



HEMODIALYSIS VERSUS CONTINUOUS VENOVENOUS HEMOFILTRATION TREATMENT OF METFORMIN ASSOCIATED LACTIC ACIDOSIS IN RENAL FAILURE PATIENTS

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Background

Renal failure patients using metformin may develop metformin associated lactic acidosis (MALA). It is unknown if hemodialysis (HD) and continuous venovenous hemofiltration (CVVH) are equally effective in metformin removal and acidosis correction in MALA.

Purpose and hypothesis

Purpose: To compare the efficacy of HD and CVVH in renal failure patients with MALA. We hypothesized that HD is more effective than CVVH, because it removes metformin faster than CVVH, leading to more effective correction of the lactic acidosis.

Materials and methods

Retrospective study of all consecutive patients with renal failure and MALA (pH < 7.35, lactate > 5.0 mmol/l) treated with HD or CVVH in our hospital. Metformin concentrations were measured in all patients. Metformin elimination half-life (Met_{1/2}), time to lactic acidosis correction and outcome were compared between HD and CVVH. The results were compared to literature data in a meta-analysis of published MALA cases

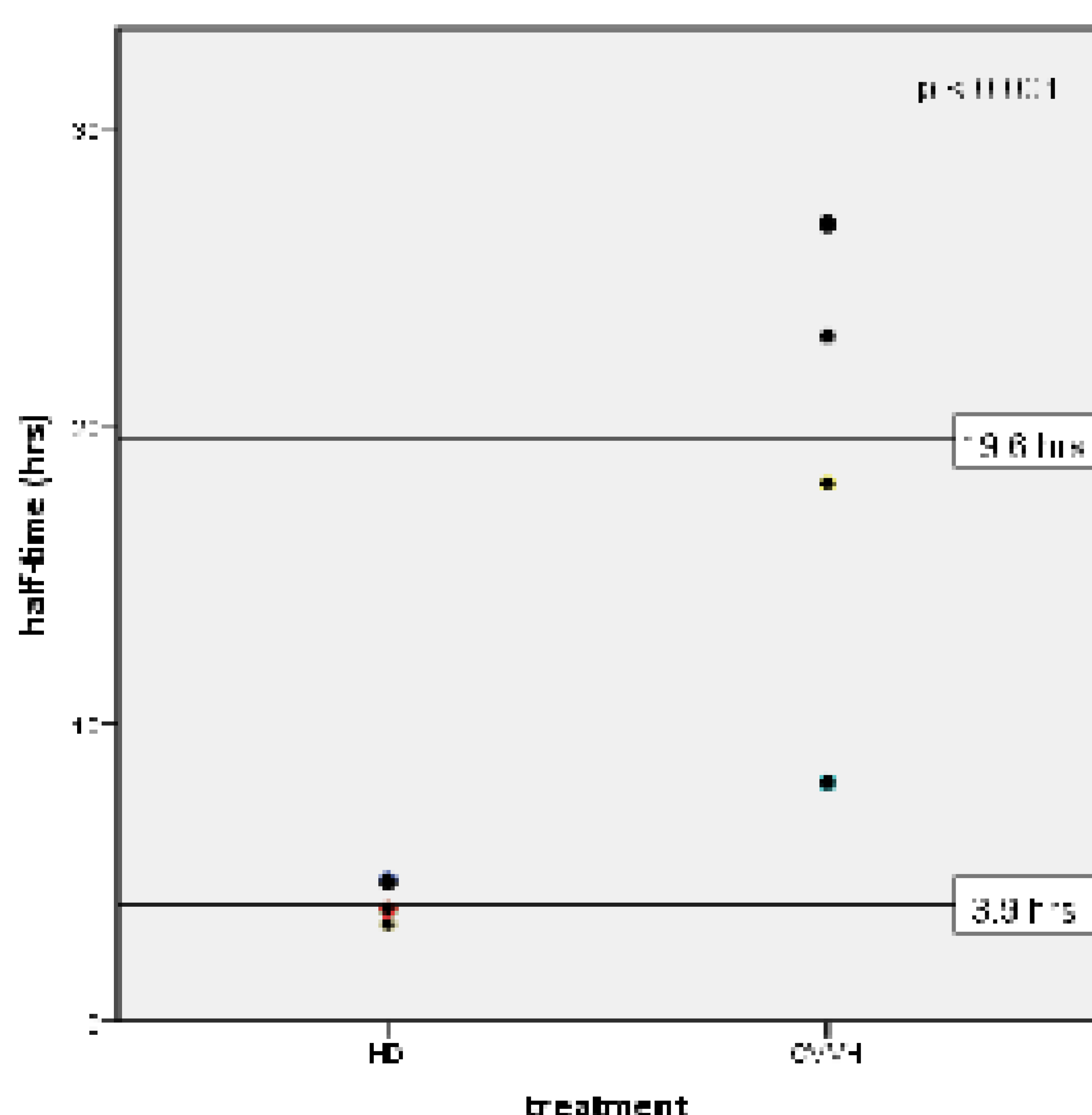


Figure 1. Metformin elimination half-life HD and CVVH

Results

Sixteen patients with renal failure and MALA were included (age 69.4 ± 7.4 years), 8 patients received HD and 8 CVVH at the discretion of the attending physician. No significant differences in admission details and outcome were observed between the two groups (Table 1). In 7 HD sessions in 5 patients the Met_{1/2} was 3.9 ± 0.7 hours (range 2.6 - 4.8), compared with 19.6 ± 6.9 hours (range 8.0 - 30.5) in 8 CVVH sessions in 4 patients ($p < 0.001$) (Figure 1). Literature data of 107 patients from a total of 43 case reports and case series were included in the meta-analysis. Forty patients were treated with HD and 67 patients received CVVH. Patient characteristics and survival did not differ between treatment groups, except for a slightly lower arterial pH in CVVH patients (6.93 ± 0.18 vs. 6.86 ± 0.18 , $p = 0.046$) (Table 2)

