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Computational dose predictions for combined treatment of hemofiltration with weekly hemodialysis

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ABSTRACT

Hemodialysis (HD) has sufficient efficacy as a conventional diffusive treatment for removing small molecules, whereas hemofiltration (HF), which is a convective treatment, has an improved the clearance of intermediate-sized molecules. This paper reports a combined treatment (CT) which combines the diffusive and convective efficacies of HF several times weekly with HD weekly. CT modalities with various schedules and prescriptions are described mathematically using a variable-volume two-compartment kinetics model, and the kinetic parameters were obtained from previous clinical reports and a hemodialysis-related database. The blood concentration profiles of the three waste molecules for 52 weeks were calculated in order to compare the capability of removing small and intermediate-sized molecules to those of other renal treatments. The results by a computer simulation show that CT can reduce the frequency of sessions and the volume of replacement fluid compared with daily convective treatment, and achieve the adequate treatment efficiency with both small and intermediate-sized molecules for chronic renal failure patients.

1. Introduction

Hemodialysis (HD) is used to treat chronic renal failure (CRF). Several decades of clinical experience has indicated that HD therapy three times weekly has sufficient efficacy to remove small molecules such as urea and creatinine. However, according to recent reports, the quality of life of a CRF patient treated with HD is still poor and the mortality rate is quite high [1,2].

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Hemofiltration (HF) therapy, which was first introduced in the mid-1970s, is based on a convective principle and had been suggested as an alternative to HD. However, its high cost and complex equipment were the main obstacles to making it an alternative treatment for CRF. Then, HF was developed into continuous renal replacement treatment (CRRT) for acute renal failure (ARF) in intensive care units (ICU) [3].

Recently, the disadvantages of conventional diffusive therapy have attracted recent attention, and convective therapy has been suggested an alternative to conventional diffusive therapy [4–6]. Convective therapy, such as filtration of the native kidney, has improved the clearance of intermediate-sized molecules that are insufficiently removed by diffusion. In particular, beta2-microglobulin (B2M), which causes HD-related amyloidosis within several years of HD treatment, can be removed effectively by convective therapy. In addition, HF treatment is strongly associated with cardiovascular stability [7]. Moreover, comparison studies between diffusive and convective therapies have supported the claims of reduced mortality of CRF patients given diffusive therapy [6,8].

Improvements in renal treatment technologies have overcome the obstacles of convective therapy such as high cost and complex equipment. The newly introduced HF equipment can be installed without additional plumbing and electrical power construction, and be operated only with several prepackaged fluid bags without a huge water treatment facility [9,10]. This device can also be used for daily home renal treatment.

Nevertheless, due to the low clearance of small molecules, HF requires significant large replacement fluid to remove the small molecules as sufficient as HD does. According to a previous kinetics study, a 70 kg patient treated with daily HF (DHF) must consume 90 l of replacement fluid per week [11]. Reducing the exchange volume within the limit of adequacy might prevent the excessive protein loss because an excessive exchange volume to improve the treatment efficacy for small molecules during convective treatment would increase the loss of protein through the effluent [12]. Although it is less than the volume of dialysate fluid required during conventional HD (CHD) or Hemodiafiltration (HDF), additional storage space for the large number of fluid bags at home or a fluid delivery service will be needed if HF is to be used as a daily home renal treatment. In the case of a patient treated with DHF at home, changing the treatment schedule of DHF into several HF procedures a week at home and a weekly HD treatment at hospital can reduce the treatment time and the volume of replacement fluid required.

In this study, various forms of combined treatment (CT) of HF with weekly HD therapy were configured, and the efficacy of these CT was calculated using a mathematical solute kinetics model. The corrected equivalent renal clearance (EKRc) and standard *Kt*/*V* (std *Kt*/*V*) were used as dose measuring parameters for comparing the efficacy with respect to the different molecular sizes. In addition, the calculated doses of combined treatment were compared with the doses of established renal therapies including CHD, daily HD (DHD), DHF, etc. The aim of this study was to determine the appropriate dose of CT for CRF patients in terms of the total treatment time and fluid resources.

2. Materials and methods

2.1. Governing mass balance equations [11,13,14]

$$\frac{d(C_p V_p)}{dt} = G - K_{ic}(C_p - C_{np}) - J_s \tag{1}$$

$$\frac{d(C_{np} V_{np})}{dt} = K_{ic}(C_p - C_{np}) \tag{2}$$

$$\frac{dV_p}{dt} = -J_v \tag{3}$$

$$\frac{dV_{np}}{dt} = 0 \tag{4}$$

- During the HF treatment session

$$J_s = Q_{uf} S C_p \tag{5}$$

$$J_v = Q_{uf} - Q_{rf} - I_w \tag{6}$$

- During the HD treatment session

$$J_s = (K_d + 0.4 Q_{uf}) C_p \tag{7}$$

$$J_v = Q_{uf} - I_w \tag{8}$$

- During the inter-session time

$$J_s = 0 \tag{9}$$

$$J_v = -I_w \tag{10}$$

2.2. Model and assumptions

A classic variable-volume two-compartment kinetic model was used [13] (Fig. 1). An anuric patient was modeled, and the dry weight and total body water were assumed to be 70 kg and 35 l, respectively. The water volume distribution of urea and creatinine in the intracellular fluid, as the non-perfused compartment, and the extracellular fluid, as the perfused compartment, was assumed to be 2:1. The B2M

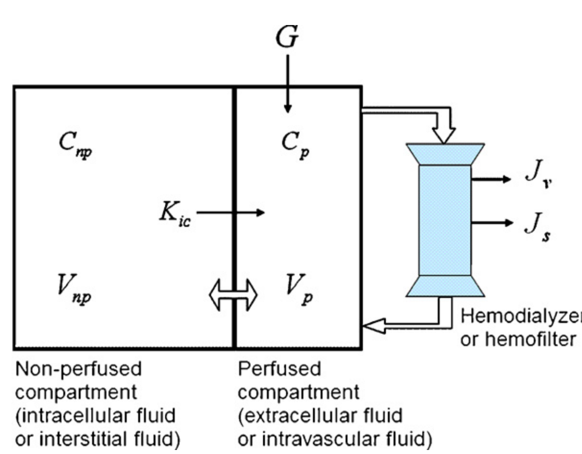

Fig. 1 – The scheme for the variable-volume two-compartment model.