Abstract

**Background.** Automatic systems for stabilizing blood pressure (BP) during dialysis are few and only control those variables indirectly related to BP. Due to complex BP regulation under dynamic dialysis conditions, BP itself appears to be the most consistent input parameter for a device addressed to preventing dialysis hypotension (DH).

**Methods.** An automatic system (ABPS, automatic blood pressure stabilization) for BP control by fluid removal feedback regulation is implemented on a dialysis machine (Dialog Advanced, Braun). A fuzzy logic control runs in the system, using instantaneous BP as the input variable governing the ultrafiltration rate (UFR) according to the BP trend. The system is user-friendly and just requires the input of two data: critical BP (individually defined as the possible level of DH risk) and the highest UFR applicable (percentage of the mean UFR). We evaluated this system’s capacity to prevent DH in 55 RDT hypotension-prone patients. Sessions with (treatment A) and without (treatment B) ABPS were alternated one-by-one for 30 dialysis sessions per patient (674 with ABPS vs 698 without).

**Results.** Despite comparable treatment times and UF volumes, severe DH appeared in 8.3% of sessions in treatment A vs 13.8% in treatment B (−39%, P=0.01). Mild DH fell non-significantly (−12.3%). There was a similar percentage of sessions in which the planned body weight loss was not achieved and dialysis time was prolonged.

**Conclusions.** In conclusion, FL may be suited to interpreting and controlling the trend of a determined multi-variable parameter like BP. The medical knowledge of the patient and the consequent updating of input parameters depending on the patient’s clinical conditions seem to be the main factors for obtaining optimal results.

**Keywords:** biofeedback control; blood pressure; dialysis hypotension; fuzzy control; haemodynamics

**Introduction**

Dialysis hypotension (DH) episodes are a severe complication of dialysis treatment. Since a number of causal factors are involved [1,2], partly related to the dialysis technique itself (ultrafiltration, dialysate sodium and temperature, membrane) and partly related to the patient (hydration, anaemia, cardiovascular pathologies, etc.), real prevention is almost unattainable.

In an attempt to introduce something really new, as compared with traditional preventative measures (bicarbonate dialysis, fasting dialysis, adequate dialysis sodium, etc. largely resulted in being ineffective), over the past decade different systems have been devised and integrated into the dialysis machine, in order to artificially modify some parameters involved in the genesis of hypotension. Most of these systems exploit the idea of preventing severe hypovolaemia and improving vascular refilling by maximizing the ultrafiltration rate (UFR) in the first part of dialysis,
thereby reducing the negative effect of fluid withdrawal over the cardio-circulatory adaptation mechanisms in the last part of the treatment. The concomitant capability of some systems to move the dialysate sodium concentration as well may further contribute to enhancing vascular refilling dynamics [3–7]. Alternatively, the control of the patient’s thermal status, by preventing the heat gain responsible for vasodilation and possibly hypotension, has been considered [8]. Different clinical trials have actually proven the efficacy of all these systems in reducing the haemodynamic instability of hypotension-prone patients during dialysis [9–13].

However, what appears to be paradoxical is that blood pressure (BP), which is the real target of any form of control, cannot enter any of the control systems devised up to now as an input parameter, so the effect on BP remains indirect. Instead, just by considering the extreme complexity of the factors and mechanisms responsible for hypotension during dialysis, BP itself should be taken as the main input parameter for an automatic system capable of moving the UFR and/or the dialysate conductivity (DC) in a feedback manner.

The bioLogic RR device (RR stands for Riva Rocci, the conceiver of the current form of sphygmanometer), implemented in the Dialog Advanced dialysis machine (B Braun), is capable of retroactively controlling BP during dialysis, whose input parameter is the BP itself, automatically adapting the UFR, thus acting in favour of BP stabilization (automatic blood pressure stabilization system, ABPS). The strategy of UFR changes is aimed at optimizing vascular refilling and, in particular, inducing only minimal variations in blood volume (BV) in the final part of the treatment.

The feedback control of BP is achieved by means of fuzzy logic (FL), based on learning about the patient’s BP behaviour during the treatment [14]. ABPS had already been tested in a previous experience [15] on a small number of patients and it provided satisfactory results.

