Biofeedback technique through the variations of the dialysate sodium concentration

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The problem of determining the optimal value of dialysate sodium concentration is still debated, because no standard dialysate sodium concentration seems ideal for everyone. For an individual patient, too low a sodium concentration may generate intradialytic discomfort (hypotension, headaches, nausea, vomiting, cramps), whereas too high a concentration is also responsible for interdialytic discomfort (thirst) and long-term complications (hypertension, left heart failure). We describe here a biofeedback technique for providing automatic adjustment of dialysate sodium concentration to each individual patient.

THEORETICAL BACKGROUND

Acting on the dialysate sodium concentration induces a modification of the sodium mass transfer through the dialyzer and thus a modification of the exchangeable sodium pool of the patient. Consequently the optimal sodium dialysate concentration is the concentration which allows the restoration of the patient's sodium pool at a physiological value by making intradialytic sodium mass transfer equal to the interdialytic sodium load. Since the interdialytic water and sodium load varies from one patient to another and from one session to another, the ultrafiltration rate and dialysate sodium must be prescribed individually, according to dietary prescriptions and patient compliance especially when it comes to water and salt intakes.

The regulation of sodium balance should be based on the same principle as the regulation of fluid balance. The ultrafiltration rate is usually adjusted according to the measured predialytic weight, in order to reach a target value (i.e. the estimated dry body weight). By prescribing the desired postdialytic dry weight, the physician determines for his/her patient the total body water to be obtained at the end of the session. If the postdialytic weight is set at a constant value, the total body water also returns to a constant value at the end of each session. Consequently the exact amount of water accumulated since the previous session is removed during the session and the fluid balance is truly regulated.

Likewise the dialysate sodium concentration should be adjusted according to the measured predialytic plasma sodium concentration, in order to reach a target value (i.e. the estimated physiological value of plasma sodium concentration). By prescribing the desired postdialytic dry weight and plasma sodium concentration, the physician determines for his/her patient the total body water and the sodium pool to be obtained at the end of the session. If postdialytic weight and plasma sodium concentration are set at a constant, total body water and sodium pool also return to a constant value at the end of each session. Consequently the exact amounts of water and sodium accumulated since the previous session are removed during the session and the sodium-water balance is truly regulated, avoiding chronic sodium-water overload.

The term «feedback» refers to a system capable of regulating a given parameter by observing a variable (measured parameter) related to it, in order, in turn, to automatically adjust the value of one or several parameters (command parameters) acting on the variable to be regulated (figure 1a). Ultrafiltration controllers are feedback systems routinely used in dialysis monitors in order to accurately control the fluid balance. From the measurement of the ultrafil-

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tration rate (measured parameter), ultrafiltration controllers set the transmembrane pressure (command parameter) at the value which makes it possible to obtain the expected weight loss at the end of the session (figure 1b).

Likewise, it should be possible to develop a feedback system which controls the sodium balance from the measurement of patient's plasma sodium concentration (measured parameter) by setting the dialysate sodium concentration (command parameter) at the value which makes it possible to obtain the expected value of plasma sodium concentration at the end of the session (figure 1c). Because the parameter measured by the feedback system is a biological variable of the patient, this system is called «biofeedback».

However, the precise determination of the optimal dialysate sodium concentration is more complex than that of the ultrafiltration rate. The management of ultrafiltration is based on an accurate relationship between the observed variable (interdialytic weight gain) and the command variable (ultrafiltration rate). In contrast, when managing dialysate sodium concentration, the observed variable (plasma sodium concentration) is not linked to the command variable (dialysate sodium concentration) by a simple relationship. The determination of this relationship requires the elaboration of mathematical models and the precise assessment of the patient's status at the beginning of the session.

We describe a biofeedback system which controls accurately the sodium balance. However, because the plasma-water conductivity is strongly correlated to the plasma sodium concentration (see below «technical validation») and because measurement of conductivity is easier than on-line measurement of sodium concentration, this system substitutes sodium measurements with conductivity measurements in order to estimate the plasma sodium concentration of the patient. Thus, from the measurement of the patient's plasma-water conductivity (measured parameter) by a system called «Diascan®», a specially designed software called «Diacontrol®» adjustes the dialysate sodium concentration by setting the dialysate conductivity (command parameter) at the value which makes it possible to obtain the expected plasma-water conductivity at the end of the session (figure 1d).

