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RESEARCH ARTICLE

RESPONSE TO METHYLPREDNISOLONE BOLUS IN CHILDREN TREATED FOR NEPHROTIC SYNDROME AT THE PEDIATRIC NEPHROLOGY UNIT IN ABIDJAN

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Abstract

Introduction: The objective of this study was to describe the modalities of the responses observed following the realization of a bolus of methylprednisolone in children treated for nephrotic syndrome in the pediatric nephrology unit in Abidjan in order to assess the need for its realization in our practice.

Methods: we carried out a descriptive and analytical cross-sectional study in patients followed up in the pediatric nephrology unit for a nephrotic syndrome and having benefited from the administration of 3 boluses of methylprednisolone at a dosage of 1g/1.73m^2 between 2013 and 2021.

Results: we collected 33 patients aged 2 to 12 years in 72.7% of cases with a male predominance (sex ratio=2.66). The bolus indication was the persistence of proteinuria (100%) after four to six weeks of corticosteroid therapy at 60mg/m^2. A biological assessment in search of a secondary cause had been carried out (48.8%) and presented abnormalities in 26.6% of cases. The bolus was done in hospitalization in 54.5% of cases. All patients benefited from gastric protection and a biological assessment before each bolus. During the realization of the bolus, incidents were observed (27.2%): arterial hypertension (22.2%), fever (55.5%), hyperglycaemia (11.2%). The post-bolus evaluation revealed 66.8% corticosteroid-resistant patients and 27.2% corticosteroid-sensitive.

Conclusion: The bolus of methylprednisolone made it possible to catch up in a third of the cases of corticosteroid-sensitive patients, hence the need for its realization when the conditions allow it.

Introduction:-

Nephrotic syndrome (NS) is the most frequent glomerular pathology in children (Boyer and al.,2017;Kikunaga and al.,2017;Ndongo and al., 2016). Its initial management is essentially based on oral corticosteroid therapy at a dosage of 60mg/m^2 of body surface area for 4 to 6 weeks, after which a bolus of methylprednisolone (MP) must be prescribed for patients who are not in remission (Loirat and al.,1997). This bolus consists of the administration of 3 intravenous infusions of MP at a dosage of 1000 mg/1.73m^2 at 48 hour intervals and is necessary to confirm corticosteroid resistance (Bahat and al.,2007; Hari and al.,2004; Loirat and al.,1997; Niaudet and al.,2000).

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However, in several African countries, its implementation is often lacking due to financial problems. Some authors have defined corticosteroid resistance as an absence of remission after 8 weeks of full dose of corticosteroid therapy (Lombel and al.,2013; Nourbakhsh and al.,2017; Trautmann and al.,2015) contrary to the recommendations of the French Society of Pediatric Nephrology,which require confirmation of the diagnosis by performing the MP bolus (Deschenes and al., 2017).

The management of corticosteroid-resistant nephrotic syndrome is difficult in our context due, on the one hand, to the difficulties of access to renal histology, which is essential to guide treatment, and, on the other hand, to the cost of immunosuppressants, which are expensive and difficult to access.

The prognosis in corticosteroid-resistant patients is generally reserved given the difficulty of bringing the nephrotic syndrome into remission. Some are refractory to multiple lines of treatment and progress to chronic kidney failure and dialysis. (Boyer and al.,2017)

The objective of this study was to describe the modalities of the responses observed following the realization of a bolus of MP in children treated for nephrotic syndrome in the pediatric nephrology unit in order to assess the need for its realization in our practice.

Methods:-

We carried out a descriptive and analytical cross-sectional study in patients treated in the pediatric nephrology unit for nephrotic syndrome and who received the administration of 3 boluses of MP at a dosage of 1000 mg/1 .73m^2/48h intravenously between 2013 and 2021. Corticosteroid therapy was continued at full dose between boluses.

Patients whose bolus of MP was interrupted for whatever reason and who presented an unusable medical file were not taken into account.

The parameters studied were: age, sex, the existence of consanguinity, the therapeutic indication, the clinical state before the bolus, the conditions for carrying out the bolus and the therapeutic response. Data were collected and analyzed using Excel 2010 and open Epi version 3.01 software.

