Measuring intradialyser transmembrane and hydrostatic pressures: pitfalls and relevance in haemodialysis and haemodiafiltration

Alain Ficheux, Nathalie Gayrard, Ilan Szwarc, Flore Duranton, Fernando Vetromile, Philippe Brunet, Marie-Françoise Servel, Joachim Jankowski, Àngel Argilés

To cite this version:

HAL Id: hal-03208425
https://hal-amu.archives-ouvertes.fr/hal-03208425
Submitted on 15 Nov 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License
Measuring intradialyser transmembrane and hydrostatic pressures: pitfalls and relevance in haemodialysis and haemodiafiltration

Alain Ficheux1,2, Nathalie Gayrard1,2, Ilan Szwarc3, Flore Duranton1,2, Fernando Vetromile3, Philippe Brunet4, Marie-Françoise Serve13, Joachim Jankowski5 and Àngel Argilés1,2,3

1RD – Néphrologie, Montpellier, France, 2BC2M, Univ Montpellier, Montpellier, France, 3Centre de dialyse de Sète, Néphrologie Dialyse St Guilhem, Sète, France, 4Hôpital de La Conception, Université Aix-Marseille, Service de Néphrologie, Marseille, France and 5Institute for Molecular Cardiovascular Research, RWTH Aachen University, Aachen, Germany

Correspondence and offprint requests to: Àngel Argilés; E-mail: argiles@rd-n.org

ABSTRACT

Background. Post-dilutional haemodiafiltration (HDF) with high convection volumes (HCVs) could improve survival. HCV-HDF requires a significant pressure to be applied to the dialyser membrane. The aim of this study was to assess the pressure applied to the dialysers in HCV-HDF, evaluate the influence of transmembrane pressure (TMP) calculation methods on TMP values and check how they relate to the safety limits proposed by guidelines.

Methods. Nine stable dialysis patients were treated with post-dilutional HCV-HDF with three different convection volumes (including haemodialysis (HD)). The pressures at blood inlet (B_i), blood outlet (B_o) and dialysate outlet (D_o) were continuously recorded. TMP was calculated using two pressures (TMP_2: B_o, D_o) or three pressures (TMP_3: B_o, D_o, B_i). Dialysis parameters were analysed at the start of the session and at the end of treatment or at the first occurrence of a manual intervention to decrease convection due to TMP alarms.

Results. During HD sessions, TMP_2 and TMP_3 remained stable. During HCV-HDF, TMP_2 remained stable while TMP_3 clearly increased. For the same condition, TMP_3 could be 3-fold greater than TMP_2. This shows that the TMP limit of 300 mmHg as recommended by guidelines could have different effects according to the TMP calculation method. In HCV-HDF, the pressure at the B_i increased over time and exceeded the safety limits of 600 mmHg provided by the manufacturer, even when respecting TMP safety limits.

Conclusions. This study draws our attention to the dangers of using a two-pressure points TMP calculation, particularly when performing HCV-HDF.

Keywords: convection volume, haemodiafiltration, haemodialysis, transmembrane pressure, ultrafiltration
INTRODUCTION

Haemodialfiltration (HDF) is an extracorporeal renal replacement technique that is based on both diffusion (passage of solutes across a permeable membrane according to a concentration gradient) and convection (passage of a fluid across a permeable membrane according to a pressure gradient). In HDF, convection is obtained by extracting fluid from the closed dialysate circuit at a given flow rate, which is then given back to the blood circuit either before the dialyser (pre-dilutional HDF) or after the dialyser (post-dilutional HDF; Figure 1). Recent evidence from randomized controlled trials suggests that post-dilutional HDF is associated with a benefit in survival, which would only be significant if it is performed with high convection volumes (HCVs), that is, 17.4 L/session for the Turkish study [1–3]. Maduell et al.’s [4] latest study on incident patients confirms this improvement in survival. However, the most recent analysis of the Dialysis Outcomes and Practice Patterns Study (DOPPS) data [5] on a larger number of patients in several European centres does not confirm this benefit. The fact that dialysis conditions and equipment to obtain HCV-HDF vary across DOPPS facilities and are more homogeneous in the Maduell study may explain the discrepancy.