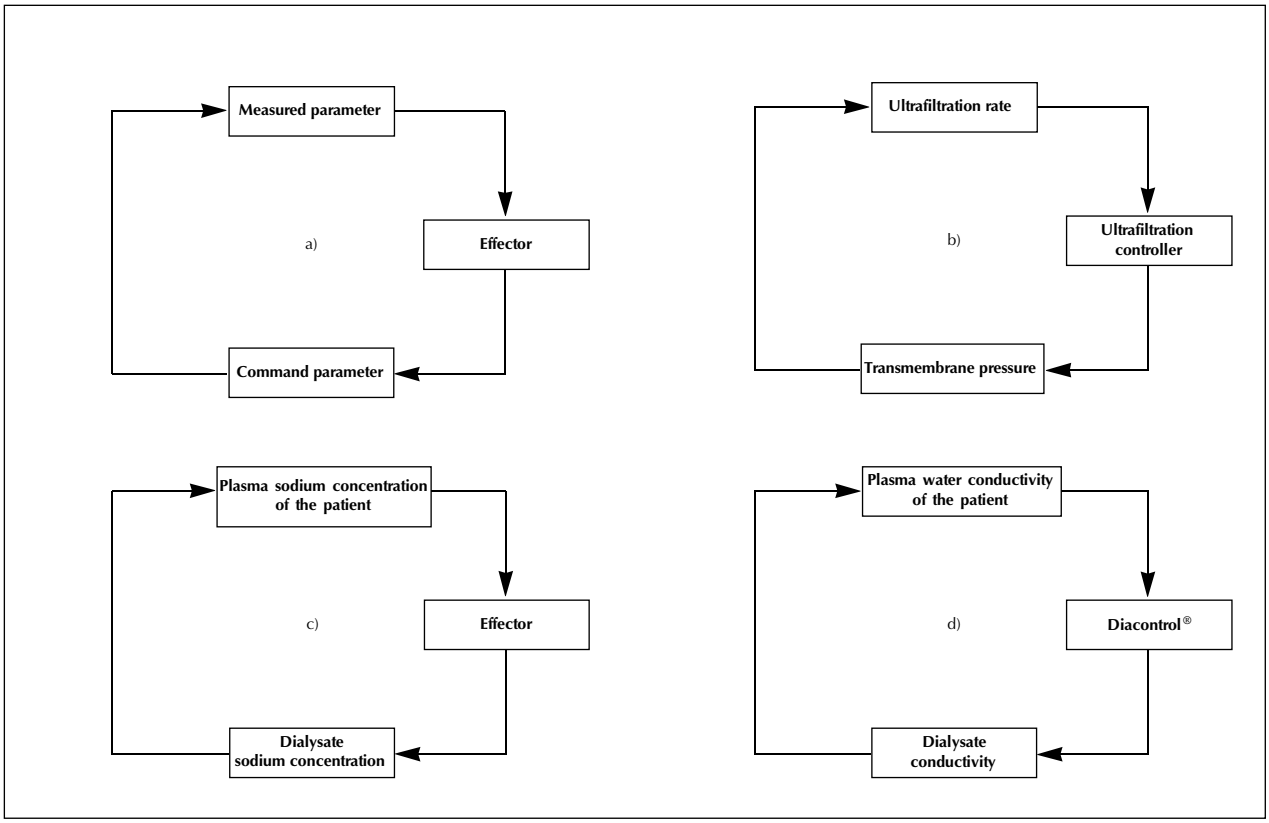

Fig.1.—Feedback loops: a) The principle of a feedback loop. b) An example of feedback loop: the ultrafiltration controller. c) An example of biofeedback loop for adjusting sodium balance. d) The biofeedback loop «Diacontrol®».

TECHNICAL IMPLEMENTATION

The biofeedback loop for controlling sodium balance consists of:

– a system, called «Diascan®», for automatic repetitive on-line measurement of ionic dialysance and of patient's plasma-water conductivity;

– an appropriate software, called «Diacontrol®», for calculating automatically the dialysate conductivity required to obtain the expected value of patient's plasma-water conductivity at the end of the session.

a) The «Diascan®»

Diascan® consists of:

– the implementation in the dialysis machine of an additional measurement of the dialysate conductivity at the outlet of the dialyzer;

– an appropriate software for measurement of ionic dialysance and of patient's plasma-water conductivity.