The qualitative variables were expressed as a proportion and the quantitative variables as an average. Fischer's exact test was used to compare frequencies with a significance level of 5%.

The NS was declared cortico-resistant in front of the persistent nephrotic proteinuria 8 days after the MP infusions (Mekhali and al.,2009; Haute autorité de Santé, 2016). In case of remission, the patient was declared cortico-sensitive. The evaluation of the response to corticosteroids was made within 2 weeks to 1 month following the administration of the bolus of MP.

Patients with initial corticosteroid resistance were diagnosed as corticosteroid-resistant during the first flare of NS and those with secondary corticosteroid resistance during a relapse, the patient being initially cortico-sensitive.

Results:-

The results of this study relate to the analysis of 33 records of patients who received a bolus of MP at the PNU for a period of 8 years.

Study population

Children aged 2 to 12 represented 72.7% of the study population with a male predominance (sex ratio=2.66).

None of the patients had consanguinity in their history, nor any malformation visible on clinical examination. A disappearance of the initial edematous syndrome was observed in 45.4% of cases after 4 to 6 weeks of oral corticosteroid therapy.

The bolus of MP had been performed in all patients in view of the persistence of proteinuria after four to six weeks of corticosteroid therapy at 60mg/m^2/day per os.

A paraclinical assessment in search of a secondary cause (mainly infection assessment) was carried out in 48.8% of cases. It presented abnormalities in 26.6% of cases. It was the positivity of malaria serology in 75% and bilharzia serology in 25% of cases.

Completion of MP bolus

The patients benefited from hospitalization in 54.5% of cases and outpatient treatment (day hospitalization) in 45.5% of cases with rigorous monitoring of temperature, pulse, blood pressure, blood sugar capillary, glycosuria and potential side effects. Premedication consisting of gastric protection by proton pump inhibitor and a biological assessment (hemogram, CRP, blood ionogram, fasting blood glucose, calcium) were systematically prescribed before each bolus in order to prevent potential complications.

During the bolus, a few incidents were observed (27.2%). (see**figure 1**).

MP bolus response

The evaluation of the response to the bolus of MP was carried out within 2 weeks to 1 month after the bolus. The response modalities are recorded in **Figure 2.**

In 86.4% of observed corticosteroid resistance, it was an initial corticosteroid resistance.

Age greater than 12 years, sex, abnormalities found during the paraclinical assessment in search of a secondary cause, the absence of disappearance of clinical signs after 4 weeks of oral corticosteroid therapy were not associated factors.to corticosteroid resistance.($p<0.05$).

Discussion:-

Over the 8-year period, 33 patients received a bolus of MP. Our cohort is superior to that of Mahé in Reunion had performed a bolus of MP in 31 patients over a period of 11 years (Mahé,2016). In our series, this could be explained by the fact that the MP bolus could not be performed in all the patients for whom it was indicated, mainly due to financial problems. Indeed, the cost of the MP bolus is currently estimated at US$328.26 in public hospitals in Côte d'Ivoire, while the extreme poverty threshold (the highest income of the poorest 10% of the whole Côte d'Ivoire) was estimated at 186.42 US dollars per head and per individual in 2015(Institut National de Statistiques Côte d'Ivoire,2015). This treatment is therefore a priori inaccessible for the majority of patients.

The patients who benefited from the MP bolus were in most cases between 2 and 12 years old, initially suggesting an idiopathic NS whose frequency varies between 50 and 84% in Africa (Bakhiet and al.,2017; Coulibaly and al.,2014; Keita and al.,2017).

These patients also showed a disappearance of the initial clinical signs after 6 weeks of full-dose oral corticosteroid therapy. These arguments confirmed our decision to perform the MP bolus.

This study made it possible to highlight in 1/3 of the cases a cortico-sensitivity whereas these patients were going to be considered wrongly as cortico-resistant in the absence of realization of the bolus of MP. This proportion is not negligible when we consider all the difficulty of taking charge of corticosteroid-resistant patients in our context. KenzaKitri in Marrakech had performed the bolus of methylprednisolone in 10 patients of his cohort, which had enabled him to demonstrate that 8 of them were cortico-sensitive (Kitri,2010). This further reinforces the need to perform the bolus of MP when possible in order to give potential corticosteroid-sensitive children the chance to be recognized and adequately cared for. The MP bolus should therefore be offered systematically to patients who do not respond favorably to oral corticosteroid therapy after 6 weeks at $60mg/m^2$.