To obtain HCV-HDF, significant pressure has to be applied to the dialyser membrane, frequently surpassing what is known as the $\zeta_{\text{K-O-UF}}$ max situation of the dialysis systems [6, 7]. $\zeta_{\text{K-O-UF}}$ stands for Global Coefficient of Ultra Filtration in the presence of Dialysate fluid. This parameter is not constant; it follows a parabolic function when convection is increased. The $\zeta_{\text{K-O-UF}}$ max is the vertex of this parabola, which corresponds to the situation where the maximum convection volume is obtained with the least applied pressure [transmembrane pressure (TMP)] [6, 7]. Then, when aiming to obtain as high as possible convection volumes [8], the dialysis systems are submitted to significantly stronger TMP constraints. The question arises to whether the resistance of the extracorporeal circuit to pressure is unlimited and what are the regulations warranting the security of the dialysis systems in terms of intra-dialyser pressure. Manufacturers specify the pressure limits of the dialysers in their notice and the European Renal Best Practice (ERBP) guidelines propose a TMP limited to 300 mmHg, as a safe maximum value [9]. However, TMP calculation is not standardized and commercially available monitors differ in their approaches [10]. Some dialysis monitors provide TMP calculated based on two pressure measurements (TMP2), whereas others use, or can use, a calculation based on three pressure measurements (TMP3). When assessing TMP2, pressures are measured at the blood outlet ($P_{\text{Bo}}$) and dialysate outlet ($P_{\text{Do}}$); when assessing TMP3, the measurement at the blood inlet ($P_{\text{Bi}}$) is also considered [10]. In presently available guidelines, there is no mention of how TMP should be measured and whether the value retained as a limitation applies to the mean observed pressure in the dialyser or the maximum pressure at any point of it [9]. Data on the influence of the two- or three-point (taking into account the pressure at the $P_{\text{Bi}}$) measurements on TMP are lacking and the actual values of pressure in the different points of the dialyser are not usually considered by clinicians when performing dialysis treatment.

The present work aimed to evaluate the influence of the calculation of TMP (2 and 3 point) on its absolute value in the clinical situation of post-dilutional HDF with different convection volumes. This study focuses on the intra-dialyser pressures in real haemodialysis (HD) and online post-dilutional HDF treatments. It analyses the data obtained from a larger study for which technical and clinical aspects have been previously published [11, 12]. In these reports, the sensitivity and reliability of determining $\zeta_{\text{K-D-UF}}$ max were demonstrated to be in the range of clinical use [11], and its application in clinics showed to be beneficial as it rendered the extracorporeal circuit more stable in terms of pressure constraints and decreased the number of alarms during treatments while allowing to reach sensibly HCVs [12].

MATERIALS AND METHODS

Preliminary study

By definition, TMP measurement requires the determination of four parameters: pressure at the blood line inlet ($P_{\text{Bi}}$), at the blood line outlet ($P_{\text{Bo}}$), at the dialysate outlet ($P_{\text{Do}}$) and at the dialysate inlet ($P_{\text{Di}}$) of the dialyser. In the clinical setting, $P_{\text{Di}}$ is usually unavailable, but some dialysis generators include this parameter such as the DBB-05 generators (Nikkiso, Tokyo, Japan). We analysed data from four patients dialysed on Nikkiso DBB-05 generators with 1.8 m² HF80 dialysers (Fresenius Medical Care, Bad Homburg, Germany), in post-dilutional HDF. We applied step increases in convection flow [cumulative 10 mL/min increases in the flow rate of the infusion pump (Figure 1)] and recorded the four pressures at the dialysate and blood inlet and outlet displayed on the generator when reaching the programmed convection at every step. We calculated and compared the resulting TMP2, TMP3 and TMP4 (formulas in Figure 1).