Measurements of ionic dialysance and of patient's plasma-water conductivity are performed as follows: for a given conductivity (C_D) of the dialysate delivered by the dialysis machine at the dialyzer inlet, the dialysate conductivity (C_{Dout}) measured at the dialyzer outlet is a function of the patient's plasma-water conductivity (C_P) and also of the performance (ionic dialysance, D_R) of the dialyzer used under the specific dialysis session conditions. Mathematical modelling yields the following equation linking these parameters :

$$C_{Dout} = \left(1 - \frac{D_R}{Q_D + Q_F} \right) C_D + \frac{D_R}{Q_D + Q_F} C_p \quad (1)$$

where Q_D and Q_F are dialysate and ultrafiltration flow rates respectively[1].

Practically, the value (X) of the conductivity of the dialysate delivered by the dialysis machine is changed by about 1 mS/cm over a short period (about 2 min), and after that is reversed to its initial value. The previous equation can be written with each measured X_1 and X_2 value corresponding to the two levels of C_D respectively, and with each respective value Y_1 and Y_2 of the dialysate conductivity measured at the dialyzer outlet, so as to obtain a system of two equations. Assuming the changes in D_R and C_P as negligible during the short period (about 5 min) required for measuring X_1, Y_1, X_2 and Y_2, we can obtain the values of the two unknown parameters C_P and D_R by solving these two equations:

$$C_p = \frac{X_1 Y_2 - Y_1 X_2}{(X_1 - X_2) - (Y_1 - Y_2)} \quad (2)$$

and:

$$D_R = (Q_D + Q_F) \left(1 - \frac{Y_1 - Y_2}{X_1 - X_2} \right) \quad (3)$$

Possible access recirculation accounts for the discrepancy between the true patient's plasma water conductivity (C_P) and the conductivity (C_B) at the dialyzer inlet. Mathematical modelling shows that the conductivity given by equation (2) is indeed the patient's conductivity (C_P), and not the conductivity (C_B) at the dialyzer inlet. Mathematical modelling shows also that the value D_R given by equation (3) is the value of ionic dialysance corrected for access recirculation[1].

Each 30 min, the «Diascan®» operates the change in C_D, records the values X_1, X_2, Y_1 and Y_2 and calculates C_P and D_R from equations (2) and (3). Because the ionic dialysance is strongly related to the actual urea clearance, the effective dialysis dose Kt can be estimated by Diascan® from the follow-up of D_R. Given an estimation of total body water, the normalized dialysis dose Kt/V can be also estimated[2, 3].

b) The «Diacontrol®»

The kinetic modelling used in the «Diacontrol software» is derived from the Gotch's single-pool model[4], but numerous modifications have been introduced:

– sodium measurement is substituted by on-line conductivity measurement;

– estimation of Donnan ratio from measurement of protidemia is useless;

– estimation of sodium dialysance from urea clearance given by the manufacturer is substituted by actual measurement of ionic dialysance corrected for recirculation.

In these conditions, if the weight loss is small enough (< 2% of total body water), a fixed-volume single-pool model can be used because total body water can be considered constant throughout the session and equal to its initial value (V_0). The patient's plasma-water conductivity (C_P) varies over time (t) during the dialysis session according to the following:

$$C_P = C_D + (C_{P0} - C_D) \exp(-Rt) \quad (4)$$

where C_{P0} is the measured C_P value at session onset, R is the D_R/V_0 ratio and C_D is the dialysate

conductivity (at the dialyzer inlet). When a significant weight loss is desired, a variable-volume single-pool model should be used and the previous equation becomes more complex:

$$C_P = C_D + (C_{P0} - C_D)\ (1 - qt)^{(R/q)-1} \qquad (5)$$

where $q = Q_F/V_0$ (Q_F is the ultrafiltration rate).

