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The Effect of Pulsatile Flow on Ultrafiltration: *In-Vitro* Study and Comparison with Roller Pump

K. Lee [1,3,4,5], J. H. Jeong[1,3,4,5], C. H. Mun[1,3,4,5], J. C. Lee[1,3,4,5], B. G. Min [2,3,4,5]

[1] Interdisciplinary Program in Medical and Biomedical Engineering Major, Seoul National University, Korea
[2] Department of Biomedical Engineering, College of Medicine, Seoul National University, Korea
[3] Institute of Medical Engineering, Medical Research Center, Seoul National University, Korea
[4] Cancer Research Center, Seoul National University Hospital, Korea
[5] Korea Artificial Organ Center, Korea University, Korea
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Abstract: Blood pulsation has been reported to have an advantageous effect on extracorporeal blood circulation. However, the study of pulsatile blood flow in renal replacement therapy is very limited. The *in-vitro* experimental results of pulsatile blood flow on ultrafiltration, when compared with the conventional roller pump, are described in this paper. **Methods**: Blood flow rate (QB) and transmembrane pressure (TMP) were considered as regulating factors that have an influence on ultrafiltration. Experiments were performed under the condition of equal TMP and QB in both pulsatile and roller pump groups. Several kinds of hollow fiber dialyzers were tested using distilled water containing chemicals as a blood substitute. Mean TMP (mTMP) varied from 10 to 90 mmHg while the QB was 200 ml/min. **Results:** Ultrafiltration rate (QUF) was found to be linearly proportional to TMP, whereas QB had little influence on QUF. In addition, QUF was higher in the pulsatile group than the roller pump group at the identical TMP. **Conclusion:** In the controlled test, QUF increased solely as a consequence of blood pulsation, which implies that the pulse frequency represents an additional and important clinical variable during renal replacement therapy.

Key words: Ultrafiltration, Pulsatile blood flow, TMP, Pulse frequency, Hemofiltration

INTRODUCTION

A number of studies have been conducted in order to clarify the effect of pulsatile blood flow on vital organ recoveries during cardiopulmonary bypass or extracorporeal circulation [1-9]. Renal replacement therapy for patients with renal failure also requires an extracorporeal circulation of blood. Two physical phenomena facilitate mass transfer in purifying blood - diffusion and convection. Diffusion caused by the concentration gradient between blood and the dialysate contributes to the removal of uremic solutes. Besides, the removal of excessive body water and mid-size molecules depend primarily on convective mass

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Corresponding Author : Byoung Goo Min, Ph.D
Department of Biomedical Engineering, College of Medicine, Seoul National University, 28 Yungun-dong, Chongno-gu, Seoul, 110-744, KOREA
Tel. +82-2-2072-3126 Fax. +82-2-2072-7870
E-mail. bgmin@plaza.snu.ac.kr

Several investigators have demonstrated enhanced clearance with pulsatile blood flow during hemodialysis transfer which results from hydraulic and osmotic pressure differences [10-13].
or hemofiltration. Runge reported increased solute clearance and ultrafiltration with pulsatile flow in 1993 [14], and more recent experiments were performed by Ruperez in a neonatal model with "pediatric-size" animals using a pulsatile blood pump [15].

Although the experimental data from these previous studies suggest an enhanced QUF with pulsatile blood flow, they are not sufficient to support the conclusion that QUF is improved solely by flow pulsation because the pressure difference between the blood and dialysate in the pulsatile and non-pulsatile groups was not uniformly controlled. We assert that the minimum requirement for demonstrating the beneficial effect of blood pulsation on QUF is equal QB and TMP in both groups. Thus, the QUF with pulsatile blood flow needs to be clarified by conducting experiments under identical TMP and QB conditions. In addition to pulsation itself, the effect of the pulse frequency was also tested. Therefore, we elucidate the effect of blood pulsation and the pulse frequency on QUF.

METHODS AND MATERIALS

Many factors contribute to the regulation of hemodialysis or hemofiltration efficiency, such as QB, dialysate flow rate, system configuration, blood hematocrit, TMP, the surface area and pore size of a dialyzer, and so on. In the same manner, the QUF can be influenced by some of these factors. Blood characteristics are specific to individual patients and are naturally outside of experimental control. If a commercially available hollow fiber dialyzer is clinically applied, the controllable variables in the regulation of QUF consist only of QB and TMP. Therefore, holding them equal in both pulsatile and roller pump group is fundamentally required in order to demonstrate the effect of flow pulsation on QUF.