Clinical study

Patients. The population under study is described in Table 1. Nine dialysis patients stable at the moment of the study were assessed. There were four men and five women and mean age was 73 ± 4 years. Their dialysis accesses were arterio-venous fistulae (n = 8) and tunnelled jugular catheter (n = 1). All patients gave their written informed consent. The study protocol was approved by the ‘Comité de Protection des Personnes’ of Nièmes (2011.10.05 bis) with the registration number at the French Agency AFSSAPS 2011-A01092-39. The study was performed in agreement with the declaration of Helsinki.
Dialysis modality. Patients were treated with post-dilutional HDF with 1.8 m² Amembris membrane dialysers (B BRAUN Avitum, Melsungen, Germany) with three different levels of convection, each applied during three consecutive treatments (total 81 sessions). The convection volumes were: (i) HD (convection volume limited to the weight loss); (ii) post-dilutional HDF with the convection flow corresponding to the maximum of the ultrafiltration flow-to-TMP ratio (HCV-HDF at $c_{Ku,UF}$ max) [11]; and (iii) post-dilutional HDF with the highest acceptable convection flow (HCV-HDF at $Q_{UF}$ max). Safety alarms were set according to the recommendations of the ERBP guidelines: ultrafiltration rate limited to 30% of the blood flow and $TMP3$ was limited to 300 mmHg [9]. No automatic system adapting convection was utilized. The nursing staff had the prerogative of modifying the infusion flow if $TMP$ alarms prevented from pursuing the dialysis at the prescribed convection volumes. Blood flow, convection volumes and dialysis times are summarized in Table 2.

Variables measured and $TMP$ calculations. HDF machines with three pressure sensors (Dialog+, B BRAUN Avitum, Melsungen, Germany) were used. The pressures $P_{Bi}$, $P_{Bo}$ and $P_{Do}$ of the dialyser (Figure 1) were continuously recorded by the dialysis monitor. Two time points of the dialysis session were specifically studied: (i) at the beginning of the treatment ($T_{start}$) and (ii) at the end of dialysis session or when $TMP$ alarms induced a manual intervention to decrease convection ($T_{end}$ or modif). The average of 10 consecutive readings per patient and time point was considered. TMP was calculated using two pressure points ($TMP2$ and $TMP3$) and three pressure points ($TMP3$) according to formulas displayed in Figure 1.

Statistical analysis

Differences between dialysis conditions were analysed by variance analysis (ANOVA) accounting for the cross-over design. Post hoc tests were performed, adjusting for multiple comparisons using the Bonferroni correction. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Tests were performed using a Type I error of 5%. Results are given as the mean ± standard error of the mean.

RESULTS

Influence of $TMP$ calculation and convection flow on $TMP$ value

In a preliminary study, the influence of using 2, 3 and 4 point measurements on $TMP$ value was assessed at different levels of convection. Figure 2 shows an illustrative example of the pressure values and resulting $TMP$ obtained, whereas the dialysis system was submitted to a full range of convection. These results, presented for one case, were reproduced in all participating patients. In Figure 2A, it can be observed that $P_{Bi}$ increases exponentially with convection flow, while $P_{Bo}$ remained constant. The dialysate pressures $P_{Di}$ and $P_{Do}$ decrease exponentially with the increase in $Q_{UF}$, in a near parallel way mirroring changes in $P_{Bi}$.