Solving equations (4) and (5) for C_D, we obtain:

$$C_D = \frac{C_P - C_{P0}.\exp\ (-Rt)}{1 - \exp\ (-Rt)} \qquad (6)$$

and:

$$C_D = \frac{C_P - C_{P0}.\exp\ [(\frac{R}{q} - 1)\ \ln\ (1 - qt)]}{1 - \exp\ [(\frac{R}{q} - 1)\ \ln\ (1 - qt)]}$$

Thus, given an estimation of V_0 (a percentage of dry weight set at a given value), the "Diacontrol®" calculates each 30 min from equations (6) or (7) the dialysate conductivity (C_D) which will bring the patient's plasma conductivity to the desired value (C_P) at the end of the remaining time of dialysis (t) as a function of the patient's plasma conductivity (C_{P0}) measured at the beginning of this period.

VALIDATION

Two aspects concern the validation of this biofeedback system:

– Is the sodium balance truly regulated by Diacontrol®? (technical validation).

– Is the control of sodium balance actually useful for the patient? (clinical validation).

a) Technical validation

Diacontrol® allows to accurately regulate the sodium balance because:

– Plasma-water conductivity measured by «Diascan®»" is strongly correlated with the plasma sodium concentration. The published correlation coefficients are comprised between 0.87 (nb of measures = 133[5]) and 0.95 (nb of measures = 24[6]).

– The measured plasma-water conductivity of the patient at the end of the session is very close to the prescribed value. The mean value (± SD) of the difference between the actual value and the prescribed value of the patient's plasma-water conductivity at the end of the session is –0.03 ± 0.09 mS/cm (nb of sessions = 133) in one study[5] and –0.04 ± 0.07 mS/cm (nb of sessions = 57) in another study[6]. In the latter, the mean confidence limits at 95% are (–0.06, –0.02) mS/cm and the individual confidence limits at 95% are (–0.18, +0.10) mS/cm, roughly equivalent to (–2, +1) mmol/l in terms of plasma sodium concentration. These results confirm the validity of the single-pool model used in the Diacontrol® software.

Figure 2 shows the efficiency of the biofeedback loop. Using the Diacontrol® (biofeedback mode), the patient's plasma-water conductivity CPpost at the end of the session is not significantly related to the dialysate conductivity, because the value of CPpost is that of the target conductivity fixed by the physician (figure 2a). The Diacontrol® is only adjusting the dialysate conductivity for the patient's conductivity reaching this target value at the end of the session. In contrast, in conventional hemodialysis (manual mode), the correlation is strongly positive (r = 0.85): higher is the dialysate conductivity imposed to the patient by the physician, higher is the plasma-water conductivity at the end of the session (figure 2b). In addition, using the Diacontrol® (biofeedback mode), there is a strong negative correlation (r = –0.93) between the mean dialysate conductivity during the session and the plasma-water conductivity of the patient at the beginning of the session: lower is the patient's plasma-water conductivity at the beginning of the session, higher is the dialysate conductivity required for reaching a target value of plasma-water conductivity at the end of the session (figure 2c).

b) Clinical validation

Two studies[7, 8] confirm the clinical interest of Diacontrol®. In the first study[7], 16 patients were treated (4 hours three times weekly) with conventional hemodialysis during a period of 4 months (control period: 724 sessions) and with Diacontrol® (666 sessions) during a period of 4 months. There was a lower intradialytic morbidity during the period using Diacontrol® in terms of percentage of sessions with symptomatic hypotension (7% vs 20%; $p < 0.001$) or nausea (2% vs 9%; $p < 0.001$). In the second study[8], 5 patients were treated during a period of 3 months with high flux hemodialysis (3 hours three times weekly). The number of episodes of symptomatic hypotension was lower when using Diacontrol® (1.6 ± 1.8 vs 6.6 ± 4.0 episodes per month).

