Calcium balance in pediatric online hemodiafiltration: beware of sodium and bicarbonate prescription in the dialysate

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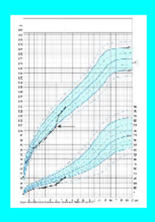
1- Background

Online hemodiafiltration (oHDF), combining hemodialysis with high convective flux and ultrapure dialysate, has been proposed as an innovative solution to clear small and middle-sized uremic toxins with a very biocompatible system. In 2013, oHDF was recognized as a **safe and efficient procedure**. However, due to specific technical requirements and lack of license in many countries, it is **not widely used in pediatrics**, even though some recent reports have highlighted its **interest to promote catch-up growth**, and decrease malnutrition (*Fischbach M et al, Nephrol Dial Transplt 2010*).



We have been using pediatric online hemodiafiltration (oHDF) since March 2009 in our pediatric unit.

Without any significant change of our daily practice, despite an adequate management of CKD-MBD as proposed by the international guidelines, we observed **in 2011 some unusually low PTH levels** (below 80 pg/mL) **in all six treated patients when using a dialysate with a 1.5 mmol/L-calcium concentration** (*Perouse de Montclos et al, Nephrol Ther 2013*).

The **'calcium balance'**, as assessed by the measurement of **total plasma calcium before and after the mid-week session**, was **strongly positive**, from 2.58 (2.42-2.84) to 2.66 (2.46-2.74) mmol/L.

We therefore concluded that dialysates containing 1.5 mmol/L of calcium may not be suitable for pediatric oHDF (5), and **we switched our patients to dialysates containing 1.25 mmol/L of calcium in December 2012.**

3- Results in the patients

The first evaluation of the biochemical profile was performed with a calcium concentration of 1.25 mmol/L in the dialysate. **Both tCa and iCa dramatically decreased in plasma during the session**: indeed, after the session, iCa was below the local reference range in three patients, just at the lower normal level in one and normal in only one patient. **Major discrepancies between the expected and the measured dCa concentrations were observed.**

With these results in mind, **we switched four children to 1.5 mmol/L-dialysates**: the second evaluation of the biochemical profile showed that **both tCa and iCa remained normal at the end of the oHDF session in all patients**; we even observed a moderate increase of tCa at the end of the session. Discrepancies between the expected and the measured dCa were still present, however in a lesser extent.

		First evaluation (N=5)		Second evaluation (N=4)	
Dialysate	Expected calcium (mmol/L)	1.25		1.50	
	Measured calcium (mmol/L)	1.01 (0.83-1.04)		1.47 (0.85-1.75)	
	Expected bicarbonate (mmol/L)	34 (30-40)		35 (34-40)	
	Measured bicarbonate (mmol/L)	32 (29-37)		31 (31-37)	
	Expected chloride (mmol/L)	112.5		112.5	
	Measured chloride (mmol/L)	101 (95-104)		109 (95-120)	
	Expected sodium (mmol/L)	136 (135-137)		136 (135-137)	
	Measured sodium(mmol/L)	132 (131-132)		139 (131-152)	
Plasma		**Beginning of the session**	**End of the session**	**Beginning of the session**	**End of the session**
	Calcium (mmol/L)	2.40 (2.26-2.43)	2.18 (2.09-2.31)	2.43 (2.15-2.19)	2.51 (2.35-2.66)
	Ionized calcium (mmol/L)	1.2 (1.1-1.2)	1.0 (0.9-1.2)	1.2 (1.1-1.2)	1.2 (1.1-1.2)
	Phosphorus (mmol/L)	1.6 (1.03-1.76)	0.61 (0.31-0.70)	1.97 (1.50-2.14)	0.70 (0.65-0.74)
	Bicarbonate (mmol/L)	23 (19-27)	27 (22-31)	20 (19-23)	27 (25-28)
	Magnesium (mmol/L)	1.04 (0.89-1.14)	0.72 (0.70-0.77)	1.10 (0.93-1.18)	0.77 (0.73-0.83)
	PTH (ng/L)	362 (88-601)	445 (217-499)	391 (224-483)	182 (126-599)
	C-terminal FGF23 (RU/mL)	2058 (708-4149)	900 (470-5605)	3942 (650-10209)	2461 (435-6631)
	Albumin (g/L)	38 (33-40)	38 (34-42)	39 (36-42)	41 (37-46)

