Light-Shielded Hemodialysis Prevents Hypotension and Lipid Peroxidation by Inhibiting Nitric Oxide Production, Sohji Nagase,1 Akira Hiramatsu,2 Atsushi Ueda,1 Takaaki Oteki,1 Kenji Takada,1 Mariko Inoue,1 Yukari Shimozawa,1 Junji Terao,2 and Akio Koyama1 (1 Department of Internal Medicine, Institute of Clinical Medicine, University of Tsukuba, Ibaraki, Japan; 2 Department of Nutrition, School of Medicine, University of Tokushima, Tokushima, Japan; * address correspondence to this author at: Department of Internal Medicine, Institute of Clinical Medicine, University of Tsukuba, Ibaraki 305-8575, Japan; e-mail sohji-n@md.tsukuba.ac.jp)

Approximately 1 million patients with end stage renal disease are surviving throughout the world with the help of renal replacement therapy (1). More than 800,000 patients are currently receiving hemodialysis (HD), the most common modality. Survival on HD has progressively improved, although vascular accidents such as cerebral bleeding and ischemic heart disease continue to be major problems. One of the possible causes of the high incidence of vascular damage is thought to be a peroxidative condition in HD patients (2–4). HD treatment is usually performed in a bright room, using transparent blood circuitry for 4 h per session, 150 times per year. No attention has been paid, however, to the potential harm of these 600 h of exposure, although fluorescent light contains variable wavelengths, from ultraviolet to visible, that are known to generate reactive oxygen species after reacting with endogenous photodynamic reagents such as tryptophan or riboflavin (5). In this study, we investigated the effect of light shielding during HD on nitric oxide (NO) generation, blood pressure control, and lipid peroxidation in HD patients.

The participants in this study were 10 stable HD patients. Their mean (SD) age was 48.1 (13.5) years, and the mean duration of HD was 8.2 (4.3) years. The cause of end stage renal failure was chronic glomerulonephritis in all patients. They were completely anuric and routinely dialyzed for 4 h, 3 times weekly. Over a period of 1 week, treatments alternated between ordinary HD and that in which the blood circuitry and the dialyzer were covered with aluminum foil (light-shielded HD). The dialysate used was bicarbonate-based, and the temperature was kept at 36.5 °C. Blood pressure was measured every 30 min. Blood samples for the measurement of plasma concentrations of NO metabolites (NO2 + NO3 = NOx) were obtained every hour, and samples for plasma lipid peroxides were obtained at the start and end of HD. HD began around 1000 in the morning; none of the patients ate lunch during the HD session.

Plasma NOx was measured by flow injection analysis based on the Griess reaction (6). For plasma lipid peroxides, we measured thiobarbituric acid–reactive substances (TBARS) and phosphatidylcholine hydroperoxide (PCOOH). TBARS were measured by the method of Ohkawa et al. (7). Separation of POCOH by reversed-phase HPLC was performed after the extraction of total plasma lipids according to the method of Bligh and Dyer (8), and quantification was by an ultraviolet detector at 235 nm and a chemiluminescence detector after the addition of luminol and cytochrome c (9).

Values are expressed as the mean (SD). The time courses of plasma NOx concentrations during HD in both treatments were compared by 1-way ANOVA. The percentage changes in mean blood pressure, plasma TBARS, and PCOOH concentrations, comparing the end to the start in ordinary vs light-shielded HD, were calculated and analyzed by the paired t-test. Differences were considered significant at P < 0.05.

The results show that plasma NOx concentrations in samples collected during light-shielded HD were significantly lower than those in samples collected during ordinary HD (Fig. 1A). Furthermore, in 4 of the 10 patients being treated with ordinary HD, the plasma NOx concentration increased at the end of HD. This increased NO generation during HD is caused by the removal of endogenous NO synthase inhibitor (10). This phenomenon was completely suppressed in all cases by light shielding (Fig. 1B). Plasma NOx is derived endogenously from NO generation and exogenously from diet. The higher NOx concentrations in samples from patients undergoing ordinary HD indicates a greater NO production during the treatment than that seen in light-shielded HD because the patients take no food during the treatment. The percentage change in mean blood pressure when comparing the end to the start of light-shielded HD was significantly less than that in ordinary HD (Fig. 1C), which suggests that light-shielded HD decreases NO generation and thereby prevents hypotension, an important problem during HD (11). In addition, plasma concentrations of POCOH at the end of light-shielded HD, expressed as the percentage of starting values, were significantly less than those in ordinary HD (Fig. 1D). Although not shown, plasma concentrations of TBARS changed in the same manner.

Plasma lipid peroxide generation is inhibited in the presence of decreased NO generation because peroxynitrite, a potent oxidant synthesized by the reaction of NO and the superoxide radical (12), contributes to the generation of lipid peroxides. However, the mechanism by which exposure to light leads to the generation of NO is essentially unknown. NO is known to be released from nitrosyl hemoglobin or nitrosoglutathione by light irradiation (13). Another possibility is NO synthase–independent NO generation from arginine, which occurs in the presence of reactive oxygen species such as hydrogen peroxide (14). However, the amount of NO released from either pathway is thought to be relatively small; therefore, still another pathway must be involved in this mechanism. In addition, although it was not measured in this experiment, there is a possibility that the plasma concentration of lipid peroxides may be decreased through changes in plasma asymmetric dimethylarginine concentrations (10, 11) by light shielding. Further study is needed to clarify these mechanisms, to explore the specific wavelength that affects NO and lipid peroxide generation, and to affect a modification of the dialyzer and blood circuitry that prevents harmful wavelengths but is other-
References


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Investigation of the Genomic Representation of Plasma DNA in Pregnant Women by Comparative Genomic Hybridization Analysis: A Feasibility Study, K.C. Allen Chan,1 Angela B.Y. Hui,2 Nathalie Wong,3 Tze K. Lau,4 Tse N. Leung,4 Kwok-Wai Lo,2 and Y.M. Dennis Lo1*

Prenatal diagnosis is part of the established obstetric care in most developed countries. However, current methods for obtaining fetal tissues for prenatal diagnosis, including chorionic villus sampling and amniocentesis, are invasive and carry a risk of fetal loss. Analysis of circulating cell-free DNA from pregnant women provides new possibilities for noninvasive prenatal diagnosis. Clinical applications of plasma fetal DNA analysis in maternal plasma include fetal RhD genotyping (1, 2), fetal aneuploidy detection (3, 4), and the prenatal diagnosis of several genetic diseases, including myotonic dystrophy (5), congenital adrenal hyperplasia (6), and β-thalassemia (7, 8). In addition to exploring the clinical applications of circulating DNA analysis, our group has investigated the molecular characteristics of cell-free DNA in maternal plasma and has shown that plasma DNA fragments in pregnant women are longer than those in nonpregnant women.