The aim of this work has been to verify the validity of this system itself, independently of any other clinical or dialysis parameter, in reducing the incidence of DH in a large number of dialysis patients prone to acute intra-treatment hypotension, at different dialysis centres, with each patient serving as his/her own control.

**Study design**

The study was designed as a prospective multicentre study, with the participation of 15 Italian dialysis centres, as follows: Aosta, Bologna (Malpighi), Castelfranco, Cernusco, Dolo, Imperia, Lucca, Pavia (Mauger), Pavia (Policlínico), Rimini, S. Giovanni Rotondo, Sanremo, Siena, Torino CTO, Tricase.

Local Ethical Committees gave their approval to the studies and patients’ informed consent was obtained before starting the planned dialysis study.

The trial was registered at the Cochrane Renal Group with number CRG080600083.

A short run-in period was planned to assess or optimize the definition of dry body weight for each patient. Classical clinical and radiological criteria were used, together with a bioimpedance evaluation on an interdialysis day, where applicable.

In the study period, each patient served as his/her own control. An overall number of 30 dialysis sessions were scheduled per patient, alternating sessions, day by day, with the use of the ABPS system with conventional dialysis sessions with constant UFR. The following abbreviations were used to identify the sessions: A = ABPS sessions, with variable UFR; B = conventional dialysis, with constant UFR.

This strategy was chosen in the study design as it represented the most immediate approach in sounding out the system’s effectiveness. Moreover, in patients on thrice-weekly dialysis, we could guarantee that in the longest interdialysis interval (where the risk of hypotension is higher, due to the higher body weight increase), ABPS was active on alternate weeks, in order to have the same number of first-day-of-the-week dialysis sessions with and without ABPS.

At the end of the study period, the number of A and B sessions per patient was comparable. Special attention was demanded of all the doctors superintending the protocol in order to achieve the highest degree of reproducibility in the operative and environmental conditions of the two treatments, considered in pairs: dialysis shift, time, drug schedule, room, nurses, snacks during dialysis, music, etc.

**Patients and methods**

**Patients**

Eligibility to the study included the following conditions:

- RDT for at least 1 year,
- any bicarbonate buffered haemodialysis treatment, not shorter than 180 min/session,
- stable clinical conditions, indicated by the absence of acute complications and by stable haemoglobin levels,
- interdialysis weight gain ≤ 5% of the body weight in the short dialysis day interval.

The only inclusion criterion was the presence of DH episodes in at least 30% of the dialysis sessions during the 2 months preceding enrolment.

In screening patients, the following criteria were adopted to define ‘acute DH’:

- if pre-dialysis systolic arterial pressure (SAP) was ≥ 100 mmHg: any event with SAP ≤ 90 mmHg, even without complaints;
- if pre-dialysis SAP was < 100 mmHg: any SAP reduction by at least 10% associated with complaints;
- any SAP reduction ≥ 25% in the pre-dialysis value, with the typical symptoms requiring specific intervention.

Any intercurrent pathological event modifying the patient’s clinical stability (persisting fever, sepsis, cardiovascular...
complications, surgery, etc.) were instead considered as exclusion criteria.

Methods

Fuzzy logic (FL) and its role in the Automatic Blood Pressure Stabilization system. FL is a problem-solving control system methodology that provides a simple way to arrive at a definite conclusion based on vague, ambiguous, imprecise, noisy or missing input information. It may control non-linear systems that would be difficult or impossible to model mathematically. Incorporating a simple, rule-based ‘if X and Y then Z’ approach to solving a control problem rather than attempting to model a system mathematically, it mimics how a person would make decisions. The desired system response is described in terms of linguistic variables rather than mathematical formulae (Appendix 1).

FL requires some numerical parameters in order to operate, such as what is considered a significant error and a significant rate-of-change-of-error. The system also needs to determine the input and output relationships and to choose a minimum number of variables for input (typically, error and rate-of-change-of-error). The number and complexity of the rules depends on the number of input parameters that are to be processed and the number of fuzzy variables associated with each parameter. Once the FL membership functions are created, defining the meaning (values) of the input/output terms used in the rules, the system is run. Then the system has to be tested, the result evaluated, the rules and membership functions tuned and retested until satisfactory results are obtained [16–18].

