ORIGINAL RESEARCH PAPER

Nephrology

THE EFFICACY OF HEMOFILTRATION WITH HEMODIALYSIS IN RELATION TO THE CLEARANCE OF INTERLEUKIN 6 AND BETA 2 MICROGLOBULIN: A RETROSPECTIVE STUDY

KEY WORDS: kidney, failure, dialysis, hemodialysis, hemodiafiltration, interleukin 6, beta 2 microglobulin

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INTRODUCTION

The kidneys being healthy fulfill the function of removing all waste from the blood and excess fluid from the body. However, when the kidneys are not working properly, these wastes and excess fluid can build up in the blood and cause health problems. To refer to hemodialysis and hemodiafiltration, it is necessary to understand about renal complications, when the kidneys stop fulfilling their function as a blood filter, in which the persistent glomerular filtration rate below 15 ml / min per 173 m2 ; said renal function reaches a level below 10% in end-stage renal failure, the most serious stage of kidney disease; during which it is necessary for survival, the implementation of a replacement treatment of renal function through transplantation or dialysis (continuous peritoneal or

hemodialysis. Chronic kidney disease (CKD) is recognized as a public health problem. Yepes et al (2009) describes that it is due to the impact caused by the rapid increase in its prevalence, and by the "iceberg" effect generated by the lack of knowledge of its real magnitude, due to both the insufficient uptake and the under-registration of patients in stages It should be added that there are several types of dialysis; hemodialysis, hemodiafiltration and peritoneal dialysis. The first are performed through a machine also known as an artificial kidney and the second is performed through a catheter that goes to the membrane peritoneal area of the abdomen to filter the blood. For the year 2015, 16776977 people with CKD were identified in Ecuador according to data from the INEC to 2019. The prevalence of this pathology was 2 people per 100 inhabitants, being more frequent in females than males. It should be mentioned that chronic kidney disease affects about 10% of the world population. According to data from the Latin American Society of Nephrology and Hypertension (SLANH), in Latin America an average of 613 patients per million inhabitants had access in 2017 to some of the treatment alternatives to replace the function that their kidneys could no longer perform.

How does hemodialysis work?

A hemodialysis machine has a special filter called an artificial kidney, which cleans the blood. In order for your blood to pass through the dialyzer, the doctor has to establish an access or entrance to the blood vessels. This is done with minor surgery, usually on the arm. Three different types of access can be created: a fistula, a graft, or a catheter. The fistula is the first option of access. It is done by joining an artery to a nearby vein, under the skin, to create a larger blood vessel. This type of access is preferred because it presents fewer complications and lasts longer. At least six months before you need to start dialysis you should be evaluated by a specialist doctor, a vascular surgeon. The fistula will need to be created early (several months before starting dialysis), so it has enough time to heal and is ready by the time it needs treatment. If your blood vessels are not suitable for a fistula, a graft can be used. In this case, an artery is attached to a nearby vein with a small, soft, synthetic tube that is placed under the skin. When the fistula or graft has healed, two needles will be placed, one on the artery side and one on the vein side of the fistula or graft, each time you receive treatment. The needles are connected to plastic tubes. One tube takes the blood to the dialyzer where it is cleaned, and the other tube returns the clean blood to your body. The third type of access, called a catheter, is inserted into a large vein in the neck or chest. This type of access is generally used when dialysis is required for a short period of time. Catheters can also be used as permanent ports, but only when a fistula or graft cannot be created. Catheters can be connected directly to dialysis tubes and therefore needles are not used. You will be referred to a specialist surgeon to establish vascular access.

How does hemodiafiltration work?

It is a technique that provides a large amount of convective transport and in which the replacement fluid is produced simultaneously from the dialysis fluid itself. For this, ultrapure water, an adequate monitor that allows the generation of reinfusion liquid with guarantee of sterility, and a high-flow dialyzer are necessary.

The dialysis fluid is produced at the expense of an ultrapure water supply, with which the acid concentrate and powdered bicarbonate are diluted. The characteristics of the water treatment systems in hemodialysis units are extensively detailed in another topic of this work (link). In summary, the dialysis fluid must be sterile and the endotoxin count must be <0.03 EU / ml.