	HD (n=8)	CVVH (n=8)	p-value
Age (years)	71.3 ± 6.5	67.6 ± 8.2	0.43
Metformin (mg/mL)	19.6 ± 16.2	29.4 ± 14.2	0.25
Creatinine (μmol/L)	569 ± 268	720 ± 241	0.21
MDRD (ml/min/1.73m ²)	12.9 ± 16.7	6.5 ± 4.5	0.22
Arterial pH	7.02 ± 0.11	7.03 ± 0.23	0.56
Lactate (mmol/L)	16.2 ± 5.2	13.8 ± 6.4	0.46
Bicarbonate (mmol/L)	6.3 ± 2.8	6.6 ± 3.8	0.87
MAP (mmHg)	84 ± 24	73 ± 16	0.19
SAPS-II	63.3 ± 26.1	67.6 ± 24.7	0.77
Outcome (survival)	6 (75%)	5 (62.5%)	0.59
T normal pH (hr)	17.7 ± 10.0	23.2 ± 10.7	0.35
T normal lactate	47.0 ± 41.5	27.0 ± 6.2	0.68
Renal recovery	71.4%	57.1%	0.57

Means (± SD) or numbers (%), MAP: mean arterial pressure; SAPS-II: simplified acute physiological score II

	HD (n=40)	CVVH (n=67)	p-value
Age (years)	67.1 ± 9.4	68.9 ± 10.5	0.35
Sex (male)	13 (32.5%)	22 (32.8%)	0.97
Systolic blood pressure	116 ± 30	104 ± 41	0.18
Serum creatinin (μmol/L)	728 ± 373	703 ± 42	0.76
Serum metformin (mg/mL)	47.3 ± 24.7	48.7 ± 31.5	0.95
Arterial pH	6.93 ± 0.18	6.86 ± 0.18	0.046
Serum lactate (mmol/L)	16.3 ± 6.0	19.8 ± 10.5	0.20
Outcome (survival)	34 (85%)	56 (83.6%)	0.85

Values are means (± standard deviation) or numbers (percentages)

Conclusions

- In renal failure patients with MALA:
- HD removes metformin faster than CVVH
 - HD and CVVH ultimately have similar efficacy in correction of lactic acidosis and outcome
 - meta-analysis of published cases confirms that both HD and CVVH are effective treatments

1. Van Berlo-van de Laar IRF et al. Metformin associated lactic acidosis: incidence and clinical correlations with metformin serum concentration measurements. *J Clin Pharm Ther.* 2011;36:376-382
2. Welsberg LS. Lactic acidosis in a patient with type 2 diabetes mellitus. *CJASN* (ePress)