The bioLogic RR is a feedback UFR control system based on FL and implemented in the B Braun Dialog Advanced monitor. The physician’s rules and experience are the basis of the algorithm that relate input to output, where input is the BP value and output the UFR rate (Figure 1). FL provides a fine control of the output similar to that of a human operator.

The system only requires two input parameters:

- the UFR max, chosen by the operator, defined as the maximum level of UFR to be applied in a specific patient, and expressed as a percentage value of the UFR used in a conventional dialysis with linear and constant UFR;
- the BP set point, defined as the BP level at which a patient generally presents his/her complaints (dizziness, yawning, pallor, etc.).

In order to be sufficiently precise, the system needs a frequent evaluation of BP. For this purpose, BP is measured before the start of dialysis and during treatment at 5-min intervals with a dedicated system implemented in the machine. This is an oscillometric manometer, (Dinamap 1846 SX, Critikon, Norderstedt) capable of automatically adapting the cuff’s inflating pressure to the patient’s BP level (at the first measurement it reaches 200 mmHg, whereas after that, it inflates up to the level of the last measurement plus 30 mmHg), thus reducing inconvenience to the patient.

At the start of haemodialysis, the UFR is at its highest level (so-called UFR max), that is subsequently retroactively reduced and adapted, depending on the BP instant variation and on how much and how fast the BP gets close to the BP set point. Figure 2 illustrates the characteristics of the multilayer control model of the UFR. If the BP set point is reached, then the UFR automatically stops, after which it re-starts, once the critical haemodynamic moment has been overcome. Figure 3 contains an example of a dialysis session course when ABPS is used and BP reaches the critical set point. (For a technical description of the system algorithm, see Appendix 1.)

Treatments. For both the treatments dialysis was carried out with the Dialog Advanced machine (B Braun) equipped with the biologic RR software for ABPS. In order to maximally reduce the technical changes as compared with what the patients were used to, and solely assess the specific effects of the ABPS system, all dialysis parameters (treatment time, membrane, dialysate composition and temperature, blood and dialysate flows, heparinization) were kept...
For data analysis, the Snedecor–Fischer test and Student’s t-test were used. Final data in the article are expressed as mean ± SD. The sign test for non-parametric data was used to compare the frequency of the ‘hypotension’ variable in ABPS treatment vs the conventional ones. Data were considered significant when \( P < 0.05 \).

### Results

Out of 61 patients selected, 55 (31 M, 24 F) completed the study. The drop-outs were due to clinical problems acutely modifying conditions in four cases, and to renal transplantation in two patients. The underlying nephropathy of patients completing the study was glomerulonephritis for 20 patients, polycystic kidney disease in 10, nephrosclerosis in 16 and ESKD in 9. The mean patient age was 55 years, while the dialysis vintage was 43.2 months. They were usually treated with bicarbonate dialysis, thrice-weekly, 210–240 min/session. An overall number of 1372 dialysis sessions were studied: 674 with ABPS (treatment A) and 698 without (treatment B).

No significant differences were found between the treatments A and B in the dialysis duration and total UF, as well as in the difference between the total UF prescribed and the one actually obtained or in the difference between the dialysis duration prescribed and the one actually realized (Table 1).

Pre-dialysis BP values showed no significant differences between the two treatments, either in the standing or in the lying position, while the post-dialysis values presented a significant difference in the standing position, even though too small to have a clinical impact (pre-dialysis, lying position: treatment A: systolic pressure 134 ± 27 mmHg, diastolic pressure 70 ± 12 mmHg; treatment B: 134 ± 21 and 69 ± 13 \((P = NS)\); standing position: treatment A: 136±24 and 73±16; treatment B: 134±28 and 68±15 \((P = NS)\). Post-dialysis, lying position: treatment A: systolic pressure 125 ± 21 mmHg, diastolic pressure 66 ± 11 mmHg \((P = NS)\); standing position: treatment A: 125 ± 25 and 67 ± 14; treatment B: 122 ± 25 and

