Journal of Nephrology
https://doi.org/10.1007/s40620-024-02112-5

RESEARCH LETTER

Feasibility of incremental haemodialysis in paediatrics: preliminary insights from a small cohort

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Received: 22 July 2024 / Accepted: 16 September 2024

Keywords Incremental haemodialysis · Paediatrics · Residual kidney function · Adequacy

Haemodialysis (HD) is rarely performed in small children but becomes more common with increasing age [1]. Incremental haemodialysis (I-HD) allows dialysis adjustment according to residual kidney function (RKF). In adults, I-HD has shown advantages over standard HD, including reduced costs, comparable mortality rates and possibly better preservation of RKF [2]. Limited data are available in paediatrics, and dialysis adequacy, following the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, still needs more research in the paediatric population [3]. However, a recent report suggests that I-HD is safe, is associated with reduced erythropoietin (EPO) use, improved cardiovascular profiles, and shows potential benefits in quality of life for caregivers compared to thrice-weekly regimens [4].

We present preliminary findings from a cohort of incident paediatric patients who underwent chronic HD for more than 3 months between January 2019 and March 2023. They were retrospectively evaluated at the Exequiel González Cortés Children Hospital's haemodialysis unit in Santiago, Chile**.** The cohort included 6 patients on twice-weekly I-HD and 9 children on standard-HD. Demographic, anthropometric, clinical, and dialysis-related variables were recorded at admission and at the end of follow-up. Patients were followed during their enrollment in the program.

Patients on I-HD met criteria for chronic kidney disease (CKD) stage 5, had diuresis greater than 500 mL/day/1.73 m^2 and residual kidney urea clearance (K_{RU}) greater than 3 mL/min/1.73 m^2. Transition to standard-HD was considered if K_{RU} fell below admission criteria, total *std*Kt/V was inadequate despite dialysis adjustments, or metabolic/fluid management was difficult to control. Baseline creatinine clearance and K_{RU} were calculated for I-HD patients. During follow-up, every 3 months K_{RU} measurements were scheduled using the Mathews et al. formula, and adjusted to body surface area (BSA) of 1.73 m^2 using the Mosteller formula [5]. Monthly *sp*Kt/V and *e*Kt/V were estimated using the Daugirdas formula. Weekly dialytic clearance was determined based on the *std*Kt/V calculated using Gotch's formula [6] and normalised to BSA and urea volume distribution (V) following Daugirdas' recommendations for paediatric patients (SAN-*std*Kt/V) [7]. The fixed target model was used for dialysis dose adequacy, calculating the equivalent continuous clearance, combining residual and dialytic *std*Kt/V [3]. Standard residual urea clearance was estimated using weekly time in minutes and V35 in mL (K_{RU} 1.73 $m^2 \times 10{,}080$ min / 35,000 mL) and added to dialytic SAN-*std*Kt/V to obtain the combined weekly urea clearance expressed as total *std*Kt/V.

The Wilcoxon, Mann Whitney or Kruskall Wallis tests were used to compare quantitative variables with non-parametric distributions between groups, and a significance level of $p = 0.05$ was adopted.

Fifteen incident pediatric patients were analysed, with 40% (6/15) undergoing I-HD and 60% (9/15) receiving standard-HD. There were no significant differences in sex distribution (males, 4/6 vs 3/9) or age at dialysis initiation [12.5 (IQR 12.03, 12.75) vs 13.5 (IQR 6.9, 14.3) years] between the I-HD and standard-HD groups, respectively. A higher prevalence of congenital anomalies of the kidney and urinary tract (CAKUT) was observed in the I-HD

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Published online: 21 October 2024

Table 1 Clinical, metabolic and dialytic characteristics of the I-HD vs St-HD group at the start and end of follow-up

