



Published in final edited form as:

*J Ren Nutr.* 2008 May ; 18(3): 301–303.

## Acute Rise of Omega-3 Polyunsaturated Fatty Acids During Hemodialysis Treatment

Allon N. Friedman, M.D.<sup>1</sup>, Rafat Siddiqui, Ph.D.<sup>2</sup>, and Bruce A. Watkins, Ph.D.<sup>3</sup>

<sup>1</sup>Department of Medicine, Indiana University School of Medicine, Indianapolis, IN 46202

<sup>2</sup>Methodist Research Institute, Methodist Hospital, Indianapolis, IN 46206

<sup>3</sup>Basic Medical Sciences, Purdue University, West Lafayette, IN 47907

### Abstract

**Objective**—Hemodialysis patients have an extremely high rate of cardiac arrhythmia-induced sudden cardiac death, though the risk during the hemodialysis procedure is curiously low. Higher blood content of long chain omega-3 polyunsaturated fatty acids (PUFA) is believed to reduce the risk of sudden cardiac death. We performed this study to measure the effect of a single standard hemodialysis treatment on plasma and erythrocyte omega-3 PUFA levels in chronic hemodialysis patients.

**Design**—This is a prospective, observational study

**Setting**—The study was performed in one outpatient hemodialysis unit

**Patients**—Study subjects were all chronic, stable hemodialysis patients

**Interventions**—There were no interventions

**Main Outcome Measure**—Plasma and erythrocyte fatty acid levels were measured before and immediately after a hemodialysis session

**Results**—Plasma levels of long chain PUFA, including the omega-3 fatty acids of interest, all rose, while those of shorter chain or more saturated fatty acids either remained unchanged or fell. A similar trend was seen in erythrocytes, though the results did not reach statistical significance.

**Conclusion**—The hemodialysis procedure induces acute increases of long chain omega-3 PUFA in the blood. This effect may help explain why malignant cardiac arrhythmias occur relatively infrequently during hemodialysis.

### Keywords

omega-3; fatty acid; hemodialysis; sudden cardiac death

### Introduction

Arrhythmia-induced sudden cardiac death is believed to account for approximately one-quarter of the exceedingly high 17% annual mortality rate seen with hemodialysis patients (1). Yet

---

Send Correspondence to: Allon N. Friedman, M.D., Division of Nephrology, 1481 W. 10<sup>th</sup> St.-111N, Indianapolis, IN 46202, allfried@iupui.edu, Tel: 317-988-4414, Fax: 317-988-2171.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

curiously few episodes of lethal arrhythmias actually occur during hemodialysis treatments (2), a time during which abrupt, non-physiological electrolyte and fluid shifts would be expected to maximize arrhythmogenic potential.

Higher blood content of the long chain omega-3 polyunsaturated eicosapentaenoic and docosahexaenoic fatty acids (n-3 PUFA) is linked to suppression of fatal arrhythmias, possibly through direct inhibition of cardiomyocyte voltage-dependent sodium and L-type calcium currents (3). Hemodialysis has been reported to quantitatively alter certain plasma fatty acids acutely (4,5), though whether the putatively anti-arrhythmic n-3 PUFA levels are affected is not known. The objective of this study was to measure the effect of a single standard hemodialysis treatment on plasma and erythrocyte n-3 PUFA levels in chronic hemodialysis patients.

## Methods

Investigational Review Board approval was given, and written informed consent was obtained from nine patients. Blood samples were obtained from dialysis tubing immediately before and after a standard mid-week hemodialysis session. Plasma and whole red blood cells (RBCs) were separated by centrifugation, washed with 0.9% saline, and stored at -80°C. Lipids from plasma and RBCs were extracted with chloroform/methanol (2:1, vol/vol) and fatty acid methyl esters prepared by derivatization using boron trifluoride in methanol (10% wgt/wgt; Supelco Inc, Bellefonte, PA), as previously described (6). Fatty acid methyl esters were extracted with isooctane and analyzed using a gas chromatograph (Agilent 6890 Plus, autosampler 7683, Chemstation Rev A.08.03; Agilent Technologies Inc, Wilmington, DE) equipped with a flame ionization detector and a DB-23 fused silica capillary column (30 m, 0.53-mm inner diameter, 0.5 µm film thickness; Agilent) using helium as the carrier gas. Fatty acid methyl esters were identified by comparison of their retention times with authentic standards (Nu-Chek-Prep Inc, Elysian, MN) and fatty acid values expressed as weight percentages. All individuals were dialyzed against Exeltra biocompatible high-flux single-use membranes (Baxter, Deerfield, IL). Changes in pre- versus post- fatty acid levels were analyzed using the Wilcoxon signed-rank test with SPSS software, version 14.0 (Chicago, IL). Statistical significance was defined by  $P < 0.05$ .

## Results

Findings are shown in the Table. While plasma levels of long chain PUFA (i.e. 20:4, 20:5, and 22:6), including the n-3 fatty acids of interest, all rose, those of shorter chain or more saturated fatty acids either remained unchanged or fell. A similar trend was seen in erythrocytes, though the results did not reach statistical significance.

