Nephrology and Renal Diseases

Editorial

ISSN: 2399-908X

Dialysis Fluid

Thomas Ryzlewicz*

Dialysis Centre, ViaMedis Riesa, Germany

Introduction

Once upon a time, there had been a dialysis centre in Tassin (south in France, near Lyon) with tremendous success in patient's long-term treatment with haemodialysis. This is *well-known*, 'The Secret of Tassin' by Charras and Lorent (treatment time was 24 hours per week, sodium of dialysis fluid was 135 mmol/l and nutrition with only 2 g NaCl by fresh cocking). They had a big group of patients with 80 years, treated 30 years with dialysis and a second (smaller) group of patients with 90 years of age, treated 40 years with dialysis. Nearly unknown is, that they had used always the dialysis prescription of Shaldon with acetate as buffer precursor → so they had *no calcification* in the dialysis fluid at all. The therapy of Shaldon and Tassin was very wise, as they never had overrun the metabolic capacity of the liver for acetate metabolism (> in his first profession, Shaldon had been *hepatologist* . . .).

In the end of the 1970-ies, there was the *cry* of shortening the treatment time of dialysis (> B.H. Scribner, *square-meter-hour-hypothesis*). Surfaces of dialyzers become big and bigger and blood flow had raised, in order to reach the same Kt/V of the former long-term treatment. This critical behaviour neglected, that the very most dialysis centres had overrun the metabolic capacity of the liver, to transform large amounts of acetate into bicarbonate. By this behaviour *like a trade union*, the *incompatibility* of acetate had introduced and the *need* for the bicarbonate dialysis fluid had proclaimed. With the re-introduction of bicarbonate in the prescription of dialysis fluid again (1978), the *calcification* accompanies the dialysis. Because of the *calcification of the monitors*, a descaling procedure for the monitors was necessary after every treatment. The patients however received *no descaling* . . .

Bicarbonate is an anion with problems of heavy solubility. In mammalians and humans, bicarbonate is the *transport form* of produced CO_2. In the lungs, this bicarbonate will re-transformed into CO_2 by carbo-anhydrase for ventilation. So *an acidification* with physically solved gas CO_2 had implemented with the amount of 4 % of the total alkali bicarbonate (> Homer W. Smith, "From Fish to Philosopher", 1953). With bicarbonate 24 mmol/l and CO_2 1,2 mmol/l (= 40 mm Hg), there is not calcification with Ca^{++} and Mg^{++} ions in humans at all. Kolff had set the bicarbonate concentration in his prescription to 32 mmol/l, because of the shorter treatment time with dialysis in relation to one week living (= 168 hours), in order to treat the metabolic acidosis. The former ways of acidification had been not sufficient concerning calcification (Kolff: acid sodium phosphate – Alwall: carbogen gas (5 % CO_2)). In 1978, 3 mmol/l acetate had introduced in bicarbonate dialysis (required double concentrate pumps). With this prescription, the calcification remains inside. With an elevated amount of acidification (> 4 or 5 mmol/l acetate, still used in France), the transfer of CO_2 gas from the dialysis fluid into the patient by the dialyzer, does reach critical pCO_2 levels for pulmonary limited patients (COLD or patients, that had just weaned from respirator). There is a critical alternative in bicarbonate dialysis: calcification or overrunning the pulmonary facilities of a group of patients.

A very interesting set-up for dialysis *without any calcification* had presented by Bené (chemist of Hospal, Lyon) in 1990, AFB (acetate free bio-filtration). Simply spoken: It was a dialysis with NaCl fluid *without any buffer or buffer precursor*, added only by small ions (Ca^{++}, Mg^{++}) and glucose. The intelligent idea: Bicarbonate will admitted as low-volume HDF (post-dilution), while the acidification of this set-up will done by the dialysis of the patient's bicarbonate against a pure NaCl dialysis fluid. With other words: Acidification will done by *robbery of the patient's own bicarbonate*. Later on in the flowchart, a higher dosage of bicarbonate will admitted to the patient in the post-dilution mode. This AFB treatment requires special monitors. The *solvent drag* is only limited (low-volume HDF post-dilution).

In 2007, a new prescription of dialysis fluid appeared with an exchanged mode of acidification, citrate 0,85 mmol/l (ART group, Seattle). First thought was, to replace the RCA (Regional Citrate Anticoagulation, done in the ICU's). Whenever this target of replacing Heparin as the single anti-coagulating drug failed, it is a very interesting prescription of acidification of dialysis fluid, as there is *no calcification at all* in this dialysis fluid. The ART prescription consists of 0,85 mmol/l citrate and 0,3 mmol/l acetate. This had fixed in patents. The *small amount* of 0,3 mmol/l acetate *is not so important*. In 2012, a second prescription with citrate appeared, Citrate 1,0 mmol/l. Comparing this new citrate acidification (1,0 mmol/l) with the classical acetate acidification (3 mmol/l): Citrate is a threefold base, so 1,0 mmol/l is equivalent to 3 mval/l. This means, that the amount of *produced* CO_2 derived of bicarbonate buffer, will be exact the same like the acidification with 3,0 mmol/l acetate. The essential is, that there is a *second principle of working inside*, the chelate ligature. This chelate ligature of citrate disguises the both problematic cat-ions of solubility in the dialysis fluid, Ca^{++} und Mg^{++}. So, they both are present in the dialysis fluid, but they cannot take part to calcify.