TMP is expressed as the difference between arithmetical average of blood pressures and dialysate pressure, because the osmotic pressure is much smaller than the hydraulic term [11, 13]. Besides, since no dialysate was applied, TMP can be expressed by the following equation as shown in Fig. 1.

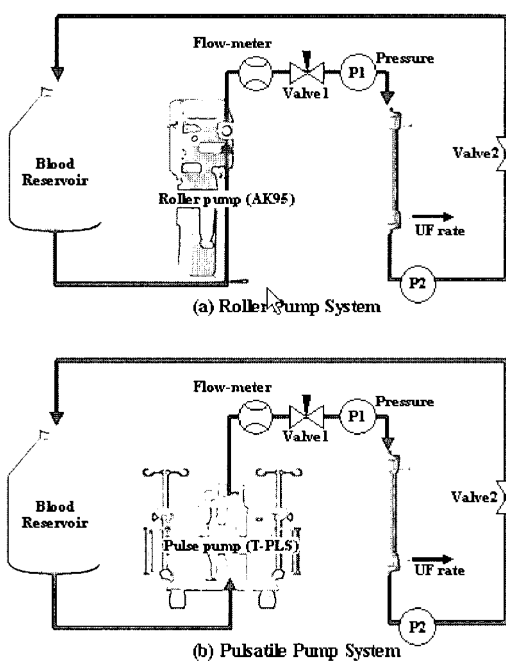


Fig. 1. Schematic Diagram of Experimental Apparatus

$$TMP = \frac{P1 + P2}{2}$$

Also, the mean transmembrane pressure and the Energy Equivalent Pressure Percentage (EEP%) were calculated as shown in the following equations.

$$mTMP = \frac{\int (\frac{P1 + P2}{2}) dt}{\int dt}$$

$$EEP\% = (\frac{EEP}{mTMP} - 1) * 100$$

$$\left(EEP = \frac{\int (QB * TMP) dt}{\int QB dt} \right)$$

Pulse Generating Blood Pump

The pulse-generating blood pump, T-PLS (Twin Pulse Life Supporter, Newheartbio Inc., Korea) consists of a blood pump, an electrical power supply, and a control panel [16]. The power supply is composed of a one-directional electronic motor (AXH450-20, Oriental Motor Co. Ltd., USA) and a pendulum-type actuator is connected to the motor via a crank and cam. The actuator is located between two silicone blood sacs and alternately applies pressure to the left and right blood sacs. When the actuator squeezes the left sac, the blood in the sac can only move in a forward direction because of polymer check-valves which prevent blood from returning back to the reservoir; at the same time, the right sac expands and blood fills up the right sac. In the same manner, blood located in the right sac moves forward when the actuator squeezes that sac, and in this alternate fashion the actuator creates pulsatile flow.

Experimental Setup for QUF

A schematic diagram of the experimental apparatus used to demonstrate the effect of pulsatility is shown in Fig. 1. Flow paths for both pulsatile and roller pump groups included three pressure-controlling devices, the reservoir and two metering valves, hollow fiber dialyzer, and pressure sensors (Sensys Inc., Korea). Besides, a flow meter (Transonic Systems Inc., USA) was inserted in order to measure the QB. Two kinds of clinically available hollow fiber dialyzers were tested in the experiments: a low flux dialyzer (Polyflux 6L, Gambro) and high flux dialyzer (Polyflux 14S, Gambro). Chemical-containing distilled water was used as a substitute for solute-bearing blood during the *in-vitro* test. The TMP varied from 10 to 90 mmHg and the pulse frequency was set at between 14 and 40 beats/minute (BPM). When the pressure reached a steady state after initiation, we measured the QUF five times at the TMP and regarded the mean value as the QUF at that point. The pressure sensors were located at the same level as the blood inlet and outlet to avoid a hydraulic effect caused by a column height of water.