Monitors prepared for HDF online include several ultrafilters in the hydraulic circuit, so that the dialysis liquid undergoes an ultrafiltration process in several phases, so that ultimately what is obtained is ultrapure dialysis liquid. In addition, ultrafilter membranes have a high endotoxin adsorption capacity, so that after the filtration and adsorption process, the resulting liquid presents guarantees of sterility, even in cases where the liquid may be previously contaminated.

Part of this resulting liquid is directed towards the dialyzer, where the ultrafiltration and diffusion mechanisms take place, and another part is directed towards reinfusion. As the ability of ultrafilter membranes to adsorb endotoxins is limited in time, it is necessary to change them periodically, according to the manufacturer's instructions.

Reinfusion can be performed before (predilution system), after dialyzer (post-dilution system). The post-dilution system is the most widely used and the most efficient. Ultrafiltration is carried out in the first phase, with which an intradialyzer hemoconcentration occurs, with an increase in hematocrit and protein concentration, which causes an increase in blood viscosity and transmembrane pressure necessary to achieve the rate of established ultrafiltration. Furthermore, the higher protein concentration can increase the protein deposition on the membrane ("protein cake"), which can decrease its permeability coefficient, making diffusive transport of small solutes difficult. The predilution system incorporates the reinfusion fluid before the dialyzer, thereby reducing the concentrations of cells and solutes. The dilution of cells and proteins gives rise to a lower viscosity and thus a better rheology within the dialyser, while the lower concentration of solutes by hemodilution reduces its efficiency. In summary, whenever possible, the post-dilution system should be the first option.

The recommended dialysis fluid flow is 400-500 ml / min plus the replacement volume, although some monitors include automatic systems for adjusting it, which allow lower flows.

Online HDF dialyzers must be made with biocompatible membranes, with high hydraulic permeability, preferably with coefficients greater than 40 ml / hour / mmHg. The new generations of dialyzers have increased the internal diameter of the capillary fibers> 200 μm to reduce the internal resistance and therefore increase the convective volume. To carry out highly convective treatments, dialyzers with a high adsorption capacity, such as polymethyl-methacrylate, should be avoided.

Hemodialysis dose. Difficulty of your measurement

Normalized urea clearance (Kt / V) and percent urea reduction (PRU) are the currently accepted parameters for calculating the hemodialysis dose. Kt / V is the quotient between two volume quantities: the volume of body fluid cleared of urea during a hemodialysis session (Kt) and the volume of distribution of urea (V), equivalent to the volume of body water. The numerator of the equation indicates the hemodialysis dose that the patient has received and the denominator is the anthropometric parameter chosen to correct said dose based on body size.

Studies have observed a positive relationship between survival and various anthropometric values, among them V. Kt / V is a mathematical construction that can induce interpretation errors because it is a ratio between two parameters with a positive influence on evolution. Pathological decreases in V increase the Kt / V value and are associated with a worse prognosis. The PRU presents the same problems: with the same hemodialysis dose the PRU is inversely proportional to body size. The cause of the higher risk of death observed in the population with higher Kt / V or PRU values was clarified when it was verified that patients with a higher degree of malnutrition were included in this group.

While Kt / V can be obtained by formulas derived from PRU, and V can be determined by anthropometric equations, the

direct calculation of Kt in a hemodialysis session is difficult to perform due to the complexity involved in the in vivo determination of K. In early studies, Kt was calculated indirectly, dividing the Kt / V obtained from Lowrie's formula (ln UreaPre ¿ln UreaPost) by the V obtained from the Chertow equation.

The advent of monitors that measure ionic dialysance solved this problem. Ionic dialysance is similar to urea (K) clearance. The ion dialysance monitor automatically provides the Kt for each hemodialysis session. The Kt obtained by ionic dialysance also has a positive relationship with survival in any range of it4.

USES FOR HEMODIAFILTRATION

In these artificial purification techniques, the membranes used have pores of considerable diameter, which allow a rapid extraction of fluids and electrolytes compared to conventional hemodialysis membranes. In transport by convection or ultrafiltration, molecules of high molecular weight (up to 10,000 Da) are eliminated, of toxins with favorable toxicokinetic characteristics (water soluble and with low binding to plasma proteins) and some less favorable (intermediate volume of distribution).

