Lactate or bicarbonate in dialysis fluid for daily home hemodialysis: advantages and disadvantages*

(Lactate ou bicarbonate dans le liquide de dialyse pour hémodialyse quotidienne à domicile : avantages et inconvénients)

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Summary

The availability since the beginning of the 21st century of hemodialysis monitors similar to the cyclers used for automated peritoneal dialysis (space-saving and easy-to-handle monitors using a low volume of dialysis fluid and suitable for daily dialysis) has led to renewed interest in home hemodialysis. As in peritoneal dialysis, these cyclers use either lactate - an anion whose metabolism leads to bicarbonate regeneration - or bicarbonate in the dialysate. The purpose of this article is to review the advantages and disadvantages of these two types of alkalinizing anion. Whichever type of anion is used, it is important to avoid over-alkalinization of the patient. Lactate dialysate, which is less expensive and easier to handle, seems to be suitable for most patients, but its use in patients with abnormal liver function should be discouraged.

Key words : acetate, bicarbonate, dialysis fluid, lactate, home hemodialysis

Résumé

La disponibilité depuis le début du XXIème siècle de moniteurs d’hémodialyse apparentés aux cyclers utilisés pour la dialyse péritonéale automatisée (moniteurs peu encombrants, de maniement simple, utilisant un faible volume de dialysat et adaptés à la dialyse quotidienne) a conduit à un regain d’intérêt pour l’hémodialyse à domicile. Comme en dialyse péritonéale, ces cyclers utilisent un dialysat au lactate - un anion dont le métabolisme conduit à la régénération du bicarbonate – ou bien un dialysat au bicarbonate. L’objet de cet article est de faire le point sur les avantages et inconvénients de ces deux types d’anion alcalinisant. Quel que soit le type de dialysat utilisé, il importe d’éviter une alcalinisation trop importante du patient. Le dialysat au lactate, moins onéreux et de maniement plus facile, semble pouvoir être utilisé chez la plupart des patients, mais son utilisation chez ceux d’entre eux présentant un bilan hépatique anormal devrait être déconseillée.

Mots clés : acétate, bicarbonate, dialysat, lactate, hémodialyse à domicile

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Introduction

Under normal dietary conditions and as a result of nutrient metabolism, the body is continuously subjected to an acid load:

- volatile acid load due to carbon dioxide ($\text{CO}_2$), mainly from aerobic glucose metabolism: carbon dioxide is present in the body in dissolved form, behaving like a weak acid (partially dissociated acid). This acid is volatile, as it is eliminated by the lungs in the form of carbon dioxide.
- load in non-volatile acids (called fixed acids) which behave like strong acids (totally dissociated at the body’s pH). The load of fixed mineral acids (mainly sulfuric acid from amino acid metabolism, but also acids from the diet) is around 1 mEq per day per kg of body weight and is normally eliminated by the kidneys. The load of fixed organic acids (lactic acid, pyruvic acid, etc.) from carbohydrate and lipid metabolism is much higher but does not affect the acid-base balance because the corresponding anion (lactate, pyruvate, acetate, citrate, etc.) is metabolizable and alkalinizing: indeed, the metabolism of these anions (consuming oxygen), which takes place mainly in the liver and muscle, leads to the appearance of bicarbonate, which takes over the $\text{H}^+$ ions provided by these acids.

As the kidneys of the dialysis patient no longer eliminate the load of fixed mineral acids, this leads to a drop in bicarbonate level (metabolic acidosis). Moreover, dialysis is responsible for the loss of alkalinizing organic anions not present in the dialysate, which exacerbates metabolic acidosis and the drop in bicarbonates.

The dialysis session must be capable of restoring bicarbonatemia. The most logical approach would seem to be to provide the missing bicarbonate using a dialysis fluid with a higher bicarbonate concentration than the patient. As dialysis fluid must also contain divalent ions (calcium and magnesium), which have a strong tendency to precipitate as insoluble calcium and magnesium carbonates, it is necessary to acidify the dialysate to prevent this precipitation.

The method used in the early days of hemodialysis consisted of acidifying the dialysate by dissolving carbon dioxide contained in a cylinder. Since this method was very cumbersome to implement, Charles Mion, then working in Belding Scribner’s team in Seattle, proposed substituting the bicarbonate in the dialysate by acetate, an alkalinizing anion that does not precipitate calcium and magnesium salts [1]. Acetate was also chosen for the same reason during the development of continuous ambulatory peritoneal dialysis (CAPD) using bags of sterile dialysis fluid.