## Discussion

The mechanism by which hemodialysis raises plasma n-3 PUFA levels is not known. Since long chain PUFA cannot be synthesized endogenously in appreciable amounts, accelerated release into plasma could be a possible explanation. In fact, the hemodialysis treatment has been shown to upregulate lipoprotein lipase and phospholipase A<sub>2</sub> activity, both of which free fatty acids from triglycerides and phospholipids, respectively (7). n-3 PUFA may be preferentially released compared with more saturated fatty acids because they have greater affinity for the sn2 phospholipid position on which phospholipase A<sub>2</sub> acts. Of note, the larger changes seen within the plasma, as compared with the RBC, compartment, were not unexpected as the former is considered more dynamic in terms of fatty acid flux.

The effects of hemodialysis on fatty acid levels may have important clinical implications. For example, could the acute rise in blood n-3 PUFA content during hemodialysis raise the arrhythmic threshold and help explain the relative infrequency of sudden cardiac death events during treatment? If so, would n-3 PUFA nutritional supplementation augment such a protective effect, especially since hemodialysis patients consume inadequate amounts in their diets (8)? Further studies are necessary to answer these intriguing questions.

#### Acknowledgements

We greatly appreciate the support of the dialysis patients and nursing staff who participated in this study. Funding was provided by the National Institutes of Health (K23 RR019615) (ANF). The corresponding author had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. None of the authors has a conflict of interest with regards to the contents of this letter.

#### References

1. Herzog CA. Cardiac arrest in dialysis patients: taking a small step. *Semin Dial* 2004;17:184–5. [PubMed: 15144539]
2. Bleyer AJ, Russell GB, Satko SG. Sudden and cardiac death rates in hemodialysis patients. *Kidney Int* 1999;55:1553–9. [PubMed: 10201022]
3. Leaf A, Kang JX, Xiao YF, et al. Clinical prevention of sudden cardiac death by n-3 polyunsaturated fatty acids and mechanism of prevention of arrhythmias by n-3 fish oils. *Circulation* 2003;107:2646–52. [PubMed: 12782616]
4. Kim KM, Jung BH, Paeng KJ, et al. Alteration of plasma total F2-isoprostanes before and after hemodialysis in end-stage renal disease patients. *Prostaglandins Leukotrienes & Essential Fatty Acids* 2004;70:475–8.
5. Marangoni R, Civardi F, Savino R, et al. Plasma lipids and fatty acid levels in chronically uremic patients undergoing blood purification with different methods. *Artificial Organs* 1992;16:625–9. [PubMed: 1482334]
6. Watkins BA, Li Y, Allen KG, et al. Dietary ratio of (n-6)/(n-3) polyunsaturated fatty acids alters the fatty acid composition of bone compartments and biomarkers of bone formation in rats. *J Nutr* 2000;130:2274–84. [PubMed: 10958824]
7. Vishwanath BS, Fux CA, Uehlinger DE, et al. Haemodialysis activates phospholipase A2 enzyme. *Nephrology Dialysis Transplantation* 1996;11:109–16.
8. Friedman AN, Moe SM, Perkins SM, et al. Fish consumption and omega-3 fatty acid status and determinants in long-term hemodialysis. *American Journal of Kidney Diseases* 2006;47:1064–71. [PubMed: 16731302]

**Table**  
**Changes in Plasma and Erythrocyte Fatty Acids During Hemodialysis \***

Fatty Acids	Pre Levels n=9	Post Levels n=9	Change <sup>†</sup>	P
<b>Plasma</b>				
16:0 (palmitic acid)	18.9 ± 1.8	17.7 ± 1.5	-1.2 ± 0.4	0.01
18:0 (stearic acid)	7.5 ± 1.1	7.9 ± 1.4	+0.4 ± 1.0	0.26
18:1 (oleic acid)	24.4 ± 3.6	22.5 ± 3.6	-1.9 ± 3.0	0.05
<i>omega-6</i>				
18:2 (linoleic acid)	27.3 ± 3.3	27.7 ± 2.6	+0.4 ± 1.6	0.37
20:4 (arachidonic acid)	8.7 ± 1.5	10.4 ± 2.4	+1.8 ± 1.7	0.02
<i>omega-3</i>				
18:3 (α-linolenic acid)	0.7 ± 0.4	0.6 ± 0.2	-0.1 ± 0.2	0.17
20:5 (eicosapentaenoic acid)	0.3 ± 0.1	0.4 ± 0.2	+0.1 ± 0.1	0.01
22:6 (docosahexaenoic acid)	1.3 ± 0.2	1.6 ± 0.3	+0.3 ± 0.3	0.02
<b>Erythrocyte</b>				
16:0 (palmitic acid)	17.0 ± 0.9	16.8 ± 0.7	-0.2 ± 0.8	0.31
18:0 (stearic acid)	16.0 ± 1.1	15.9 ± 1.1	-0.1 ± 0.1	0.02
18:1 (oleic acid)	14.4 ± 0.9	14.3 ± 1.0	-0.03 ± 0.2	0.17
<i>omega-6</i>				
18:2 (linoleic acid)	9.3 ± 0.8	9.3 ± 0.9	-0.01 ± 0.2	0.86
20:4 (arachidonic acid)	17.7 ± 0.8	17.9 ± 0.9	+0.2 ± 0.4	0.11
<i>omega-3</i>				
18:3 (α-linolenic acid)	0.1 ± 0.02	0.1 ± 0.02	+0.002 ± 0.01	0.75
20:5 (eicosapentaenoic acid)	0.3 ± 0.1	0.3 ± 0.1	+0.001 ± 0.01	0.86
22:6 (docosahexaenoic acid)	4.0 ± 0.6	4.1 ± 0.6	+0.1 ± 0.2	0.11

\* mean ± standard deviation

<sup>†</sup> post minus pre levels