Hemofiltration (HDF) is a form of hemofiltration that consists of adding another continuous dialysis system to the hemofiltration system (using the same hemofilter). In this way, transport or clearance of solute is achieved by convection (ultrafiltration) and by diffusion (dialysis). Both techniques are already in routine use in most ICUs, easy to apply, and relatively inexpensive.

HDF will be used only if HD is not available (clearance with HD is 70 to 170 ml / min, compared to about 20 ml / min with HDF). In intoxicated by the antiarrhythmic disopyramide (class I) with manifestations of clinical severity (electrocardiographic alterations such as marked prolongation of the QT interval, widening of the QRS or blockages and coma, advanced age and renal failure), HDF would be indicated.

Another indication for HDF is procainamide or N-acetylprocainamide overdose, as they have low plasma protein binding (15%), an intermediate volume of distribution (1.4 l / kg) and spontaneous renal elimination (50% for procainamide and 85% for N-acetylprocainamide).

INTERLEUKIN 6

Interleukin 6 (IL-6) is a key cytokine in the immune system with widely varied functions.

Stimuli such as infections, injuries (eg a burn) or other cytokines such as interleukin 1 favor the synthesis of interleukin 6 in T cells, macrophages, fibroblasts or even in muscle cells.

Furthermore, this cytokine plays a very important role as a mediator of fever and the so-called acute phase reaction, a process in which the production of certain proteins is activated or inhibited respectively in the liver (or other organs). These proteins play an important role in the regulation of immune function as well as in coagulation and wound repair processes.

A decrease in IL-6 levels is associated with poor defense against various pathogens. On the other hand, its overproduction can be the primary cause of many inflammatory and autoimmune diseases, such as arthritis, multiple sclerosis or osteoporosis. That is why it is vitally important to control the levels of this cytokine, especially in those pathologies in which IL-6 is involved.

STUDY

The results of interleukin 6 and beta 2 microglobulin were measured in 4 patients during 1 year of treatment, alternating between dialysis techniques (hemodialysis and Hemodiafiltration); Furthermore, it was compared with PRU and KTV levels to assess the efficacy of each dialysis technique. The selection criteria were: 1. Chronic kidney disease, 2. Having been on dialysis for more than 4 years, 3. Patients who underwent three-week sessions , 4. Patients undergoing short daily sessions.

There are antibody therapies in which the action of IL-6 is inhibited, demonstrating its efficacy in rheumatoid and juvenile idiopathic arthritis. On the other hand, in microimmunotherapy, this cytokine is used at different levels of dilution, in order to stimulate, modulate or slow down its biological action, depending on the pathology to be treated.

BETA 2 MICROGLOBULIN

The beta 2 microglobulin is a small protein that was first identified by Beggard and Bearn (1964) in the urine of patients with renal tubular disease. In said urine, it was possible to isolate a protein that had an immunoglobulin-C domain structure (amino acid sequence similar to that of the constant region of Ig) and an electrophoretic activity similar to that of beta globulins, so this, together Due to its small size, he gave it the name beta 2 microglobulin.

It is found in most nucleated cells, except trophoblasts. It is synthesized by numerous cells, particularly lymphocytes, and released into the blood where it is found in the highest concentration. Later it is degraded in the kidneys, and reabsorbed and catabolized

Due to its presence in most body fluids, it is used as a marker for a large number of diseases, such as cancer, central nervous system involvement, infectious and cerebrovascular disorders ... It is also often used to check kidney function, since it totally depends on her.

BIOMEDICAL SIGNIFICANCE

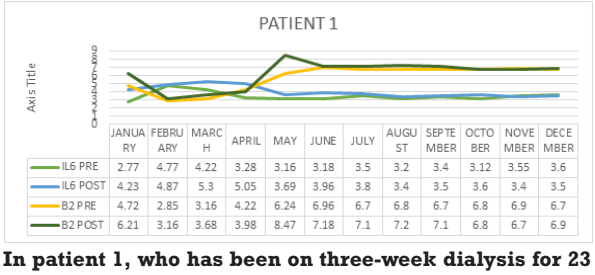
Due to its presence in the kidneys, when there is a failure in renal activity (proximal tubular dysfunction) or an overproduction of beta 2 microglobulin, your serum (blood) levels will increase. Cell membrane renewal also affects these levels.