Progressive improvements in access to hemodialysis have made it possible to care for increasingly frail and elderly patients. However, the deleterious effects of acetate often make such treatment impossible. Technological advances have made it possible to manufacture a bicarbonate dialysate extemporaneously, without the need for a CO2 cylinder, and this type of dialysate became increasingly popular in the last two decades of the 20th century [2]. At the same time, acetate was found to be responsible for sclerosing peritonitis in patients treated with CAPD [3] and was replaced by lactate.

At the start of the 21st century, the benefits of short daily hemodialysis are becoming increasingly apparent, both in medical terms and in terms of quality of life. Its main (and perhaps only!) disadvantage is that, when performed in a center, it doubles the time and cost of transport, which
are already very high. The development of simplified monitors to promote short daily home hemodialysis is therefore justified. This type of hemodialysis is carried out using low-flow dialysate [4], based on the example of peritoneal dialysis cyclers: space-saving, easy-to-handle monitors, suitable for daily dialysis and requiring only a small volume of dialysis fluid supplied in bags in which the alkanizing ion is lactate or bicarbonate.

To my knowledge, there are as yet no published studies comparing the use of lactate and bicarbonate in short daily home hemodialysis. That’s why we’ll start with conventional hemodialysis. Although acetate dialysate is virtually no longer used, it will be mentioned in the preamble because acetate is a metabolizable alkanizing ion and, as such, shares properties with lactate. In chronic hemodialysis, there have been far more publications in the literature on acetate dialysate than on lactate dialysate.

**Acetate buffered dialysate**

The replacement of bicarbonate with acetate in the dialysate results in a significant loss of bicarbonate in the dialysate. A high acetate concentration (35 to 45 mmol/L) is therefore required to compensate for both bicarbonate consumption during the interdialytic period and bicarbonate and inorganic anions loss during the dialysis session. The result is a significant rise in acetatemia (normal: 0.01 to 0.3 mmol/L) during dialysis, which can reach over 4 mmol/L in some patients with particularly slow acetate metabolism [6].

The presence of acetate in the dialysate is responsible for several deleterious effects. The higher the acetate level, the greater the vasodilatation. This vasodilatation leads to a drop in blood pressure despite the increase in heart rate, resulting in hemodynamic instability. The presence of acetate in the dialysate is also responsible for abnormalities in lipid and carbohydrate [7] metabolism as well as stimulation of inflammation (production of TNF and IL1-β), explaining a mild febrile reaction [8,9].

In addition, the loss of dissolved CO₂ in the dialysate, due to its absence in the dialysate, induces respiratory alkalosis, as evidenced by the decrease in PCO₂ of around 4 mmHg during the session [7]. This respiratory alkalosis explains the maintenance or even slight increase in pH during the session, despite the loss of bicarbonate (beneficial effect), but is responsible for hypoventilation.

Finally, the presence of acetate in the dialysate is responsible for a hypoxia-inducing decrease in PO₂ during the dialysis session. This decrease is due in part to hypoventilation, but mainly to the increase in oxygen consumption associated with acetate metabolism, which also explains why the decrease is more pronounced in patients with rapid acetate metabolism.

All these deleterious effects, and in particular the hemodynamic instability that can be major in frail or elderly subjects, explain why acetate dialysate is virtually no longer used in Europe.

**Dialysate with bicarbonate buffered dialysate**

Technological advances now make it possible to produce bicarbonate dialysate extemporaneously, without the need for a CO₂ cylinder, by diluting two different concentrates, thereby separating the divalent ions (calcium and magnesium) and the bicarbonate. One of the concentrates (concen-
trate A) is an acidic concentrate containing, in particular, divalent ions and an acid. This prevents bacterial contamination and, above all, ensures that the dialysate obtained after dilution is sufficiently acidified to prevent calcium and magnesium precipitation when it meets the bicarbonate provided by the second concentrate (concentrate B). The latter currently consists of a sodium bicarbonate powder cartridge rather than a liquid concentrate in order to limit bacterial proliferation and reduce weight and bulk.