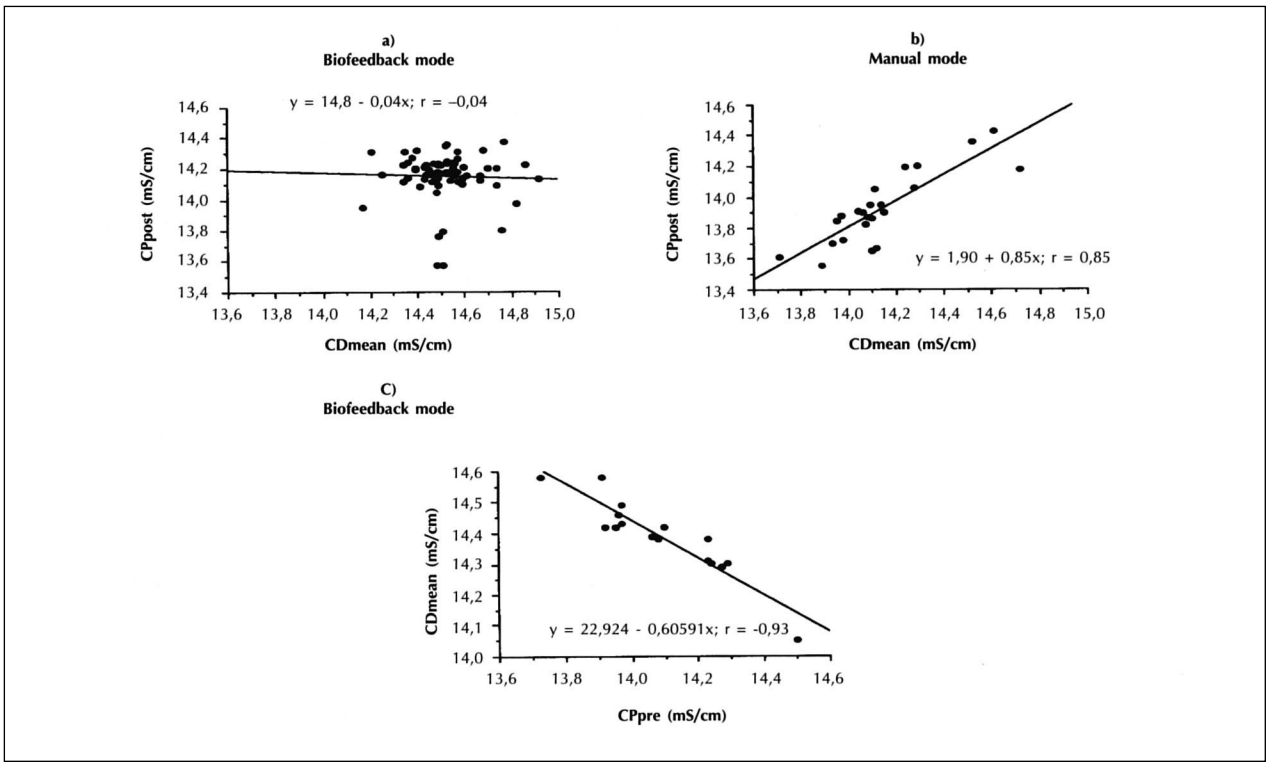

Fig. 2.—Efficiency of the Diacontrol®: a) Plasma-water conductivity CPpost (mS/cm) of the patient at the end of the hemodialysis session vs mean value of the dialysate conductivity CDmean (MS/cm) during a session with the Diacontrol®. b) Plasma-water conductivity CPpost (mS/cm) of the patient at the end of the hemodialysis session vs mean value of the dialysate conductivity CDmean (mS/cm) during a conventional session without the Diacontrol®. c) Mean value of the dialysate conductivity CDmean (mS/cm) during a hemodialysis session with the Diacontrol® vs plasma-water conductivity CPpre (mS/cm) of the patient at the beginning of the session.

The improvement in hemodialysis tolerance is probably due to the better refilling rate with a lower decrease in blood volume (13% vs 18%) obtained with Diacontrol®, as shown by di Giulio[9] which also reports a decrease in the number of hypotensive episodes (12 vs 26).

CONCLUSION

Diacontrol® is a feedback system which enables the physician to prescribe a patient parameter (desired end-of-session plasma-water conductivity) instead of a dialysis parameter (dialysate conductivity), just as an ultrafiltration controller enables the physician to prescribe a patient parameter (desired end-of-session weight loss) instead of a dialysis parameter (transmembrane pressure). In the short-term, Diacontrol® leads to a significant decrease in intradialytic morbidity. In the long-term, Diacontrol® makes it possible to maintain the sodium pool of the patient at a constant value and should help avoid chronic sodium overload and its related complications (hypertension, left heart failure...). Thus the automatic optimization of dialysate sodium by Diacontrol® can be considered safer for the patient than a prescription based on empirical and intuitive knowledge.

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