Clinical characteristics	Initial			Final		
	I-HD ($n=6$)	St-HD ($n=9$)	P [a]	I-HD ($n=6$)	St-HD ($n=9$)	P [a]
24-h CrCl and K_{RU} at HD initiation	10.03 (8.7, 10.7)	Not measured(*)				
Median (IQR), mL/min/1.73 m^2	5.46 (5.01, 6.51)					
U.O median (IQR), mL/kg/h	2.26 (1.81, 2.85)	0.06 (0, 0.31)	< 0.001	2.46 (1.91, 2.83)	0 (0, 0.09)	< 0.001
and mL/1.73 m^2/day	2917 (2596, 4393)	90.74 (0, 373)	< 0.001	3373 (2993, 4295)	0 (0, 97.4)	< 0.001
Z-Score H/A, median (IQR)	– 1.5 (– 2.11, – 0.91)	– 2.28 (– 3.96, – 1.58)	NS	– 1.75 (– 2.11, – 0.39)	– 2.13 (– 4.24, – 1.55)	NS
Laboratory characteristics						
Albumin, median (IQR), g/dL	3.9 (3.84, 3.97)	3.68 (3, 3.8)	NS	3.95 (3.83, 4.08)	4.21 (4, 4.6)	NS
Potassium, median (IQR), mEq/L	4.2 (3.8, 4.3)	5.1 (3.9, 5.4)	NS	4.1 (3.73, 5.4)	4.3 (4.2, 4.6)	NS
Bicarbonate, median (IQR), mEq/L	22.6 (21.1, 24.1)	22 (19.9, 23.5)	NS	20.9 (20.1, 22.9)	22.9 (20.6, 23.7)	NS
Calcium, median, (IQR), mg/dL	9.4 (9.1, 9.7)	8.9 (8.7, 9.2)	NS	9 (8.9, 9.3)	9.6 (9.2, 9.7)	NS
Phosphorous, median (IQR), mg/dL	5.1 (4.35, 5.78)	5.1 (4.9, 5.7)	NS	4.85 (4.45, 5.18)	5.1 (4.5, 6.1)	NS
iPTH, median (IQR), pg/mL	446.6 (99.3, 193.7)	403.9 (260, 426)	NS	189.6 (184, 592)	160 (187, 1020)	NS
Ferritin, median, (IQR), ng/mL	90.6 (49.6, 117.8)	217 (142, 325)	NS	188 (130, 253)	241 (62.6, 321)	NS
Haemoglobin, median (IQR), g/dL	10.2 (9.83, 11.4)	9 (8.5, 9.3)	NS	12.5 (12.08, 12.7)	10.8 (10.6, 12.5)	NS
EPO dose, median (IQR), (UI/kg/week)	95.3 (91.7, 117.1)	181.8 (100, 217.4)	NS	81.7 (52.8, 90.43)	187.5 (171.4, 253.2)	0.003
Antihypertensives, *n* (%)	1 (17)	6 (67)	NS	0 (0)	8 (89)	0.0007
LVH[a], *n* (%)	0 (0)	4 (44)	NS	0 (0)	5 (56)	0.02
Dialysis characteristics	I– HD ($n=6$)	St– HD ($n=9$)		I– HD ($n=6$)	St– HD ($n=9$)	
UFR, *n* (%) and	1 (16)	9 (100)	< 0.001	2 (33)	9 (100)	0.002
Median (IQR), mL/kg/h	0 (0, 2.92)	6.71 (3.62, 7.99)	< 0.001	0 (0, 0.71)	5.9 (4.69, 8.04)	0.01
Number of minutes per HD session, median (IQR)	210.2 (192, 221.1)	237.2 (235,239.8)	< 0.04	225 (221.7, 240.2)	239.5 (238.1, 241.3)	NS
Number of hours on HD per week, median (IQR)	7.05 (6.4, 7,35)	12.2 (12.9, 13.9)	< 0.001	7.75 (7.4, 8.1)	12.5 (12, 15.2)	< 0.001
Pre-HD BUN, median (IQR), mg/dL	64.8 (54.5, 72.3)	58.1 (48.3, 67.7)	NS	58.5 (50.45, 64.4)	57.8 (45.7, 61)	NS
*sp*Kt//V per session, median (IQR)	1.67 (1.42, 1.86)	193 (1.69, 2.26)	NS	1.7 (1.46, 1.79)	1.93 (1.87, 2.02)	NS
Dialysis SAN-*std*Kt//V, median (IQR)	1.39 (1.33, 176)	2.52 (2.2, 2.7)	< 0.001	1.56 (1.39, 1.79)	2.6 (2.46, 2.98)	< 0.001
$K_{RU,}$ median (IQR), mL/min/1.73 m^2	7.03 (4.8, 8.9)	–		6.94 (4.3, 8.2)	–	
Residual *std*Kt/V, median (IQR)	1.33 (1.23, 2.37)	–		2.01 (1.39, 2.57)	–	
Total *std*Kt/V, median (IQR)	2.89 (2.8,3.8)	2.22 (2.15, 2.89) $n=5$	0.006	3.4 (2.8, 4.2)	2.6 (2.44, 2.75) $n=7$	0.002