By combining with an equivalent quantity (in mEq/L) of bicarbonate, the acid contained in concentrate A disappears and is transformed into dissolved CO$_2$ acid and the corresponding anion. Acetic acid, at a concentration of 3 to 7 mEq/L after dilution, has historically been the first choice. However, it leads to the appearance of 3 to 7 mmol/L of acetate in the dialysate, which is enough to significantly raise acetatemia (to more than 10 times its value at the start of the session in some slow-metabolism patients) [10] and can be deleterious (sensation of general malaise, muscular impatience, post-dialytic asthenia) in susceptible patients. It’s important to note that, during bicarbonate dialysis with acetic acid concentrate, acetate and bicarbonate loading is proportional not to the concentration of acetate and bicarbonate in the dialysate, but to the difference in acetate and bicarbonate concentration between plasma and dialysate. This difference averages 6 to 10 mmol/L for bicarbonate and 2 to 7 mmol/L for acetate, so the acetate load represents around one-third (and the bicarbonate charge two-thirds) of the alkalizing ion load.

The trend is therefore to replace acetic acid with hydrochloric acid. However, hydrochloric acid concentrates, because of their very high acidity before dilution to 1/45, are more difficult to manufacture and more dangerous to handle, so citric acid is now being proposed. Lactic acid is also used to acidify bicarbonate dialysis fluid during continuous renal replacement therapy in intensive care but does not appear to have been proposed for chronic bicarbonate hemodialysis.

When acetic acid, citric acid, or lactic acid is used, the corresponding anion is acetate, citrate, or lactate, which is metabolized to bicarbonate, compensating for its consumption during the conversion of acetic, citric, or lactic acid to dissolved CO$_2$ acid. When hydrochloric acid is used, the corresponding anion is chloride, which is not metabolized, requiring an increase in the bicarbonate concentration of the dialysate.

It’s important to note that we don’t dialyze with acetic acid (vinegar), citric acid, lactic acid, or hydrochloric acid, which are strong acids totally dissociated at the body’s pH! In all cases, the acid contained in concentrate A has disappeared and dialysis is carried out with the weak dissolved CO$_2$ acid (2 to 7 mmol/L corresponding to a PCO$_2$ of 65 to 230 mmHg), which acidifies the dialysate (pH between 6.8 and 7.2).

The acidity of the dialysate, compared with that of plasma (pH between 7.2 and 7.4), is responsible for the acidification of plasma during its passage through the dialyzer because the acidifying dissolved CO$_2$ load is greater than the alkalinizing bicarbonate load. This does not prevent the desired alkalinization of the patient, since the dissolved CO$_2$ load is normally eliminated immediately by the lungs, leaving only the alkalinizing bicarbonate load. In patients with ventilatory disorders, however, it can lead to respiratory acidosis, causing drowsiness and even disturbances of consciousness. In addition, the acidification of blood during its passage through the dialyzer may induce an anaphylactoid reaction in susceptible patients.
Bicarbonate dialysis, when carried out at high efficiency with dialysate of high bicarbonate concentration, can lead to a rapid increase in bicarbonatemia, with the onset of poorly tolerated metabolic alkalosis (headache, dizziness) resulting in a decrease or absence of increase in ionized calcium which, together with the increase in bicarbonates, can contribute to hemodynamic instability [9]. This metabolic alkalosis is also responsible for stimulating the production of organic acids [10]. Their metabolism leads to an increase in oxygen consumption, explaining the slight decrease in PO2 during the session. The greater the bicarbonate concentration in the dialysate, the greater this decrease [11,12]. The persistence of organic acid production during the hour following the end of the session explains the abrupt drop in pH and bicarbonatemia, as well as the persistence of the decrease in PO2 during this period [13].

**Lactate buffered dialysate**

Why was acetate chosen as a substitute for bicarbonate in dialysate for chronic hemodialysis? Perhaps because acetate was proposed in 1949 by Gilbert Mudge as a substitute for bicarbonate in parenteral rehydration when both calcium and an alkalinizing ion are required [14]. However, as early as 1934, Alexis Hartmann had proposed introducing 36 mmol/L lactate to the saline solution to which Sidney Ringer had added calcium to improve cardiac function [15]. This solution (commonly known as “Ringer lactate”) has been used for decades in critical care units in cases of hypovolemia or extracellular dehydration and avoids the vasodilatory effect of acetate.