What is the problem with citrate acidification? This *second principle of working*, the chelate ligature, will not well understood by Medical Doctors, as this requires *some chemical knowledge*. Medical opinion leaders will complain the well-known calcification of coronary vessels and heart valves of CKD-5 patients, but the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with Medical Doctors. This means a limited chemical knowledge. Additional to this, a Medical Product (Dialysis concentrates) has absolutely no

Correspondence to: Thomas Ryzlewicz, Dialysis Centre, ViaMedis Riesa, Germany, E-mail: thomas.ryzlewicz@web.de

Received: January 01, 2018; **Accepted:** January 10, 2018; **Published:** January 13, 2018

vigilance!

What will remain? An interested Nephrologist or a Dialysis Provider will be the best option in order to reach the dialysis fluid *without any calcification*, the citrate acidification. We will not wait until the Medical Societies and Medical Authorities will have finally understood this problem of *chemical solubility*, as it is a real clinical problem!

Naturally, the problems of calcification of CKD-5 patients have several different reasons, e.g. secondary hyperparathyreoidisme, nutrition intake of protein and phosphate or reduction of the FGF-23 principle. With this background, there is the *medical obligation*, to avoid any further reason for calcification. Mourning and complaining of the patient's calcification will not stop them.

An important point: When switching to citrate acidification, the concentration of Ca^{++} should slightly elevated in order *to prevent* a hypo-calcaemic reaction of the patient, as a smaller part of the patient's Ca^{++} will bound by citrate. For example, instead of Ca^{++} 1,25 mmol/l (3 mmol/l acetate), Ca^{++} 1,5 mmol/l should use with citrate.

Smaller points: Toxicity of citrate. In former times, RCA had done with 30 % citrate as regional anticoagulation in case of bleeding problem. The known danger was the metabolic alkalosis, due to the three-fold buffer precursor citrate *additional* to the bicarbonate concentration of 32 mmol/l. One third of this total dosage had run into the patient, up to 450 mval. This was an over-treatment with alkali and *not* a specific effect of citrate. RCA today will done in most cases with 4 % citrate (in pre-dilution mode). With this set-up, citrate levels will reach about 10 mmol/l in the patient's blood today. For successful anticoagulation with citrate as the single anticoagulating drug, a level between 4 – 6 mmol/l is the target. With citrate acidification, the reached level of citrate will be about 1 mmol/l. - Taking-up these citrate levels, there will be a *partial effect* of anticoagulation in the citrate acidification. Different studies had shown a possible reduction of Heparin up to 50 % bolus and 50 % of the continued dosage of Heparin (H. Wolf, Ahrenholz). A dialysis with citrate acidification needs for anticoagulation *a second principle*, e.g. a disorder of the patient's anticoagulation or the half dosage of Heparin. - Stimulation of the MPO (Myeloperoxidase): In the ART prescription, there will be today 0,3 mmol/l acetate inside. This is a reduction of two ten-potencies, when comparing with the acetate dialysis of Shaldon. In this set-up, there will be no effect of acetate on the MPO. - Kt/V will be slightly higher with citrate acidification in comparison to the classical acetate acidification, due to the additional anticoagulation effect of citrate. - Citrate will metabolized quantitative in high turn-over mode in the Krebs cycle, as this is the oxidative metabolism (> proven by the Calcium gap smaller than 0,2 %):

Ca^{++} GAP = (total Ca^{++} post – total Ca^{++} pre) – (ion Ca^{++} post – ion Ca^{++} pre), Gabutti).

Conclusion

Several curious points you will observe:

1. The Medical Authorities had casted with Medical Doctors. They do not ask a chemist for consulting concerning the problem of *chemical solubility* of the classical dialysis concentrate of bicarbonate dialysis (acidification with 3 mmol/l acetate). Moreover, there absolutely no existing vigilance for Medical Products.
2. Medical Societies and their Opinion Leaders are also Medical Doctors, who do not really assess the problem of *chemical solubility* of the classical dialysis concentrate. This remains the duty of a chemist. Therefor the Medical Societies complain the clinical calcification problems of the CKD-5 patients.
3. Lectures by a chemist to this theme are seldom. When these will presented, the context will only deal with the *smaller points* concerning the extent (Kt/V, IL concentration, MPO activation). The best of them will report concerning the reduction of Heparin dosage. – Nearly all chemists, who are involved in the production of dialysis fluid, had employed by the companies. There are *conflicts of interests*: Not to damage *a running product* (> the classical bicarbonate dialysis prescription). It is *not* a deficit of knowledge of them . . .
4. It remains to the *interested doctors and interested dialysis providers*, to switch to the citrate based dialysis concentrates in order to prevent the important additional effect of calcification *by the wrong bicarbonate dialysis prescription*. The citrate based dialysis concentrates are licensed and available on the market. We should not wait *"ad calendas graecas"* until Medical Societies or Medical Authorities will awake . . .