

Dosing renally cleared drugs in critically ill children: mind the trap of glomerular hyperfiltration !



De Cock P^{1,2}, Van Der Heggen T^{2,3}, Dhont E⁴, Boeykens N¹, Roelandt K², Leenknecht B², Peperstraete H⁵, Delanghe J⁶, Vande Walle J⁷, De Paepe P^{1,2}

[1] Department of Pharmacy, Ghent University Hospital - [2] Heymans Institute of Pharmacology, Ghent University - [3] Department of Pediatrics, Ghent University Hospital - [4] Department of Pediatric Intensive Care, Ghent University Hospital - [5] Department of Cardiac Intensive Care, Ghent University Hospital - [6] Department of Laboratory Medicine, Ghent University Hospital - [7] Department of Pediatric Nephrology, Ghent University Hospital

1. BACKGROUND

Glomerular hyperfiltration (GHF), defined as an elevated glomerular filtration rate (GFR), induces the enhanced elimination of circulating solute by the kidneys. Recently, this phenomenon has received increasing attention in critically ill adults. The incidence in this setting is high, varying between 28-65%. In critically ill children, data on the incidence of GHF are scarce.

2. AIM

Primary objective:

To investigate the incidence of GHF in critically ill children.

Secondary objective:

To identify factors associated with the development of GHF.

3. METHODS

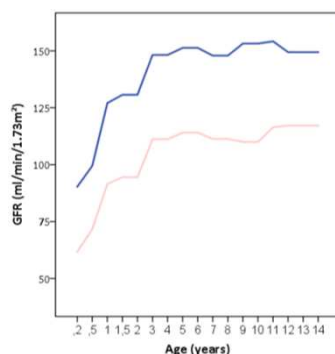


Fig 1. Age dependent normal GFR (pink) and limit for GHF (blue)

This study was a single center, prospective, observational study, conducted at the pediatric intensive care unit (PICU) and the cardiac surgery intensive care unit (CSICU) of the Ghent University Hospital, Belgium. Patients between 1 month and 15 years of age with a bladder catheter were enrolled. GFR was measured by means of a calculated 24 hours creatinine clearance (24h ClCr) during a maximum of 4 consecutive days. GHF was defined as a GFR exceeding normal values for age plus two standard deviations. Logistic regression analysis was used to identify covariates for GHF. The following variables with a clinical plausibility were entered in univariate analysis: age, weight, length, body surface area (BSA), amount of IV fluids administered, and vasopressor support. Those with an a priori determined p value < 0.10 in univariate analysis were entered in multivariate regression analysis

4. RESULTS

Data were collected from 65 patients (median age 1.7 years, IQR 3.0). On the first day following admission to the ICU, 80% of patients expressed GHF. **In total, GHF was seen at least once in 84.6% of patients.** Smaller BSA, strongly correlated to younger age, and the absence of vasopressor support were found as independent associated factors with the development of GHF (table 1).

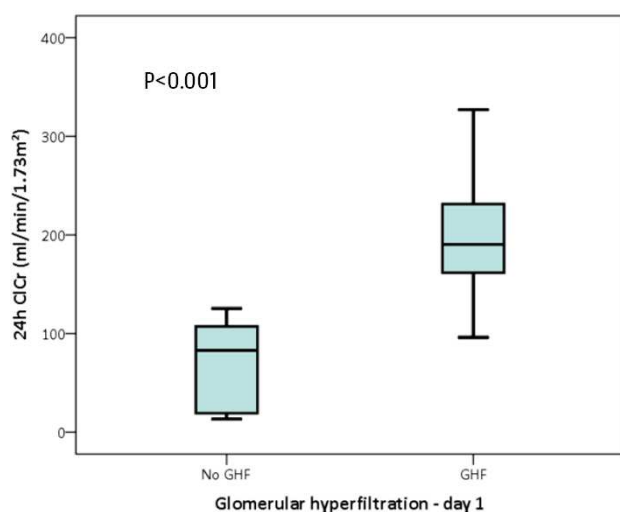


Fig 2. Creatinine clearance in patients with vs. without GHF.

GHF patients had a median 24 hours creatinine clearance of 181.8 ml/min/1.73m² (IQR 75.0) on the first day, compared to 40.2 ml/min/1.73m² (IQR 78.9) in patients without GHF.

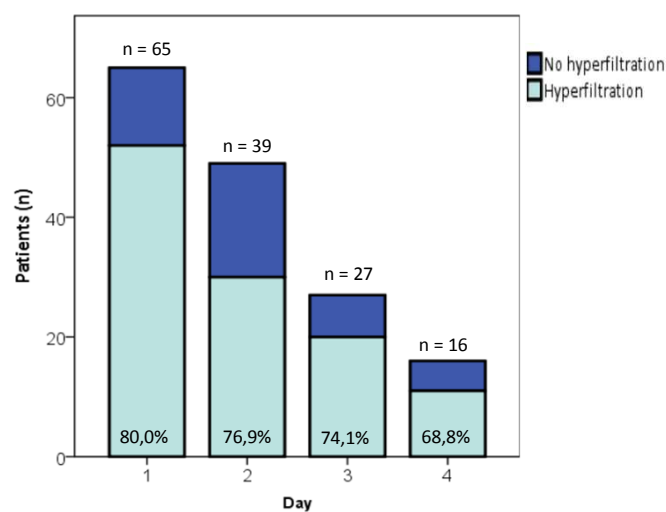


Fig 3. Evolution of GHF during the study.

The percentage of patients presenting with GHF slowly decreases during consecutive days following admission to the ICU.

Factor	OR	95% CI	P-value
BSA	0.078	0.019-0.319	< 0.001
Vasopressor support	0.258	0.097-0.687	0.007

Table 1. Variables associated with GHF (logistic regression, multivariate analysis)

Smaller BSA and the absence of vasopressor support were independently associated with the development of GHF. OR = odds ratio, CI = confidence interval. Hosmer-Lemeshow (goodness-of-fit): $\chi^2 = 11.972$, df = 8, P=0.152.

5. CONCLUSION

- GHF is a common phenomenon in the pediatric ICU, especially in the youngest children and those not on vasopressor support.
- We recommend using an age dependent definition of GHF, related to renal maturation processes.
- As GHF may lead to subtherapeutic treatment of renally eliminated drugs, early detection of patients at risk is of main importance.