Dialysis-associated amyloidosis:

As we have mentioned, the serum levels of this protein depend on the glomerular filtration rate and the protein synthesis rate. In patients with proximal renal dysfunction, the glomerular filtration rate decreases and there is an increase in the concentration of beta-2-microglobulin, which accumulates.

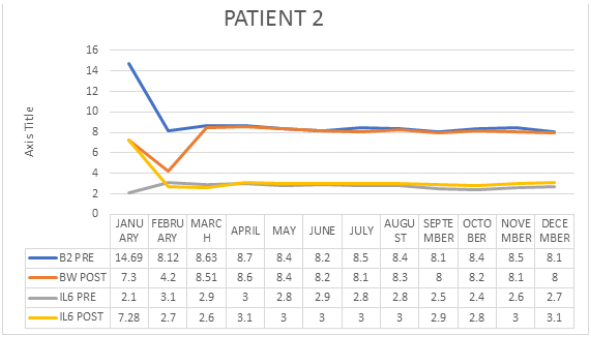
Beta-2-microglobulin precipitates resulting in circular arrangements of two beta sheets. These precipitates accumulate in tissues (extracellular deposit) and give rise to the variety of dialysis amyloidosis.

RESULTS



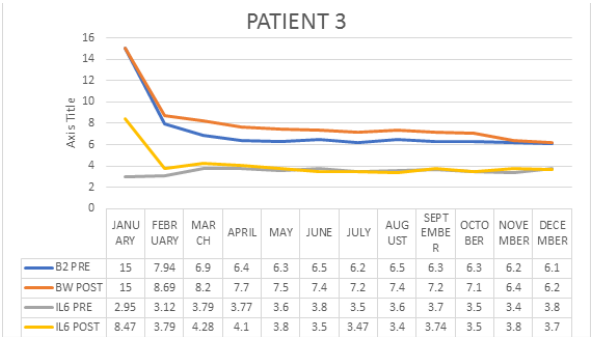
	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
IL6 PRE	2.77	4.77	4.22	3.28	3.16	3.18	3.5	3.2	3.4	3.12	3.55	3.6
IL6 POST	4.23	4.87	5.3	5.05	3.69	3.96	3.8	3.4	3.5	3.6	3.4	3.5
B2 PRE	4.72	2.85	3.16	4.22	6.24	6.96	6.7	6.8	6.7	6.8	6.9	6.7
B2 POST	6.21	3.16	3.68	3.98	8.47	7.18	7.1	7.2	7.1	6.8	6.7	6.9

In patient 1, who has been on three-week dialysis for 23 months, it was observed that with the change from conventional hemodialysis technique to hemodiafiltration, the values were decreasing, with which the mean molecule clearance is better with the hemodiafiltration Technique



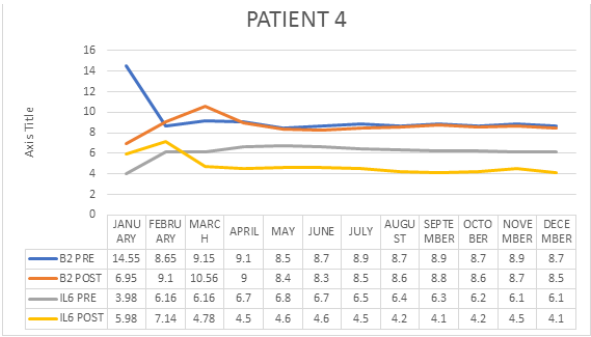
	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
B2 PRE	14.69	8.12	8.63	8.7	8.4	8.2	8.5	8.4	8.1	8.4	8.5	8.1
BW POST	7.3	4.2	8.51	8.6	8.4	8.2	8.1	8.3	8	8.2	8.1	8
IL6 PRE	2.1	3.1	2.9	3	2.8	2.9	2.8	2.8	2.5	2.4	2.6	2.7
IL6 POST	7.28	2.7	2.6	3.1	3	3	3	3	2.9	2.8	3	3.1