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment A M ± SD</th>
<th>Treatment B M ± SD</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Weight gain (kg)</td>
<td>3.28 ± 1.32</td>
<td>3.2 ± 0.85</td>
<td>NS</td>
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<tr>
<td>UF (l)</td>
<td>3.28 ± 1.32</td>
<td>3.2 ± 0.85</td>
<td>NS</td>
</tr>
<tr>
<td>HD time (min)</td>
<td>233.2 ± 18</td>
<td>233 ± 17.7</td>
<td>NS</td>
</tr>
<tr>
<td>HD sessions (%) with actually achieved UF &lt; UF prescribed</td>
<td>28.9 ± 3.1</td>
<td>34.4 ± 3.39</td>
<td>NS</td>
</tr>
<tr>
<td>Difference (ml) between total UF prescribed and UF achieved</td>
<td>150 ± 190</td>
<td>180 ± 180</td>
<td>NS</td>
</tr>
<tr>
<td>HD session (%) with actual treatment time &lt; prescribed</td>
<td>9.31 ± 2.01</td>
<td>6.67 ± 1.4</td>
<td>NS</td>
</tr>
<tr>
<td>Difference (ml) between actual and prescribed treatment times</td>
<td>16.8 ± 15.2</td>
<td>16.2 ± 12.0</td>
<td>NS</td>
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</tbody>
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**Fig. 3.** A typical course of a dialysis treatment with the use of the ABPS. A feedback control of the UFR (blue columns) is automatically activated if the systolic pressure (red line) decreases. If, in spite of the control, BP decreases below the critical set point (dotted red line), the minimum UFR will be applied.

unchanged as compared with the usual treatments and dialysis sessions were carried out according to the customary practices of the various dialysis centres (bed or armchair, snacks or fasting, etc.).

In treatment A (ABPS), the operative parameters for the fuzzy system were as follows:

(i) UFR max: up to 160% of the mean UFR;
(ii) BP set point:
   (a) if pre-dialysis SAP was ≥140 mmHg, BP set point = 110 mmHg;
   (b) if pre-dialysis SAP was <140 mmHg, BP set point = SAP – 30 mmHg.

This type of setting was the result of a previous experimental period, performed in other patients at the Malpighi Nephrology and Dialysis Department, so that they might become familiar with the system. While for patients with normal–high BP we found that 110 mmHg could be considered a ‘universal critical level’, for those patients with normal–low BP values this value was personalized as a function of the pre-dialysis level.

In treatment B (no ABPS), constant UFR, equal to the body weight increase divided by the treatment time, was applied.

In both the treatments, BP was measured during dialysis every 5 min with the automatic oscillometric manometer inserted in the machine.

Any constraints, apart from those illustrated earlier in the article, were indicated by the different centres. Pre- and post-dialysis BP, together with any event appearing during dialysis (hypotension, muscle cramps, nausea, vomiting or other symptoms) and specific interventions, were recorded by the nurses in a specific form for each dialysis session.

A comparison of the different frequency of DH in the two dialysis strategies was made, as well as in the target of total UF in the programmed time and the need for therapeutic action.

**Statistics**

For data analysis, the Snedecor–Fischer test and Student’s t-test were used. Final data in the article are expressed as mean ± SD. The sign test for non-parametric data was used to compare the frequency of the ‘hypotension’ variable in ABPS treatment vs the conventional ones. Data were considered significant when \( P < 0.05 \).
Dialysis was complicated by the appearance of at least one episode of hypotension (mild and severe) in 21% of the sessions (n = 142) with ABPS (treatment A), and in 28.1% of the sessions (n = 196) without ABPS (treatment B). An overall reduction in the DH frequency equal to 25.3% was obtained (P = 0.02).

