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Editorial:

ARTIFICIAL KIDNEY PHYSIOLOGY

Carlos G. Musso[1] and Gerardo Torres Torres[2]

[1]Nephrology Department. Hospital Italiano de Buenos Aires. Argentina
[2]Nephrology Department. Hospital General Yagüe. Complejo Asistencial de Burgos. España

carlos.musso @ hospitalitaliano.org.ar

Versión en español

Introduction
The extrarrenal depurative techniques are based on the indirect contact of the patient´s blood with the dialysate. Such contact, performed via a semipermeable membrane (dialytic membrane), allows for the exchange of substances in both: the blood and dialytic compartment. It is during this process that toxic substances such as urea are removed from the body and substances that are necessary, such as bicarbonate enter it. If such contact happens outside the patient´s body, in fact in the hemodialysis filter (for which an external blood and dialysate circulation circuit are necessary): this is a *hemodialytic* procedure, while if this procedure happens inside the body (peritoneal cavity), with the peritoneum acting as a filter: this procedure corresponds to *peritoneal dialysis*[1].

Physiology of the artificial kidney: methods
The artificial kidney offers a series of depurative/infusion methods, each of which allows for the extraction/incorporation of particular substances in the body. These methods are: difusion, ultrafiltration, convection, adsorption, buffer system, heating.

Difusion: it is the passage of solutes through a semi permeable membrane of the compartment where it is most concentrated to where it is less concentrated. In general it is based on the use of low permeability membranes, which only allows the passage of small molecules (< 500 daltons: for example: urea, potassium, etc)[1]

Ultrafiltration: it is the passage of water from one compartment to the other

motivated by an osmotic gradient between them.

Convection: it is based on the transportation of solutes from one compartment to the other as a consequence of the passage of fluid through a high permeability membrane. This process allows for the removal of medium sized molecules (up to 30.000 daltons) among which are most of the inflammation mediator[1]. In order for this removal to be significant the amount of fluid displaced has to be high (35 ml/Kg / h). A typical example is hemofiltration[2]. Theoretically, a convective method can also eliminate solutes (small molecules) when they are dragged through the solvent passage, but for this to be significant, the removal of fluid should be so much that in practise it makes it necessary to use diffusive methods for achieving this objective[3]. The convective methods remove mediators that participate in the systemic inflammatory response syndrome: TNF, IL 6, etc. Such depuration would be achieved through the removal of a high volume of liquid (for some authors 50 litres/day), and through the adsorption of these molecules in the hemofilter membrane (it is necessary to change the filters often in order to make this effect to be significant). However, research has shown that despite this effective depuration, no significant modifications are achieved in the serum levels of the mediators, not even in the mortality of the treated patients. On the other hand, these procedures also remove protecting mediators (anti-inflammatory ones) such as the IL 10.[3-5]

Adsorption: This process consists of the removal of solutes through its adhesion to the filter membrane. Such property is used to depurate the substance in question from the blood compartment, as it happens with some toxic substances which can be removed by using filters with charcoal [1].

Buffer System: The buffer solution to be used can be based on bicarbonate or lactate base (which becomes bicarbonate, in equimolar proportion, at hepatic level). Nevertheless, bicarbonate must be used instead of lactate in some situations such as lactic acidosis, hepatic insufficiency and post - surgical treatment immediately after hepatic transplant[6-7].

Heating: in continuous techniques body temperature must be controlled and it should be evaluated whether to heat the replacing solution since there is loss of heat and subsequent risk of hypothermia[8].

Artificial kidney physiology: prescription schemes
The methods offered by the artificial kidney can be applied in a simple or combined way following schemes of different duration, frequency and pump speed depending on the objective you want to achieve.