The KDIGO and Ibadan consensus guidelines both recommend defining steroid resistance as a lack of response to daily prednisone after 8 weeks of treatment (Esezobor and al., 2021). The IPNA (International Pediatrics nephrology Association) proposes the 6-week period to define resistance to corticosteroids in the NS. These guidelines seem more appropriate if it is impossible to perform the bolus when the financial means and the technical platform are lacking.

However, emphasis should be placed on the family history of children with persistent nephrotic proteinuria after 4 to 6 weeks of corticosteroid therapy at $60mg/m^2$ by looking for a history of consanguinity and familial nephropathy.

During the clinical examination of the patient, it would be necessary to insist on the search for extra-renal manifestations (skeletal, neurological, ocular, auricular and urogenital) in the absence of renal histology allowing to direct towards a genetic cause.

Conclusion:-

The bolus of MP made it possible to catch up in a third of the cases of cortico-sensitive patients in a context where the management of cortico-resistant patients is difficult, hence the need for its realization when the conditions allow it.

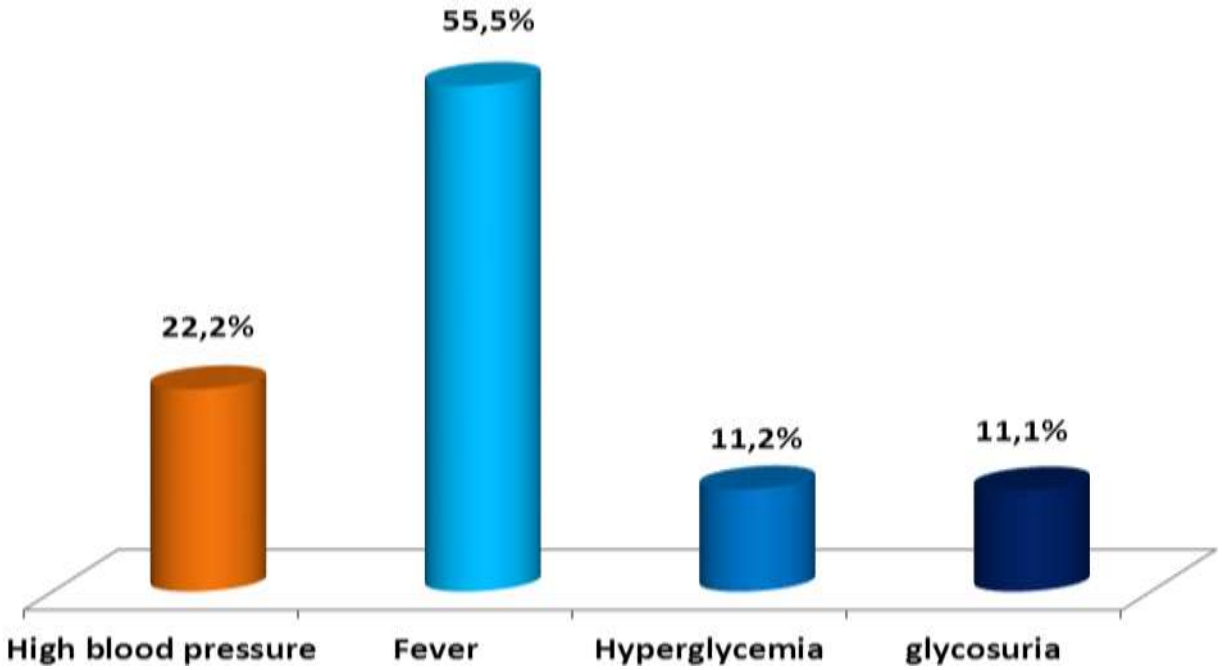

Fig 1:- Incidents observed during the bolus of methyl prednisolone.

