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Influence of Temperature on dialysis in the artificial kidney

Since Kolff introduced clinical extra-corporeal hemodialysis in 1943, many improvements have been made on the physical apparatus, design, and technique of dialysis. One of the variables that has received relatively little attention has been the effect of the temperature of the bath solution in the dialyzer on the efficiency of dialysis in the clinical setting. Brown and Schreiner², by in vitro studies, have shown that between 37°C. and 10°C., a linear reduction in dialysance of urea and creatine of about 1% per degree occurs.

In vitro studies cited by Lyman⁶ showed that using a cuprophane membrane, urea in water dialyzed 1.20 times as fast at 40° as at 30°. Freeman, et al.³ demonstrated improved dialysance, in an in vivo setting, by increasing dialysate temperature from 10°C. to 37°C. The once popular low temperature (cold) dialysate is now seldom used, and it has been replaced by a warm (37°C.) bath. These results

suggest that an investigation of temperature variation under clinical conditions was needed. We present the results of such a study, using dialysate bath temperatures of 37°C. and 40°C.

Method

A two-layer, single-pass, counter-current flow Kiil dialyzer was used. Cuprophane membrane (cellophane regenerated by the cuprammonium process)⁵ was employed throughout this study. The experimental population consisted of patients on maintenance dialysis, for an average of 2 years, most of whom were on a bi-weekly, 12-hour dialysis schedule. All of them had end-stage renal disease (Creatinine clearance of 0-2ml./min.).

A heat exchanger was employed in the dialysate affluent line to maintain the dialysate at the specified temperatures within 0.1°C. when entering the dialyzer. Calibrated thermister probes were utilized within the dialysate flow line to measure the temperature of the

dialysate as it entered and exited the dialyzer (Fig. 1).

The patient's arterial pressure pumped the blood through the dialyzer. The dialysate flow was maintained at approximately 500 cc./min. and monitored by periodic timed collection in a graduated cylinder. The blood flow rate was measured by timing the passage of a small bubble of air injected into the blood tubing, as it transversed a measured length of tubing.

Each patient's blood was dialyzed with a 37.0 and 40.0 dialysate, and the clearances of urea and creatinine at these temperatures were calculated.

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Blood samples were drawn from the arterial and venous sides of the dialyzer simultaneously. Thus, each patient acted on his own control during the 37° dialysis, with 40° dialysis being the experimental variable.

Dialysance was calculated according to the formula:

$$D = Q (C_i - C_o) / C_i$$

where D = dialysance

Q = blood flow through dialyzer

C_i = concentration of substance dialyzed in inflow blood

C_o = concentration of substance dialyzed in outflow blood.

Results

Forty-three different comparisons were made. Dialyses were accomplished, starting at 37°, followed immediately by a 40° bath, and then another 37°C. "run", and vice versa. The results of each of these comparisons is shown in Table 1. Inflow-outflow temperature differences were approximately 3°. The average initial BUN in all runs was 58.8 mg. %; initial creatinine average 10.6 mg. %. The average blood flow at 37 was 173 ml./min.; the average blood flow at 40 was 176 ml./min. The dialysate flow averages were 473 ml./min. at the lower temperature, and 470 ml./min. at the higher temperature.

The average clearance at 37°C. for blood urea nitrogen was 77 ml./min.; this value at 40°C. was 83 ml./min.: an 8% increase. The average creatinine clearance at 37° was 65 ml./min.; at 40° this value was 68 ml./min.: a 5% increase. These increases have been calculated to be statistically significant to the 1% level in the case of the BUN and to the 5% level in the case of creatinine, using the student t-test (Fig. 2).

Discussion

We regard these results as an indication that an elevated dialysate temperature does have a favorable influence on the efficiency of the dialyzer. It should be pointed out, as discussed by Sweeney and Galletti⁸, that dialysance efficiency increases as the ratio of dialysate flow to blood flow increases, whereas in our studies, this ratio slightly decreased as the dialysance increased with temperature, which would tend to bias our results adversely.

Figure 2. Tests of Statistical Significance.

BUN changes (37°-40°C)

Paired t test N=43

Average change $\bar{d} = +6.98$

$$t = \frac{6.981}{1.362} = 5.12 \quad P < .01$$

Significant at 1% level

Creat. changes (37°-40°C.)

Average change $\bar{d} = +3.0$

$$t = \frac{3.067}{1.345} = 2.28 \quad P < .05$$

Significant at 5% level.