The $TMP$ values calculated from the 2, 3 or 4 pressure measurements for the same treatment are presented in Figure 2B. It can be observed that $TMP2$ underestimates $TMP3$ of 45–100 mmHg. The difference between $TMP2$ and $TMP3$ increases with increasing convection flow due to the exponential increase in $P_{Bi}$, while $P_{Bo}$ remains constant (Figure 2A). The patterns of $TMP3$ and $TMP4$ are similar and absolute values differ by around 50 mmHg across the $Q_{UF}$ range (Figure 2C). This value, according to the $TMP$ formulas, is the half of the pressure drop in the dialysate $[|P_{Di} - P_{Do}|]/2$. It is around 100 mmHg (Figure 2A), well above the in vitro pressure drop measured at sites strictly corresponding to the dialyser length (25 ± 3 mmHg, in agreement with the values given by the manufacturer). The discrepancy can be explained by the position of the $P_{Di}$ sensor in the Nikkiso DBB-05 machine, away from the dialyser inlet. In this setting, the difference between $TMP3$ and $TMP4$ is about 12.5 mmHg (half of 25 mmHg) when dialysate pressure sensors are adjacent to the dialyser. It can be concluded that the fourth pressure measurement ($P_{Do}$) has a minimal influence on $TMP$ estimation.

Intradialyser transmembrane and hydrostatic pressures during treatment

In the clinical study, we collected pressure records every 30 s from three-pressure sensors generators to assess the clinical relevance of different $TMP$ estimations for dialysis session monitoring.
TMP and hydrostatic pressures in HD and HDF

**DISCUSSION**

TMP was the main parameter that allowed the pioneers in dialysis to control ultrafiltration and thereby weight loss and extracellular volume. With the advent of ultrafiltration controllers [13], weight loss was accurately driven by automatic setting of TMP by dialysis monitors. TMP turned into an informative value properly assessing TMP has allowed identification of the fact that the global ultrafiltration coefficient of a dialysis system is not constant, but follows a parabolic function when convection increases [6].

It is known that TMP varies greatly along the fibres of the dialyser [14]. However, in practice, it is not possible to measure TMP...
FIGURE 3: Pressure readings during dialysis treatments with different convection flows. Illustrative examples of three treatments performed in HD (left panels), high convection HDF at \( \tilde{Q}_{\text{UF, max}} \) (central panels) or at maximum possible convection (\( Q_{\text{UF, max}} \), right panels) in the same patient. The continuous recordings of pressures measured at the Bi and Bo (top panels) and TMP calculated based upon 2 or 3 measurement points (TMP2 and TMP3, lower panels) are displayed. Asterisks indicate infusion modification due to TMP alarms.

FIGURE 4: Pressure readings at two time points of dialysis treatments performed with different convection flows. Distribution of blood line pressures (top panels) and TMP (lower panels) observed in 79 treatments from 9 patients in HD (left panels), high convection HDF at \( \tilde{Q}_{\text{UF, max}} \) (central panels) or at maximum possible convection (\( Q_{\text{UF, max}} \), right panels). Values were obtained at the start of the treatment (\( T_{\text{start}} \)) and at the end of the treatment (\( T_{\text{end}} \)) or at the moment of adapting the convection because of TMP alarms (\( T_{\text{modif or end}} \), whatever was first. Box plots display median, first and third quartile, Tukey’s fences and extreme values.
the pressure of the fibres within the dialyser and external pressure sensors located outside the dialyser are used instead. To estimate an average TMP value, dialysis machines are equipped with two, three or four pressure sensors measuring pressures at the inlet and outlet of the dialyser, at both the blood and dialysate sides. The present work was performed to evaluate the influence of TMP calculations using two and three pressure measurements on its absolute value and on its variations during sessions in the clinical situation of post-dilutional HCV-HDF. Almost no information is available on these aspects, and the rare criteria included in dialysis guidelines are not adequately described or sustained by solid data. Our study provides information on the direct effects of convection on the pressures at the dialysate and blood sides, on the resulting TMP value. It also provides a description of longitudinal changes in pressure observed throughout the treatment, and how they are induced by convection.