In patient 2, who has been in a short daily dialysis session for 195 months, it could be observed that with the change from conventional hemodialysis technique to hemodiafiltration, the values decreased more rapidly, with which the mean molecule clearance is better with the hemodiafiltration technique



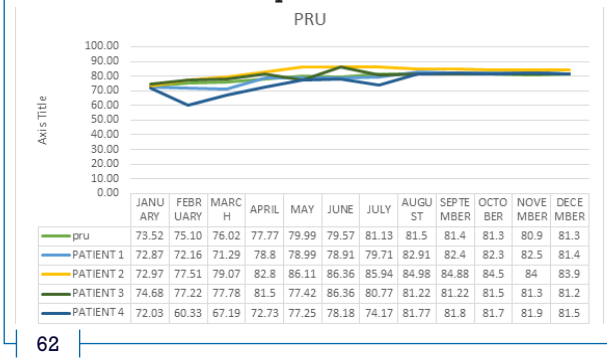
	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
B2 PRE	15	7.94	6.9	6.4	6.3	6.5	6.2	6.5	6.3	6.3	6.2	6.1
BW POST	15	8.69	8.2	7.7	7.5	7.4	7.2	7.4	7.2	7.1	6.4	6.2
IL6 PRE	2.95	3.12	3.79	3.77	3.6	3.8	3.5	3.6	3.7	3.5	3.4	3.8
IL6 POST	8.47	3.79	4.28	4.1	3.8	3.5	3.47	3.4	3.74	3.5	3.8	3.7

In patient 3, who had been in a three-week dialysis session for 48 months, it could be observed that with the change from conventional hemodialysis technique to hemodiafiltration, the values decreased from 8, which began to minimum values of 3 in il6, with which the Medium molecule clearance is better with hemodiafiltration technique



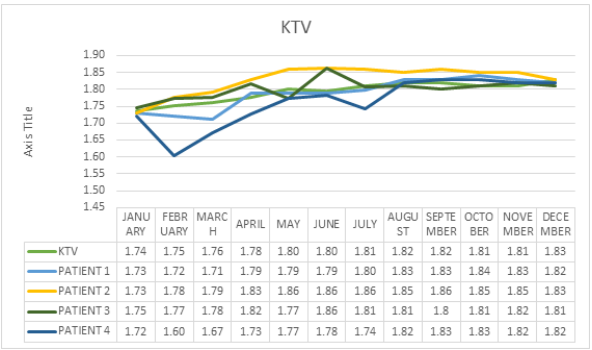
	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
B2 PRE	14.55	8.65	9.15	9.1	8.5	8.7	8.9	8.7	8.9	8.7	8.9	8.7
B2 POST	6.95	9.1	10.56	9	8.4	8.3	8.5	8.6	8.8	8.6	8.7	8.5
IL6 PRE	3.98	6.16	6.16	6.7	6.8	6.7	6.5	6.4	6.3	6.2	6.1	6.1
IL6 POST	5.98	7.14	4.78	4.5	4.6	4.6	4.5	4.2	4.1	4.2	4.5	4.1

In patient 4, who had been on three-week dialysis for 161 months, it was observed that with the change from conventional hemodialysis technique to hemodiafiltration, the values were decreasing from 5.98, which began to minimum values of 4 in il6, with which the clearance of medium molecule is better with hemodiafiltration technique



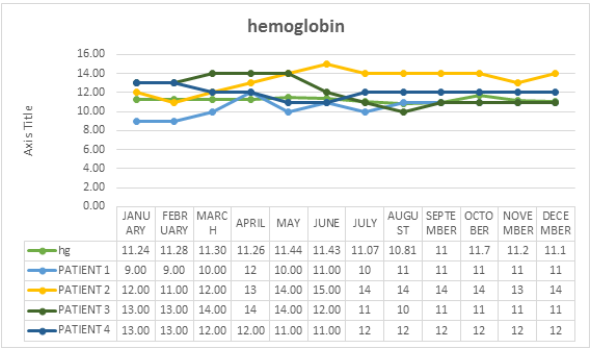
	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
pru	73.52	75.10	76.02	77.77	79.99	79.57	81.13	81.5	81.4	81.3	80.9	81.3
PATIENT 1	72.87	72.16	71.29	78.8	78.99	78.91	79.71	82.91	82.4	82.3	82.5	81.4
PATIENT 2	72.97	77.51	79.07	82.8	86.11	86.36	85.94	84.98	84.88	84.5	84	83.9
PATIENT 3	74.68	77.22	77.78	81.5	77.42	86.36	80.77	81.22	81.22	81.5	81.3	81.2
PATIENT 4	72.03	60.33	67.19	72.73	77.25	78.18	74.17	81.77	81.8	81.7	81.9	81.5