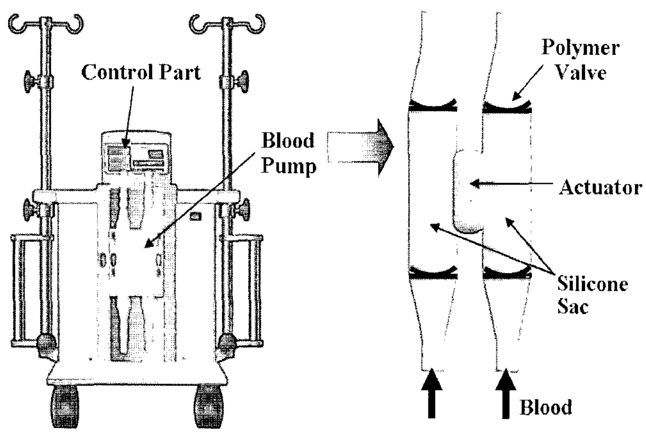
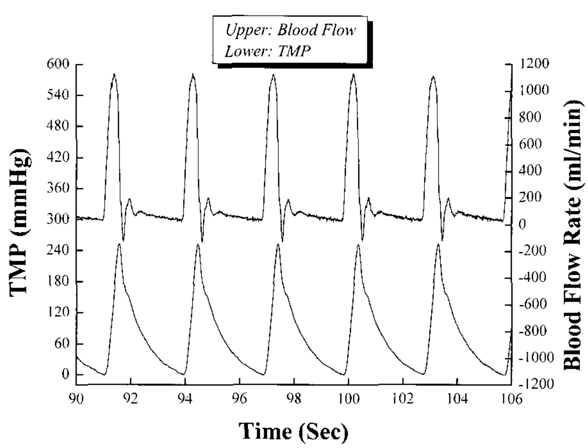


Fig. 2. Pulsatile Pump, T-PLS

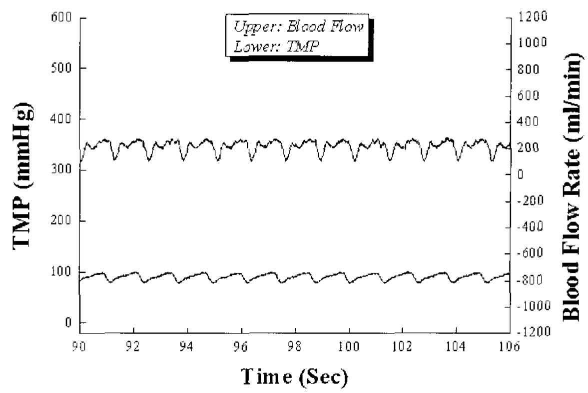
RESULTS

Pressure and Flow Profiles

Adequate and desirable pressure and flow profiles were obtained with both the pulsatile and roller pump. The selected pressure profile, shown in Fig. 3, represents that the mean TMP of the pulsatile and roller pump are 76 and 88 mmHg respectively. The frequency of pulsatile pump is 20 BPM.



(a) Pulsatile Pump



(b) Roller Pump

Fig. 3. Pressure and Blood Flow Profile Sampled from the Total Data

Ultrafiltration Rates

The results definitively confirmed the QUF was much higher with high flux dialyzers than low flux dialyzers and it was linearly proportional to the TMP. Additionally, the QUF was higher in the pulsatile pump group than in the roller pump group regardless of the type of dialyzer, as illustrated by Fig. 4.

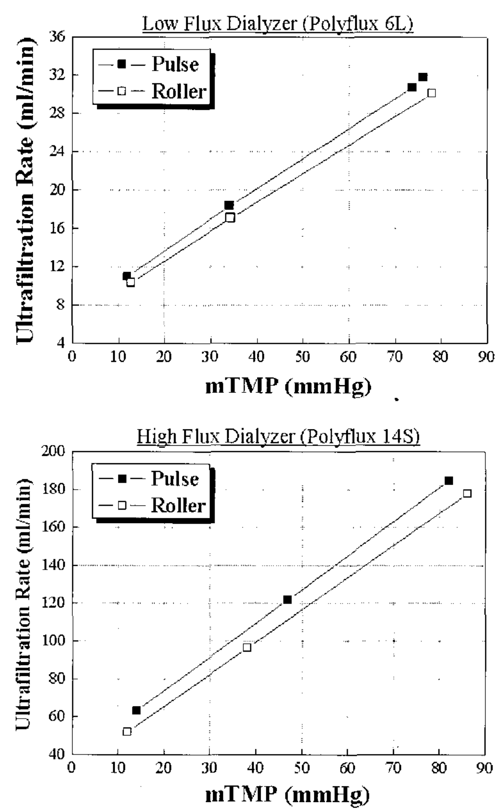


Fig. 4. Ultrafiltration Rate

In case of the low flux dialyzer, the TMP varied from 12 to 76.1 mmHg with the pulsatile pump and 12.7 to 78 mmHg with the roller pump. At the moment, the QUF changed from 11 to 31.8 ml/min and 10.3 to 30.1 mmHg respectively. At 76.1mmHg, the QUF was increased by 6.8% (from 29.6 to 31.6 ml/min) due to the flow pulsation.