In order to attain some more accurate results as to the effects on haemodynamic stability, DH episodes, defined as in the patient screening phase, were further subdivided into mild and severe on the grounds of the following criteria:

- **Mild hypotension**: successfully treated with an UF withdrawal ≤5 min, with or without the infusion of 250 ml saline ± 20 mEq NaCl.
- **Severe hypotension**: needing >5 min UF stop, plus plasma expander.

The most important effect of the ABPS system was to reduce the severe hypotension episodes, which showed a significant decrease as compared with what was observed in conventional treatments B (−39.1%, P = 0.01), whilst the change in the mild hypotension episodes (−12.3%) was not significant (Figure 4).

The scatterplot comparing the frequency of severe hypotension episodes in treatments without and with ABPS (Figure 5) shows that for most of the patients the switch from the conventional treatment to the use of ABPS resulted in a real improvement in haemodynamic treatment tolerance. In effect, most of the patients are allocated below the identity line in the scatterplot, indicating that, on the whole, for a certain frequency of severe hypotension in the conventional treatments, the corresponding frequency in the ABPS treatments was, in most cases, more or less reduced.

To verify the system's efficacy in reducing the frequency of DH, the sign test for non-parametric data was used. By means of this test we compared the negative differences (number of patients in whom DH frequency was higher with the use of ABPS than without it) the positive differences (number of patients in whom DH frequency was lower with use of ABPS than without it) and the condition of equality (number of patients in whom the frequency of hypotension was comparable between the two treatments). This test resulted highly significant (P = 0.02), indicating that the null hypothesis is highly unlikely.

Fluids for the therapeutic interventions proved lower in the ABPS sessions, significantly for hypertonic sodium (386 ± 9.3 ml in A vs 442 ± 10.6 in B; −13%, P < 0.05) and plasma expanders (1982 ± 66 ml in A vs 2783 ± 84 ml in B; −29%, P < 0.03), which are usually employed for treating the most severe hypotension events. Instead the amount of normosaline did not turn out to significantly different between the two dialysis strategies.

**Discussion**

The prevention of dialysis-induced hypotension is still one of the hardest objectives to achieve. Moreover, the almost complete willingness to deliver dialysis treatment to every patient, independently of their age or degree of comorbidity, largely aggravates the problem, in spite of the well-known progress made in dialysis technology (UF control, biocompatible membranes, convective treatments, acetate-free techniques) which have, instead, reduced the natural unphysiology of dialysis and have enhanced the patient’s treatment tolerance.

The intrinsic multifactorial nature of DH [1,2] makes an actual prevention of the onset of hypotension...
virtually impossible. The most traditional and simplest measures generally adopted (fasting dialysis, the avoidance of hypotensive drugs before treatment, the avoidance of short treatments, bicarbonate-buffered dialysis, etc.) actually prove quite insufficient in the most compromised patients, like diabetic or heart-compromised subjects.

In the past decade, many attempts have been made to devise new systems aimed at improving the haemodynamic tolerance to dialysis by working on the variables mainly involved in the problem, such as blood volume. With a view to adapting fluid removal to the patient’s fluid status, profiling systems, both for UF and sodium, have been set up [3–7]. Generally speaking, these systems seek to enhance the cardiocirculatory tolerance to fluid withdrawal by removing more fluid at the beginning of the session, when the patient is more water-repleted, thus gaining an advantage to be used in the second part of the treatment when the UFR can instead be progressively decreased. Fluid shifts from the extra- to the intravascular space are facilitated [3], and the blood volume trend should result in being similar to what is observed in most stable patients [19], that is a more or less steep decline in the first part of dialysis and an almost linear trend in the last part of the treatment. However, dialysis profiling systems are, even from a strictly conceptual standpoint, self-limiting, in some way ‘rigid’, i.e. a pre-set profile of UF (or sodium) is applied throughout treatment, not adaptable to the different conditions of body fluid distribution and, above all, to the continuously changing fluid equilibrium at the arteriolar–capillary–venous level [20].

Since there is no retroactive control, but only a unidirectional one (i.e. from the machine to the patient), they are purely open-loop control systems. Biofeedback systems to control BP during dialysis [7,8], were the real leap ahead, in that they have revolutionized the technological approach to DH by introducing artificial intelligence and the self-control concept, by means of a closed-loop control retroactively managing some machine parameters (UF, sodium, dialysate temperature) akin to what is already available in some other fields of medicine, such as, for example, in the infusion pumps for insulin.