Within the PRU values, it could be observed that there is an increase in urea clearance with the hemodiafiltration technique



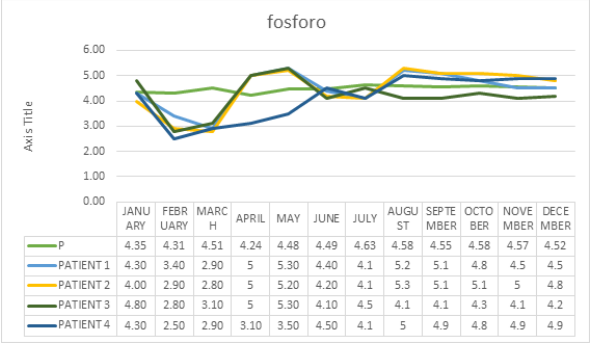
	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
KTV	1.74	1.75	1.76	1.78	1.80	1.80	1.81	1.82	1.82	1.81	1.81	1.83
PATIENT 1	1.73	1.72	1.71	1.79	1.79	1.79	1.80	1.83	1.83	1.84	1.83	1.82
PATIENT 2	1.73	1.78	1.79	1.83	1.86	1.86	1.86	1.85	1.86	1.85	1.85	1.83
PATIENT 3	1.75	1.77	1.78	1.82	1.77	1.86	1.81	1.81	1.8	1.81	1.82	1.81
PATIENT 4	1.72	1.60	1.67	1.73	1.77	1.78	1.74	1.82	1.83	1.83	1.82	1.82

In relation to KTV, it was observed that with hemodiafiltration it is closer to normal values for patients with chronic kidney disease



	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
hg	11.24	11.28	11.30	11.26	11.44	11.43	11.07	10.81	11	11.7	11.2	11.1
PATIENT 1	9.00	9.00	10.00	12	10.00	11.00	10	11	11	11	11	11
PATIENT 2	12.00	11.00	12.00	13	14.00	15.00	14	14	14	14	13	14
PATIENT 3	13.00	13.00	14.00	14	14.00	12.00	11	10	11	11	11	11
PATIENT 4	13.00	13.00	12.00	12.00	11.00	11.00	12	12	12	12	12	12

In hemoglobin values there were no significant changes with the change in technique.



	JANUARY	FEBRUARY	MARCH	APRIL	MAY	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	DECEMBER
P	4.35	4.31	4.51	4.24	4.48	4.49	4.63	4.58	4.55	4.58	4.57	4.52
PATIENT 1	4.30	3.40	2.90	5	5.30	4.40	4.1	5.2	5.1	4.8	4.5	4.5
PATIENT 2	4.00	2.90	2.80	5	5.20	4.20	4.1	5.3	5.1	5.1	5	4.8
PATIENT 3	4.80	2.80	3.10	5	5.30	4.10	4.5	4.1	4.1	4.3	4.1	4.2
PATIENT 4	4.30	2.50	2.90	3.10	3.50	4.50	4.1	5	4.9	4.8	4.9	4.9

Within the phosphorus values there was a decrease in the values.

CONCLUSIONS:

With the four patients it was possible to detect that regardless of the number of months they have been on dialysis, hemodiafiltration had better clearance values of both interleukin 6 and beta 2 microglobulin, in addition that no amyloidosis occurred in any patient due to dialysis, with In which the patients passed without complications and adapted correctly to their dialysis treatment, the use of Hemodiafiltration is recommended to obtain better results in clearance of IL 6 and microglobulin.

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