Dalal et al. clearly showed the different effects of lactate, compared with acetate and bicarbonate, in chronic hemodialysis [16]. The use of lactate dialysate (46 mmol/L) is responsible for an increase in lactatemia (nle: 0.5-5 mmol/L), which can reach 8 mmol/L at the end of the session. Lactate is much better tolerated than acetate, in particular because its vasodilatory effect is less pronounced, as evidenced by the smaller decrease in blood pressure and the smaller increase in cardiac output during the dialysis session.

Due to the loss of bicarbonate during the session, the increase in pH and bicarbonatemia is less marked during the session (which limits the risk of alkalosis), whereas 1 hour after the end of the session, pH and bicarbonatemia are the same as in bicarbonate dialysis due to continued lactate metabolism and perhaps less or no increase in organic acid production. Lactate metabolism consumes oxygen, which explains why the fall in PO2 is greater than in bicarbonate hemodialysis, but less than in acetate hemodialysis, since lactate metabolism is slower than acetate metabolism. This slower rate also explains why the correction of acidosis (increase in pH and bicarbonatemia) is slower than in acetate hemodialysis, which reduces the risk of alkalosis at the end of the session, and why the fall in PCO2 is greater due to greater respiratory compensation. During high-efficiency dialysis, the frequency of intradialytic symptoms observed with lactate dialysate is of the same order as that observed with bicarbonate dialysate and much lower than that observed with acetate dialysate [17].

**Home hemodialysis with a cycler**

In daily home hemodialysis, dialysis can be performed with bicarbonate or lactate.

Daily bicarbonate hemodialysis with a low-flow dialysate cycler is possible using the S3 cycler (Physidia) and 5-liter bags S3 (Physidia) with two compartments: a small compartment (0.25 L)
containing potassium, calcium, magnesium, and glucose, plus the amount of chloride needed to ensure electroneutrality, and a large compartment (4.75 L) containing sodium, bicarbonate, and the amount of chloride needed to ensure electroneutrality. The two compartments are thoroughly mixed just before the dialysis session. The presence of hydrochloric acid in the small compartment enables acidification of the dialysate after mixing (pH = 7.2), thus avoiding carbonate precipitation. The use of hydrochloric acid enables acetate-free bicarbonate dialysate to be obtained.

The two cyclers currently available in France (S3 from Physidia and System One from NxStage-Fresenius) allow the use of lactate dialysate bags. To my knowledge, there are no published studies comparing lactate and bicarbonate dialysis with low-dialysate-flow hemodialysis cyclers. However, a few studies have been carried out on intensive care patients. In 20 patients treated by intermittent hemofiltration with lactate dialysis fluid, the 8 patients with acute liver failure had, compared with the other patients, a greater rise in lactatemia and a greater fall in pH and bicarbonatemia (probably reflecting slower metabolism), as well as a greater fall in blood pressure [18]. In contrast, a study comparing continuous hemofiltration with lactate replacement fluid or bicarbonate replacement fluid (acidified with 3 mmol/L lactic acid) in 40 ventilated intensive care patients without severe liver failure showed no difference between the two replacement fluids in terms of acid-base balance (pH, PCO₂, base-excess) [19]. Another study in 8 intensive care patients without severe liver failure showed that lactate dialysis fluid used in continuous hemodiafiltration had no adverse effects [20].

All in all, lactate dialysate is contra-indicated for patients with reduced lactate metabolism (severe liver failure, hypoxia, lactic acidosis) [21,22], but these patients are not good candidates for home hemodialysis. For all other patients, lactate dialysis fluid, which is less expensive and easier to handle, appears to be as suitable as bicarbonate dialysate fluid. However, it seems prudent to avoid using lactate dialysate in patients with liver disease and to check transaminases from time to time to ensure that they are not elevated: this will ensure that lactate intolerance is not overlooked this intolerance will be strongly suggested if the switch to bicarbonate dialysate is accompanied by progressive normalization of transaminases.

Regardless of the type of alkalinizing anion used (lactate or bicarbonate), it is important to avoid over-alkalinization of the patient, whose bicarbonatemia at the start of the session must not exceed 24 mmol/L, in order to avoid metabolic alkalosis and the induced decrease in ionized calcium, the deleterious effects of which can be significant, even life-threatening [23]. NxStage dialysis fluid bags (Fresenius) are available with a lactate concentration of 35, 40, or 45 mmol/L, enabling a concentration adapted to the patient’s acid-base balance to be prescribed.

Conflict of interest

The author declares no conflict of interest for this article.

Références

Lactate or bicarbonate in dialysate?