In a similar manner with high flux dialyzers, the TMP varied from 14 to about 82 mmHg with the pulse pump and from 12 to 86 mmHg with the roller pump. In response to the increasing TMP, the QUF rose from 63.2 to 183.7 ml/min for the pulse pump, and from 52 to 178.1 mmHg for the roller pump, which shows the QUF increase by 7.8% (from 171.4 to 185 ml/min) due to the blood pulsation at 82 mmHg of TMP.

Finally, we also found the higher pulse frequency generated a greater QUF as displayed in Fig. 5. The increased pulse frequency facilitated the increase in the TMP and consequently contributed to the QUF increase in the regular dialysis system.

Even though some quantitative differences between the *in-vitro* and *in-vivo* experimental results are anticipated, the regulating effect of the pulse frequency in our experiments implies that it will constitute an additional clinical variable for convective mass transfer and thus mid-size molecular clearance. For this reason, we will pursue an *in-vivo* study as the next step, in order to re-confirm the functional efficacies of the blood pulsation and pulse frequency in increasing the QUF.

DISCUSSIONS

The QUF under the condition of equal QB and TMP in both the pulsatile and roller pump groups were measured in our work. The blood flow rate and transmembrane pressure were considered as regulating factors that have an influence on the QUF. These variables can be independently controlled and holding them constant across experiments is essential to conclusively demonstrate the superiority of blood pulsation. In a previous study [14], greater ultrafiltration was reported to have resulted from a higher energy of pulsation, which implied a greater mean pressure in the blood part than in the dialysate part. In the work, the increased QUF probably resulted from the greater pressure in the blood part, not through only the blood pulsation. For this reason, we assembled an experimental apparatus with which identical TMP and QB in both groups could be attained. Actually, we found that the QB had little effect on the QUF based on the preliminary study.

The experimental results conclusively demonstrated enhanced QUF with pulsatile flow, which proved the superiority of blood pulsation. Previous investigators suggested the pulsatile flow was generated from an energy gradient rather than the pressure gradient so it was imperative to adopt the energy equivalent pressure in order to make a direct comparison between the pulsatile and non-pulsatile flow [17-24]. Based on the QB and TMP graphs in Fig. 3, the EEP% was 1.4% with the roller pump and 58% with the pulsatile pump respectively, which means a roller pump rarely generated the flow pulsation. Flow pulsation is reported to reduce the channeling and layering effect [14]. In addition, the higher kinetic energy with blood pulsation contributed to enhancing the QUF. In a microscopic perspective, we postulate the improved QUF with flow pulsation results from reduced shear resistance at the inner separation layer of each fiber composed of densely compacted granules of hundreds of nanometers in size [25], leading to higher hydraulic permeability.

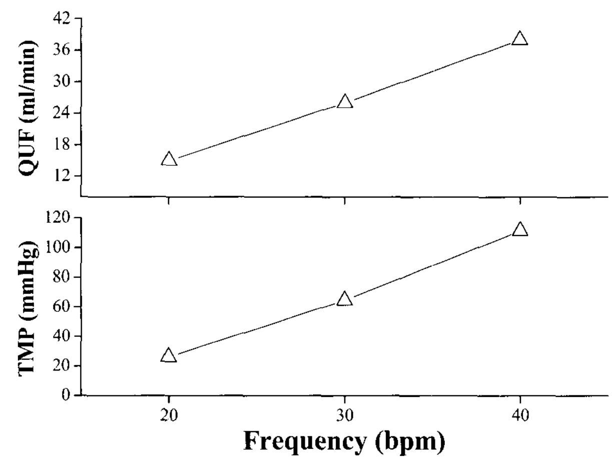


Fig. 5. Pulse Frequency versus TMP and QUF

CONCLUSIONS

The QUF increased solely by applying blood pulsation at the identical TMP. In addition, the QUF can be easily enhanced by regulating the pulse frequency. In a strictly controlled test, the superiority of the pulsatile flow in terms of ultrafiltration was proven. Additionally, the pulse frequency can be indicated as an additional regulating variable in clinical settings for patients with renal failure.

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