No attempt was made in this study to investigate the mechanism of apparent improvement in dialysis with increased dialysate temperature. In speculating on such a mechanism, several factors must be considered. Cellulose membranes consist of fibers interlacing in an ill-defined, irregular fashion, which create "pores". This has been compared to a "flattened hay stack"¹. It has been proposed that solute molecules pass through the membrane by moving segments of the polymer out of the way, rather than passing through preformed pores⁷. Increased temperature may make polymer segments more "pliable".

In addition to the membrane barrier, there are thin films of fluid on each side of the membrane which act as additional membranes in series. Kolff has argued⁴ that diffusibility through these thin fluid films seems to be the limiting factor in dialysance. Other factors influencing solute permeability are the monolayer of leukocytes found to coat the membrane's

blood surface, and the phenomenon of membrane molecular polarization. For the purposes of our study, we have assumed that increased dialysance with increased temperature could be a result of the kinetic energy added to the system.

Patient reaction to the experiment varied. Some complained of a feeling of warmth, but this was infrequent and inconsistent with actual temperature level of the bath. Observed patient temperatures were generally normal or subnormal during dialysis. No adverse effects were noted. To what extent these results may be useful in the day-to-day operation of a dialysance center is not known. Long-term evaluation of the efficacy of using increased dialysate temperatures is now being conducted at our center.

Summary

A study of the effect of dialysate bath temperature on dialysance efficiency in the clinical setting, using 37°C. baths, has shown that use of the warmer bath improves dialysance.

References

Table 1. DIALYSANCE AT DIFFERENT TEMPERATURES

No.	Temp. Sequence	BUN ml./min.		Creatinine ml./min.		
		Di37°C.	Di40°C.	Di37°C.	Di40°C.	
¹ Bluemle, L. W., Jr.: Session I—Dialyzing membranes. <i>Proceedings, Conference on Hemodialysis, National Institutes of Health</i> , 1964, p. 9.						
² Brown, H. W., and Schreiner, G. E.: Prolonged hemodialysis with bath refrigeration: The influence of dialyzer membrane thickness, temperature, and other variables on performance. <i>Trans. Amer. Soc. Artif. Intern. Organs</i> 8: 189, 1962.						
³ Freeman, R. B., Setter, J. G., Maher, J. F., and Schreiner, G. E.: Characteristics and comparative efficiencies of coil and parallel flow hemodialysis. <i>Trans. Amer. Soc. Artif. Intern. Organs</i> 10: 174, 1964.						
⁴ Kolff, W. J.: The artificial kidney—past, present, and future. <i>Circulation</i> 15: 288, February 1957.						
⁵ Leonard, E. F., Bluemle, L. W.: Evaluation of dialysis membranes. <i>Trans. Amer. Soc. Artif. Intern. Organs</i> 8: 182, 1962.						
⁶ Lyman, D. J.: New synthetic membranes for the dialysis of blood. <i>Trans. Amer. Soc. Artif. Intern. Organs</i> 10: 19, 1964.						
⁷ Michaels, A.: Session I — Dialyzing membranes. <i>Proceedings, Conference on Hemodialysis, National Institutes of Health</i> , 1964, p. 32.						
⁸ Sweeney, M. J., and Galletti, P. M.: A practical point of reference for evaluation of mass transfer capacity of hemodialyzers. <i>Trans. Amer. Soc. Artif. Intern. Organs</i> 10: 6, 1964.						
				* Started at 37° - 40° - 37°		
				** Started at 40° - 37° - 40°		
29	**	71.3	66.3	59.8	51.4	
31	**	78.5	82.0	80.1	69.9	
32	**	92.1	99.3	74.0	75.0	
34	**	73.7	76.6	63.7	66.2	
35	**	86.6	81.8	70.1	64.6	
36	*	72.6	74.6	62.0	62.6	
37	**	73.5	84.5	58.9	65.7	
38	*	80.1	80.2	67.8	68.9	
40	**	61.0	105.2	63.0	50.0	
41	*	94.9	101.4	82.2	76.0	
42	**	59.2	62.5	50.7	52.4	
43	*	99.6	99.0	87.0	81.4	
44	**	73.8	79.8	75.9	71.0	
45	**	68.0	79.3	54.1	68.0	
47	**	66.2	69.6	50.1	55.0	
48	**	55.9	64.1	43.2	54.6	
49	*	51.7	46.4	42.8	37.8	
50	**	78.0	85.5	60.1	57.5	
51	**	64.6	70.9	62.9	69.0	
52	**	78.6	80.5	62.3	68.1	
5-2	*	70.4	73.6	61.2	64.5	
5-16	**	79.0	75.7	71.8	70.6	
Average		77.0	83.0	65.0	68.0	
				* Started at 37° - 40° - 37°		
				** Started at 40° - 37° - 40°		