studied polymorphisms in the study by Moussa et al. [1]. Since the change in molecular weight is proved to be the important contributing factor to susceptibility and resistance phenotype in several medical disorders [2,3], the similar observation should be observed in any studied polymorphisms in the study by Moussa et al. [1]. As already noted, the number of studied subjects in the report by Moussa et al. might be too few to statistically assess the effect of genetic polymorphism on a population scale.

Declaration of Interest:
None.

References:

1. Moussa A, Mabrouk S, Hamdouni H, et al. MDR-1 and CYP3A5 Polymorphisms in Pediatric Idiopathic Nephrotic Syndrome: Impact on Susceptibility and Response to Steroids (Preliminary Results). Clin Lab 2017;63:1233-42 (PMID: 28792718).

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RESPONSE

Response to the Letter to the Editor Regarding "Polymorphisms in Pediatric Idiopathic Nephrotic Syndrome"

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TO THE EDITOR

We would like to thank Mr. Joob for his interest in our study entitled ''MDR-1 and CYP3A5 Polymorphisms in Pediatric Idiopathic Nephrotic Syndrome: Impact on Susceptibility and Response to Steroids (Preliminary Results)'' [1] and we appreciate the valuable comments. Several studies in different ethnic populations have evaluated the distribution of the MDR1 polymorphisms (1236T>C, 2677T>G/A, and 3435T>C) in children with NS and controls to investigate their usefulness as markers of responsiveness of the disease to steroids, and they have shown inconsistent results [2-5]. We agree that the number of our studied population is too few for meaningful interpretation. We have already mentioned it in our limitation section and we have said that they are preliminary results (in the title). We have found that even with the reduced number, the G2677A polymorphism was the only polymorphism showing significant association, so it seems to be the most associated. Whereas other polymorphisms could further be associated after increasing the number of our study population. A Polish study conducted in a reduced NS population found that prednisone TR may be influenced by histology, age at the onset of NS, and MDR1 3435T>C polymorphism. Also, they reported that the MDR1 1236T>C and 2677T>G polymorphisms were significantly associated with age at onset [6].

Among the three MDR-1 polymorphisms, only the G2677T/A is a missense variant (Ser893Ala) whereas the two others are both synonymous variants: C1236T (Gly418=) and C3435T (Ile1081=). The molecular weight change occurs only with the G2677T/A polymorphism so similar findings may not be observed in the other studied polymorphisms.

Concerning the CYP3A5*3 polymorphism, which is a splice acceptor variant, creating an acceptor splicing site and thus leading to aberrant mRNA (SV1-mRNA) and a nonfunctional protein [7], the number of studied subjects might be too few to statistically assess the effect of this polymorphism on a population scale. In addition, glucocorticoid metabolism is also ensured by CYP3A4 which has an analogous enzymatic activity to that of CYP3A5. Therefore, the failure of CYP3A5 may not alter the response to the corticoids due to the CYP3A4 compensation [8].

Declaration of Interest:

The author reports no actual or potential conflicts of interest.

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