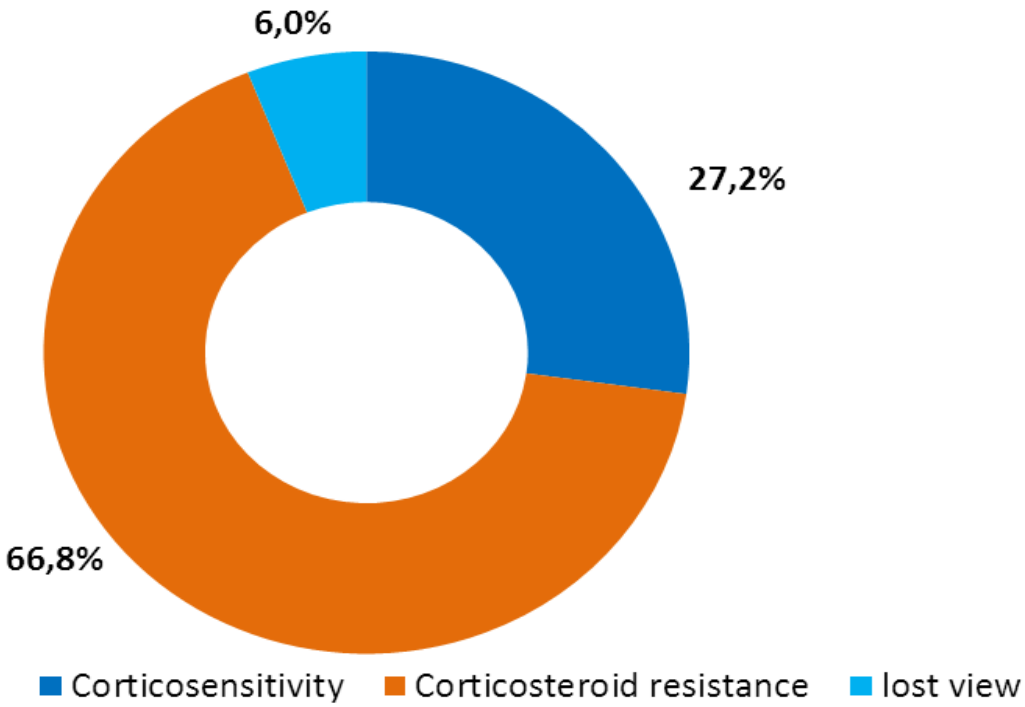

Fig 2:- Modalities of response to the bolus of methyl prednisolone.

References:-

1- Bahat E., Akkaya B.K. (2007) Comparison of pulse and oral steroid in childhood membranoproliferativeglomerulonephritis.Jnephrol MAR 20(2): 234-45.

2- Bakhiet Y.M., Mudi A., and al.(2017). Idiopathic nephrotic syndrome in south African children. AfrHealthSci [Internet] [consulté le 15/09/22]; 17 (4): 1130-6. Disponible sur : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5870266/

3- Boyer O., Baudouin V., et al.(2017). Aspects cliniques du syndrome néphrotique idiopathique de l'enfant. Arch Pediatr [Internet] [consulté le 15/09/22] ; 24(12) : 1338-43. Disponible sur : https://www.sciencedirect.com/science/article/abs/pii/S0929693X17304086

4- Coulibaly P.N.A., Adonis-Koffy L.Y. et al.(2014). Réponse initiale à la corticothérapie dans le syndrome néphrotique de l'enfant en Côte d'Ivoire. Afr J PaedNéphrol [Internet] [consulté le 15/09/22]; 1 :52-6. Disponible sur : https://www.ajol.info/index.php/ajpn/article/view/133515

5- Deschenes G, Vivarelli M and al. (2017). Variability of diagnostic criteria and treatment of idiopathic nephrotic syndrome across European countries.Eur J Pediatr 2017; 176: 647–54.