Closed-loop systems indeed enable a continuous adaptation of the output parameters depending on the patient response. The controlled variable re-enters the system, which ‘sees’ the result of the previous parameter change. Two systems of this type are today widely known: one of them, BVT (blood volume tracking), automatically controls blood volume [7], while the other, BTM (blood temperature monitoring) controls the patient’s temperature [8].

A number of papers have described the excellent results in improving haemodynamic instability during haemodialysis in hypotension-prone patients [9–13] when these systems are used as compared with conventional treatments.

However, the most striking drawback of the biofeedback systems known up to now is that, although BP is the real control target, it is not possible for BP itself to enter the system as an input parameter. Adding this parameter has always been thought to be troublesome as it would be necessary to know, first of all, which BP level is actually ‘critical for the single patient’; secondly, it is necessary to fine-tune the system’s response to the changes in BP in that particular patient, and lastly which type of response (magnitude, duration) the system should give.

ABPS is a biofeedback system, a typical closed-loop control, solely based on the chance to use BP itself as the input parameter: the system counter-response is to modulate the only output parameter, i.e. the UFR, according to the BP trend. This possibility is offered by FL, which processes the BP’s instant value, a parameter with no absolute significance, but rather individually patient-related, thus involving the clinical experience and the physician’s knowledge of the single patient. A combination of these two aspects, the medical knowledge of the patient, expressed by the critical pre-set parameter BP level, and the fuzzy interpretation of the patient’s BP trend, enables an effective personalization of the treatment. In other words, the automatic system is indeed modelled upon the patient.

In 1995, Nordio et al. [14] first described the results of their experience with the adaptive fuzzy control on a simulation model of BP and blood volume implemented in a personal computer with satisfactory results in stabilizing BP as well as in achieving the dry weight.

Schmidt et al. [15] first tested this system in seven hypotension-prone patients in 237 treatments overall, achieving less frequent and less severe hypotension events, as compared with control group patients who were treated by conventional haemodialysis.

Instead, our experience was carried out in hypotension-prone patients alternately treated with ABPS-controlled BP or with conventional haemodialysis in a one-to-one ratio (one session ABPS, one session without ABPS, and so on) so that each patient was his/her own control. Moreover, the large number of dialysis centres involved attached a particular importance to the results obtained. In fact, owing to the very nature of the system, the role played by physicians and nurses in the adequate running of ABPS is a critical factor: in this case, a single-centre study would provide results that are somehow conditioned by the customary practices of that specific centre or a single doctor.

The results of this multicentre study confirm that the FL seems well-suited to analysing BP trends during dialysis, provided a correct critical BP parameter has been introduced.

The results obtained on the DH incidence (a 25% reduction overall, with a 39% reduction in the most severe episodes) proves quite similar to what was obtained in a multicentre trial with the BVT system, aimed to retroactively control blood volume [9].

This is a well-confirmed result, considering that the ABPS system, by moving the UFR, influences the
blood volume behaviour, similarly (but not equally) to BVT. It could be argued that the 25–30% ‘saving’ in DH obtained with both the systems is what can be avoided when reducing the effect of uncontrolled blood volume behaviour on the cardiocirculatory response to fluid withdrawal.

As with any automatic system modulating the UFR throughout the treatment, there actually is the risk that the target of the ideal dry body weight, by completing the schedule of the programmed total UF, is not accurately reached. This drawback may be reflected in the treatment time, that, more or less often, must be prolonged in order to complete the fluid removal. On the other hand, the gain in BP stability reduces the risk of the temporary zero-setting of the UF, or its stable reduction, which are, instead, routine manoeuvres in the event of tendency to hypotension. In effect, as illustrated in Table 1, no significant differences appeared when comparing the actual dialysis time and total UF, as well as the percentage number of dialysis sessions in which the total programmed UF was not achieved or the actual treatment time was longer than that programmed. Even the difference in the UF volume or the minutes of treatment time (actual — prescribed) was comparable between the two treatment strategies.