2- Objectives and methods

The objective of this **service evaluation audit** designed as a **retrospective study** was to evaluate our current practice and to measure the main parameters of mineral metabolism in in our centre.

In **September 2013**, we therefore **assessed plasma and dialysate electrolytes** in the **five children undergoing chronic oHDF** with a 1.25 mmol Ca/L-dialysate.

Plasma total calcium (tCa), **ionized calcium** (iCa, local reference value between 1.1 and 1.3 mmol/L), bicarbonates, phosphate, magnesium (routine biochemical assessment), PTH (ECLIA, Cobas, Roche®) and C-terminal FGF23 (2nd generation, Immutopics®) were measured.

Blood samples were drawn **before and after the mid-week session** while blood and dialysate flows were decreased to less than 100 mL/min and substitution stopped during the last 3 minutes of the session.

We also assessed the **concentration of electrolytes in the dialysate** just before beginning the session (calcium dCa, bicarbonates, chloride, sodium), using the routine biochemical technique for urines.

All children underwent **oHDF with a Fresenius 5008® device** and Helixone dialyzers (Fresenius Medical Care); dialysates were all 7076 bags (Baxter®).

Due to the low number of patients, results are presented as median(range).

4- 'Ex-vivo' results : dCa directly measured on the Fresenius device

To **explain the discrepancies observed between expected and measured dCa**, electrolytes were measured in the dialysate produced by a Fresenius 5008 machine at the end of successive ten minute-periods following the modification of sodium and bicarbonate conductivity requested to the machine, when no patient was connected to the machine.

Theoretical calcium (mmol/L)	Required sodium (mmol/L)	Required bicarbonate (mmol/L)	Measured sodium (mmol/L)	Measured chloride (mmol/L)	Measured bicarbonate (mmol/L)	Measured calcium (mmol/L)
1.5	138	32	135	106	30	1.53
	135	32	131	103	30	1.48
	132	32	128	100	30	1.44
	138	35	135	103	33	1.48
	138	38	134	100	35	1.43
	138	40	135	98	37	1.39
	135	40	132	96	36	1.36
1.25	138	32	134	104	30	1.25
	135	32	132	102	30	1.24
	132	32	128	98	30	1.20
	138	35	134	101	33	1.23
	138	38	133	98	36	1.20
	138	40	134	97	37	1.18
	135	40	131	94	37	1.15

Decreased calcium concentrations in the dialysate were observed when the required sodium concentration was decreased and/or when the requested bicarbonate concentration was increased.

5- Discussion and conclusion

The **differences between expected and measured dCa** can be explained by **technical characteristics** on the Fresenius® system.

Indeed, during the reconstitution of the dialysate, **the priority is given to the final sodium concentration**: **increasing bicarbonate concentration** in the dialysate induces a decreased sodium (and calcium) extraction from the acid preparation, thus decreasing dCa. Similarly, **decreasing the sodium requested in the dialysate** (for cardiovascular protection) induces a decreased calcium extraction from the acid preparation, therefore also decreasing dCa.

Proof of this concept was given when measuring dCa after changing sodium and/or bicarbonate prescriptions directly on the 5008 machine.

Prescription of high bicarbonate and/or low sodium in the dialysate decreases calcium concentration in the dialysate.

Monitoring iCa in addition to classical mineral biomarkers may help to adapt pediatric oHDF.

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M) Dialysis. M6) Bone disease in dialysis patients.

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