When performing HD without added convection, the pressures of the system remain particularly stable. When convection is added, the pressures change during the procedure and the greatest changes are observed at the blood side at the entrance of the dialyser: pressure increases in a proportional manner to the rate of convection $Q_{\text{UF}}$. Since the pressure at the outlet at the blood side of the dialyser remains constant during dialysis, we observe an increase in the pressure drop in the blood compartment of the dialyser. Therefore, any method to assess the pressures in the dialysis system performing HCV-HDF that does not take into account the pressure values at the $B_i$ of the dialyser is not accurate and does not reflect the phenomena occurring inside the dialyser. This is the case when calculating TMP from only two points ($P_{B_i}$ and $P_{D_o}$). Since the blood pressure variations occurring during dialysis are overlooked, TMP2 should not be used to monitor a dialysis system performing HCV-HDF. Only machines performing at least a three-point TMP measurement including the $B_i$ site should be used to monitor the dialysis systems, particularly in HCV-HDF.

Is it necessary to monitor the four points? Our preliminary study shows that TMP3 and TMP4 follow the same pattern and that the difference between the two is relatively constant. The value of this difference is the result of adding the readings from the dialysate inlet into the formula ($P_{D_i}$ will be averaged with the $P_{D_o}$ value). In our study, this value was further increased by the location of the sensor on the dialysis machine, situated at a distance of the entrance of the dialyser. The pressure drop in the dialysate compartment is stable during the dialysis treatment, relatively independent of the convection rate and available from manufacturer documentation. In consequence, measuring the pressure at the dialysate inlet of the dialyser is not mandatory. However, should the reading of the pressure at the dialysate inlet be incorporated in the formula, it has to be corrected by the pressure drop before reaching the dialyser. Otherwise, using the crude value given by the sensor would artifically decrease the estimated TMP4.

Secondly, we aim to increase safety and want to avoid problems occurring during treatment. Focussing on the blood side of the extracorporeal circuit, the pressure measured in the blood outlet reflects the return or venous pressure. Therefore, any sudden changes in $P_{B_i}$ require immediate attention to the needle and blood access. The pressure at the $B_i$ ($P_{B_i}$) reflects changes on the resistance to flow between the blood pump and the entrance of the dialyser. Therefore, with constant blood and convection flows, a sudden increase in $P_{B_i}$ may be due to a decrease in effective dialysate surface or an increase in blood viscosity, both markers of initiated or premonitory of clotting in the dialyser fibres, respectively [15]. As we have shown in Figure 5, left panel, this complication may be prevented if monitored TMP is calculated using three or four pressure points, as they include the pressure measured at the $B_i$. TMP3 and TMP4 will warn about a sudden increase in pressure at the $B_i$ and preventive measures may be implemented, whereas TMP2 will not. Some machines presently available still use a TMP2 monitoring though.
Furthermore, with the advent of the HCV-HDF, the knowledge on the pressure changes in the system will help in establishing safety limits for this type of treatment. The ERBP has emitted an advice limiting the TMP to 300 mmHg [9]. However, our data clearly show that any given TMP limit should be associated to a type of TMP calculation. We have seen that 300 mmHg of TMP3 is already associated with increases in pressure at the Bi that may be beyond those advised by the manufacturer and that the use of TMP2 overlooks them. We think it may also be appropriate to monitor pressure at the Bi and propose to set a limit to be the dialyser manufacturer limit.

In summary, our study provides new information on the behaviour of dialysis systems, particularly relevant when performing HCV-HDF, which may help to establish pressure safety. We show that a strong discrepancy exists across TMP calculations, whereas appropriately monitoring pressures should be sought.

ACKNOWLEDGEMENTS

P.B., J.J. and A.A. are members of the European Uraemic Toxin (EUTox) working group of the European Society of Artificial Organs, endorsed by the European Renal Association–European Dialysis and Transplant Association.

CONFLICT OF INTEREST STATEMENT

A.F., N.G., F.D. and A.A. are employees of RD—Néphrologie, owner of the patent protecting the exploitation rights of the patents EP2362790, JP5587891 and US8298427. The results presented in this article have not been published previously in whole or part, except in abstract format.

REFERENCES