Nevertheless, the present study does have some limitations. The work was performed using a single-blind procedure (blind to the patient), and inevitably the ABPS sessions received special attention from the nursing staff, involved in understanding the workings of the automatic system in response to the patient’s BP behaviour. Data concerning dialysis-sodium concentration or temperature were not collected, meaning that some dialysis-related factors affecting the BP stability were not taken into account. At the same time, we did not consider the specific cardiac conditions of the population studied, thus we are unable to state whether the benefits were obtained in the presence of a certain cardiological pattern. Although the present study should therefore be considered as somewhat preliminary, we believe that this experience actually has its own intrinsic value, despite its manifest limitations. Actually, this was a pilot study with the specific aim of assessing, in a large number of patients from different centres, the applicability of this new system during dialysis, in terms of user-friendliness, and the FL’s capacity to interpret a changeable, volatile variable such as BP, and finally to actually reduce the hypotension events in critical patients. From this point of view, the fact of not having over-emphasized the other parameters (dialysis time, conductivity, membranes, various habits, etc.) apart from the use of the system itself, enhances the result obtained.

The aims we intended to pursue were all achieved. We believe that it is now worth applying this system further and studying it within other more complex protocols, also aimed at identifying those patients who might draw the greatest benefits from it.

Conclusions

FL has proven capable of adequately interpreting and controlling the BP trends during haemodialysis.

In our experience, the automatic ABPS system based on this logic has allowed for an overall reduction in the dialysis episodes in hypotension-prone subjects, equal to 25%, and nearly 40% as concerns the most severe episodes. The system is quite straightforward to use and only a few specific parameters are needed.

Patients with a poor tolerance to fluid withdrawal, due to an instability in plasma refilling or to an inadequate cardiovascular and/or autonomic nervous system response to dialysis, could accrue benefits from the use of ABPS during dialysis treatment.

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Conflict of interest statement. None declared.

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**APPENDIX 1**

In the *bioLogic RR*, the feedback control of the UFR rate is maintained by non-invasive BP measurements via arm cuff, which are initiated automatically by the fuzzy controller at 5-min intervals.

Three linguistic variables are calculated from the measuring values:

(i) Relative difference of systolic pressure and pre-adjusted set point pressure,
(ii) Short-term pressure trend (15 min),
(iii) Long-term pressure trend (25 min).

Each of the linguistic variables i–iii is defined by specific fuzzy sets that are described by trapezoid and triangular membership functions for the interesting ranges of the variable.

FL is applied to the procedures of the feedback control in the following steps:

- **Fuzzification** of input data by matching of actual measuring values i–iii and relevant fuzzy sets inclusive weighing of the results by set operators,
- **Fuzzy inference** by probabilistic reasoning extended to specific rule bases for control of UFR,
- **Defuzzification** of conclusions obtained from fuzzy inference by conversion into crisp outputs for adaptation of UFR to patient’s actual BP behaviour.

The feedback control is provided by on-line transmission of the crisp outputs for UFR control to the dialysis machine (Figure 1).

Since on most of hypotension-prone patients the frequency of hypotensive events is increasing with ongoing haemodialysis, the biofeedback control is focused on UFRs as low as possible during the final phase of the session. This goal may be achieved by applying maximum UFRs (up to 200% of the average UFR) during the initial phase of treatment so long as it is tolerated by the systolic BP.

Figure 2 shows a simplified model of multilayer control characteristics, illustrating the interrelations between the following:

- **UFR n–1**: UFR applied during the previous 5 min-interval (n–1);
- **UFR n**: UFR calculated from Fuzzy-Controller for the actual 5 min-interval n.

Following a single layer (same colour) along the axis ‘conclusions’ for a fixed value UFR n–1, the figure demonstrates the control range of UFR n, which is available for the actual interval n after UFR n–1 was applied during the previous interval n–1.

Following a single layer (different colours) along the axis ‘UFR n–1’ for an individual conclusion, the figure shows how UFR n will be varied for the same conclusion depending on UFR n–1.