- **Speed of external pumps:**
  In general, in critical patients it is common to use slow procedures (with blood and dialysate slow speed pumps) so as not to induce hypotension. Thus, in this situation is better to use procedures which have more chances of being tolerated: such as semi continuous and continuous therapies. Among the reasons why convective methods involve a lower risk of arterial hypotension are; the slow removal of fluids which allow the refilling of the intravascular compartment, the slow removal of the intravascular solutes which prevents the massive osmotic passage of intravascular liquid to the

intracellular compartment (as it happens in hemodialysis), decrease of body temperature in 2-3 degrees (vasoconstriction), the removal of mediators with heart-depressor properties (only in high volume exchanges).
These methods allow to use bigger volume of ultrafiltration with better hemodynamic tolerance, which leads to a better handling of the volume absorbed by the patient through parentenal feeding and from intravenous drugs[3, 8].

- **Time and frequency of the sessions:**
From this perspective, the substitutive methods of the renal function can be intermittent such as hemodialysis three times a week, semicontinuos: daily and prolonged in time between 8-18 hours, such as low efficiency prolonged dialysis (SLED) or daily prolonged dialysis. Finally, there are the continuous procedures which are daily and last 24-48 hours, with an additional requirement of fluid restitution so it allows a high volume of fluid displacement. Example: veno venous hemofiltration, hemodyafiltration, etc.

  Regarding the speed of the blood pumps and the dialysate, 300 ml/min and 500 ml/min respectively usually are the speeds of the intermittent procedures, with speeds similar or lower to the previous ones for semicontinuous procedures, and finally slower speeds (100 ml/min y 300 ml/min respectively) for continuous treatments.

It is worth noticing that in every extra renal depuration procedure the solutes extracted are removed from the blood compartment to the dialyzed, which in turn creates a favourable gradient for the passage of such solutes from the intracellular compartment (which is the one we wish to depurate) to the intra-vascular one. This phenomenon increases the gradient of solutes between the intravascular and dialytic compartments, thus increasing the efficiency of the depurative process. However, in intermittent procedures (hemodyalisis) the passage of solutes between the blood and the dialytic compartments is faster than the one between the intracellular and the blood compartment. This phenomenon explains why in intermittent procedures the most significant removal of solutes is achieved in the first 2 hours of the session, which is the moment of the bigger blood-dialysate gradient; it also explains why after interrupting the dialytic session there are still solutes passing from the intracellular to the intravascular compartment, in which approximately 30 minutes after disconnection the serum levels of solutes being removed increased in a 10-20% (rebound effect)[1].

On the contrary, in slow procedures the speed of the passage of solutes between the different compartments happens approximately at the same speed, so the depuration of the solutes is virtually constant throughout the procedure and consequently the slow methods do not cause rebound effect after disconnection.

It is very important to keep hemodynamic stability during extrarenal depuration treatments: since when a hypotense patient is dialyzed it is common to dialyse only the intravascular and not the intracellular compartment, which is the objective of the substitutive treatment. This happens because in a hypotense patient, as their tissues are badly perfused they accumulate solutes, since there is little passage of them to the vascular compartment, thus they are not dialyzed properly out of the body. When the dialytic session is finished and the hemodynamic condition of the patient improves, the tissues that are now better perfused begin to pass solutes to the

intravascular compartment which generates a significant increase in serum levels of the solutes (urea), reflecting the low efficiency reached during the dialytic session[3].

Artificial kidney physiology: types of circuits
In the extra-renal depurative methods, based on extra body circulation circuits, these systems require a circuit for blood goes of the body and another for its reentry once it has been depurated.

While the reentry circuits are always venous systems, the exit circuit can be an arterial or venous one. In the first case the motor of the system is the circulation of the patient itself while in the second case it is necessary to use a pump to mobilize the blood. These are the arterial-venous and venous-venous circuits respectively. The first of these circuits presents a special risk of bleeding, ischemia of the part of the body involved, as well as thrombotic events. Veno-venous circuits present a lot less complications, they require only one access (a venous one) since it is possible to use a double lumen catheter, they can hold a continuous blood flow despite presenting the patient arterial hypotension since it uses an extra-body blood pump. Because of all the above exposed reasons the preferred access is the veno-venous one. (3,9)

Conclusion:
The knowledge of the physiology of the artificial kidney enables us to understand which are its potential therapeutic benefits as well as its limitations when substituting the native renal function.

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