# Effect of Sevelamer on Bone Profile in High Flux Regular Haemodialysis Patients

***Thesis***

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***in Nephrology***

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***Emad Mohamed Kotb Abu-Elyazid***

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# List of Abbreviations

| | | |
|---|---|---|
| 25-OHD | : | 25-hydroxyvitamin D |
| ABD | : | Adynamic bone disease |
| ALP | : | Alkaline phosphatase |
| BMC | : | Bone mineral content |
| BMD | : | Bone mineral density |
| BSA | : | Body surface area |
| CI | : | Confidence interval |
| CKD | : | Chronic kidney disease |
| Da | : | Dalton |
| DCOR | : | Dialysis Clinical Outcomes Revisited |
| DOPPS | : | Dialysis Outcomes and Practice Patterns Study |
| ESKD | : | End stage kidney disease |
| FGF | : | Fibroblast growth factor |
| GH | : | Growth hormone |
| HD | : | Hemodialysis |
| HDF | : | High-efficiency haemodiafiltration |
| kD | : | Kilodalton |
| KDIGO | : | Kidney Disease: Improving Global Outcomes |
| LMWPs | : | Low-molecular weight proteins |
| LPS | : | Lipopolysaccharide |
| MBD | : | Mineral and bone disorder |
| MW | : | Molecular weight |
| NCDS | : | National Cooperative Dialysis Study |

# List of Abbreviations (Cont.)

| | | |
|---|---|---|
| PCR | : | Protein catabolic rate |
| PTH | : | Parathyroid hormone |
| QCT | : | Quantitative computed tomography |
| SEN | : | Spanish Society of Nephrology |
| spKt/V | : | Single pool Kt/V |
| TACurea | : | Time-averaged concentration of urea |
| tHcy | : | Total homocysteine |
| UKM | : | Urea kinetic model |
| URR | : | Urea reduction rate |
| VC | : | Vascular calcification |
| VDR | : | Vitamin D Receptor |
| Wnt | : | Wingless-int |

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# Introduction

Standard hemodialysis is a far from ideal treatment for uremia since the morbidity and mortality of patients on hemodialysis are still significantly higher than those of non-hemodialysed subjects with similar demographic characteristics. Because it has been suggested that the cause could lie in the inadequate removal of "middle molecules" by standard hemodialysis, two alternative treatments have been proposed: high-efficiency hemodialysis and high-flux hemodialysis ***(Manzoni et al., 2009).***

Currently, high-flux hemodialysis is the most common mode of dialysis therapy worldwide. Its steadily increasing use is largely based on the desire to reduce the excessively high morbidity and mortality of end-stage renal disease patients maintained on conventional dialysis (low-flux, mostly cellulosic membranes) by offering better biocompatibility and enhanced removal of uremic toxins ***(Schiffl, 2011)***.

High-flux dialysis membranes are more efficient in removal of intact PTH and they might help in minimizing the consequences of bone disease associated with hyperparathyroidism in patients with ESRD) ***(Makar et al.,2010).***

It was also suggested that high flux dialysis improves plasma lipoprotein profiles, especially lowering plasma triglyceride concentrations, and also increases HDL cholesterol. ***(Goldberg et al.,1996).***

The major disadvantage of high-flux hemodialysis relates to the use of dialysis fluid, which is commonly not pure and may endanger patients treated with high-flux hemodialysis. Endotoxin fragments and other bacterial

substances derived from bacteriologically contaminated dialysis fluid may, even at bacterial counts or endotoxin concentrations within the limits of accepted standards of dialysis fluid purity, enter from the dialysate into the patient's blood either by convective transfer (backfiltration) or by movement down the concentration gradient (backdiffusion) ***(Schiffl and Lang, 2010).***

Sevelamer hydrochloride, as a phosphate binder that contains neither aluminum nor calcium, is expected to improve the prognosis of dialysis patients. However, sevelamer hydrochloride has been reported to lower the serum bicarbonate level ***(Oka et al., 2007).***

***Oka et al. (2008)*** reported that sevelamer hydrochloride exacerbated metabolic acidosis in hemodialysis patients, depending on the dosage.

***De Santo et al. (2006)*** reported that a 24-week sevelamer administration caused a statistically significant ($p<0.05$) reduction (0.8g/dL) in serum albumin concentration, without affecting iPTH. And, ***Ohno et al (2009)*** reported sevelamer to reduce the serum urate concentration in maintenance hemodialysis patients

***Inoue et al. (2007)*** reported that Sevelamer was useful for reducing the serum calcium level and calcium x phosphate product.

***Akatsuka et al. (2008)*** recommended the use of sevelamer hydrochloride in combination with calcium carbonate in hemodialysis patients.

Yet, it is important to mention that sevelamer hydrochloride binds bacterial endotoxin in the intestinal tract, leading to lower circulating endotoxin levels, and offering a novel anti-inflammatory mechanism ***(Sun et al., 2009).***

# Aim of the Work

Study of the effect of sevelamer on bone profile in high flux regular haemodialysis patients.

# Hemodialysis

Patients with end stage kidney disease (ESKD) are progressively increasing and the demand for renal replacement therapies is expanding ***(Lysaght, 2002).*** Hemodialysis and peritoneal dialysis represent reliable forms of therapy leading to significant and longlasting survival times ***(Ledebo and Ronco, 2008)***. Nevertheless, hemodialysis is still performed intermittently leading to a significant degree of unphysiology due to fluid and electrolyte shifts during intra and interdialytic periods.

## I. Solute Removal by Dialysis:

Uremia could theoretically be treated by reducing solute production, but this is not part of current practice. High protein intake increases the production of many solutes, including various guanidines, indoles, and phenols. Patients with kidney failure tend to reduce their protein intake spontaneously, and before dialysis became available, physicians found that marked protein restriction relieved uremic symptoms ***(Kopple et al., 2000).***

Protein restriction can have ill effects, however, and it is now recommended that patients undergoing dialysis receive 1.2 g of protein per kilogram of body weight per day, which is nearly the amount provided by an average diet in the United States. Since a number of the best-known uremic solutes-such as aliphatic amines, D-amino acids, methylguanidine, hippurate, and many indoles and phenols-are produced entirely or in part by gut bacteria, the use of sorbents to reduce the load of such solutes has been considered but has not been systematically studied.