I-HD incremental haemodialysis, *St-HD* standard haemodialysis, *IQR* interquartile range, *HD* haemodialysis, *CrCl* creatinine clearance, K_{RU} residual kidney urea clearance, *U.O* urinary output, *H/A* height-for-age, *iPTH* intact parathormone, *EPO* erythropoietin, *LVH*[a] left ventricular hypertrophy was diagnosed using bidimensional M-Mode echocardiography, *UFR* ultrafiltration rate, *BUN* blood urea nitrogen, *spKt/V* Kt/V single pool, *SAN-std Kt/V* surface area normalised standard Kt/V, *std*Kt/V standard Kt/V, *(*) CrCl and* K_{RU} were not measured by low urinary output: anuria, $n=5$ and oliguria < 0.35 mL/kg/h, $n=4$

[a] *P* value means comparison between I-HD and St-HD, *NS* non statistically significant

patients (83%) compared to the standard-HD patients (11%, $p = 0.005$). Anthropometric data showed slightly better median *Z*-score height-for-age in the I-HD group; however, this finding had no statistical significance. Dialysis vintage and median follow-up time of the entire cohort were 289.8 and 18.8 months, respectively. Creatinine clearance and K_{RU} at dialysis initiation are shown in Table 1. The urine collection schedule in the I-HD group could not be strictly followed. In practice, a total of 19 K_{RU} measurements were made. In the standard-HD group, 5 patients were anuric at baseline and 2 more were included over time. The remaining 2 patients had very low diuresis (< 0.35 mL/kg/h), therefore RKF was not measured. No differences were found in laboratory characteristics between the groups at the start or end of the study, as shown in Table 1. However, EPO dosage, prevalence of antihypertensive therapy, and left ventricular hypertrophy were lower in the I-HD group at both time points. In both groups, pre-dialysis blood urea nitrogen and *sp*Kt/V showed no differences. Total *std*Kt/V achieved in the I-HD group was significantly greater than for the anuric patients in the standard-HD group due to preserved RKF throughout the study period (Table 1). During follow-up, 4 I-HD patients underwent kidney transplants, 2 were switched to a thrice-weekly regimen, though only one due to low dialysis adequacy. In the standard-HD cohort, 5 patients received kidney transplants, and 4 remained on dialysis until the study conclusion. Patients treated with I-HD spent more median time on dialysis than those treated with standard-HD [24.9 (IQR 16.6, 30.2) vs 8.2 (IQR 7.4, 18.9) months], saving 669 dialysis sessions over time.

I-HD might optimise RKF advantages by minimising dialysis exposure while preserving RKF [8]. Within our cohort, 6 patients exhibited significant urinary output for RKF measurement without diuretic therapy, allowing to initiate twice-weekly I-HD. Similar findings have been published by Gurevich et al. in Israel [4].

Preserving RKF in HD patients could provide benefits in sustaining cardiovascular health, and enhancing endogenous EPO activity. Shafi et al. [9] highlighted these benefits, which we also observed in our cohort.

Dialysis adequacy is crucial to avoid underdialysis, and we carefully estimated K_{RU} and delivery of the correct dialysis dose following established formulas. Combining dialytic clearance and K_{RU} into a total *std*Kt/V could be considered in the decision-making process, leading to dose adjustments or transitioning to a thrice-weekly regimen. In the I-HD group, this strategy allowed us to switch one patient to standard-HD and improve dialysis efficiency in another.

Our sample is small, but we are applying this policy to new patients and hope to improve our statistical power in the next 2 or 3 years.

In conclusion, I-HD seems to be a safe, beneficial strategy for selected children with kidney failure and preserved RKF, especially in the CAKUT subgroup. It is worth emphasising the importance of accurate RKF measurement to prevent suboptimal dialysis, while reducing dialysis burden and healthcare costs without compromising clinical outcomes compared to standard-HD. Further research is warranted to validate these findings and optimise I-HD approaches in the pediatric population.

Author contributions J.G conceived and designed the study. All authors provided intellectual content, revised the drafts and approved the final version.

Funding No funds, grants, or other support was received.

Data availability Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Competing interests The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval The study was approved by the Ethics Committee of the Southern Metropolitan Health Service, and is in accordance with the Helsinki Declaration.

Human and animals rigths This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Due to the nature of the retrospective study and the anonymisation of patient data, the Ethics Committee approved the study without written informed consent.

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