6- Esezobor C., Ademola A.D and al. (2021). Management of idiopathic childhood nephrotic syndrome in sub-Saharan Africa: Ibadan consensus statement. Kidney International [Internet] 2021 [consulté le 15/09/22]; 99, 59–67. Disponible sur : https://www.kidney-international.org/article/S0085-2538(20)30966-2/fulltext

7- Hari P., Bagga.(2004) A Short term efficacy pf intravenous dexamethasone and methylprednisone therapy in steroid resistant nephrotic syndrome.Indianpediatr 41:993-1000.

8- Haute Autorité de Santé.(2016) Centre de Référence Syndrome Néphrotique Idiopathique. Protocole National de Diagnostic et de Soins (PNDS) : Syndrome néphrotique idiopathique de l'enfant [Internet] [consulté le 15/09/22]35p.Disponible sur : https://www.has-sante.fr/upload/docs/application/pdf/2016-04/pnds_-_syndrome_nephrotique_idiopatique_de_lenfant_2016-04-29_15-02-42_382.pdf

9- Institut national de statistiques.(2015). Enquête sur le niveau de vie des ménages en Côte d'Ivoire (ENV 2015) [Internet] [consulté le 15/09/22]35p.Disponible sur : https://www.has-sante.fr/upload/docs/application/pdf/2016-04/pnds_-_syndrome_nephrotique_idiopatique_de_lenfant_2016-04-29_15-02-42_382.pdf

10- Keita Y., Lemrabott A. T.et al. (2017) Le syndrome néphrotique idiopathique (SNI) de l'enfant à Dakar : à propos de 40 cas. Pan Afr Med J. [Internet][consulté le 15/09/22]; 26 : 161. Disponible sur : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5429445/

11- Kikunaga K., Ishikura K.et al. (2017) High incidence of idiopathic nephroticsyndrome in east Asian children: a nationwide survey in Japan (JP-SHINE study). Clin ExpNephrol [Internet] [consulté le 15/09/22]; 21 (4): 651-7. Disponible sur: https://link.springer.com/article/10.1007/s10157-016-1319-z

12- Kitri K.(2010) Aspects thérapeutiques et évolutifs du syndrome néphrotique chez l'enfant [Internet] [thèse Med]. Marrakech :Faculté de medecine et de pharmacie Université Cadi Ayyad; 2010 [consulté le 15/09/22]22. 153 :118p.Disponible sur : http://wd.fmpm.uca.ma/biblio/theses/annee-htm/FT/2010/these22-10.pdf

13- Loirat C, Baudoin V.(1997). Néphrose. ln:AujardY, Bourrillon J. Paris: Ellipses Pédiatrie 335-41.

14- Lombel RM, Hodson EM, Gipson DS. (2013). Treatment of steroid-resistant nephrotic syndrome in children: new guidelines from KDIGO. PediatrNephrol 28: 409–14.

15- Mahé R. (2016). Le syndrome néphrotique idiopathique de l'enfant à la Réunion Epidémiologie, description clinique et aspect évolutifs sur une période de 11 ans [Internet] [thèse Med]. Bordeaux : UFR Sciences Médicales Université de Bordeaux [consulté le 15/09/22] 96 :118p.Disponible sur : https://dumas.ccsd.cnrs.fr/dumas-01346716/document

16- Mekahli D, Liutkus A, et al. (2009). Long-term outcome of idiopathic steroid resistant nephrotic syndrome: a multicenter study. PediatrNephrol 2009;24:1525–32.

17- NdongoAA.,Sylla A. and al. (2016). Nephrotic syndrome in children at the Dakar University Hospital.Arch Pediatr[Internet] [consulté le 15/09/22]; 23 (6): 653-4. Disponible sur: https://sci-hub.se/https://doi.org/10.1016/j.arcped.2016.03.008

18- Niaudet P. (2000) Syndromes néphrotiques chez l'enfant. EncyclMèdChirNephrologie-Urologie 18-039-0-10,pédiatrie 4-084-C-25, 12P.

19- Nourbakhsh N, Mak RH.(2017). Steroid-resistant nephrotic syndrome: past and current perspectives. Pediatric Health Med Ther 2017; 8: 29–37.

20- Trautmann A, Bodria M, et al. (2015). Spectrum of steroid-resistant and congenital nephrotic syndrome in children: the PodoNet registry cohort. Clin J Am SocNephrol 10: 592–600.