# 6. Acidosis: target bicarbonate levels

**Draft CARI Guidelines**

**Haemodialysis**

- **Aim for a predialysis serum bicarbonate in the range 23-24 mmol/L. (Level A evidence)**

**Peritoneal dialysis**

- **Aim for serum bicarbonate in the range 26-27 mmol/L. (Level A evidence)**



## Practice tips

- Due to the large variability in acid base status between patients, a choice of dialysis buffer concentrations should be available to help achieve targets.
- Identify the cause of the acidosis: for example, inadequate dialysis, excessive weight gain due to fluid retention, excessive animal protein intake, bicarbonate loss.
- In haemodialysis patients, avoid hypotension during dialysis as this may contribute to acidosis via lactate production.
- Bicarbonate levels can be increased by:
  - addition of oral alkali: for example, calcium carbonate or sodium bicarbonate (recognising that in haemodialysis patients this agent has been associated with increased fluid gain)
  - Altering both the dialysate concentration and possibly the base type, aiming for a post-haemodialysis bicarbonate of < 28 mmol/l.
- Avoid alkalosis, which has been associated with nausea, vomiting, lethargy, soft tissue calcification and hypoxemia. Alkalosis can be diagnosed in haemodialysis patients by measuring post-dialysis bicarbonate.
- Peritoneal dialysate buffered with bicarbonate may offer benefits compared to lactate buffer.

## What is the evidence?

Serum bicarbonate ($HCO_3$) and pH in dialysis patients are determined by the dialysis process, exogenous alkali ingestion and endogenous acid production. The best data (based on sample size) concerning the relationship between acidosis and mortality in humans is probably the epidemiological study of Lowrie and Lew (1992) conducted in a cohort of over 12,000 haemodialysis patients in the USA. (Level B evidence) They reported that a predialysis serum bicarbonate of < 12 mEq/L was associated with

increased mortality, as was predialysis serum bicarbonate > 20 mEq/L. This J curve relationship was, however, not analysed for the influence of confounders that might influence serum bicarbonate levels and/or mortality, such as nutrition and dialysis dose. Hence there is no clear evidence in the published literature that serum bicarbonate is an independent predictor of mortality.

RCTs (Level A evidence) concerning the morbidity of acidosis are limited to endpoints such as markers of bone metabolism, nutrition and hospitalisation rates.

Two RCTs in small numbers of haemodialysis patients demonstrated that raising the predialysis serum bicarbonate from 15 to 24 mmol/L (n = 11) and from 18 to 24 mmol/L respectively improved indices of bone turnover and PTH responsiveness to calcium (Lefebvre et al, Graham et al 1997a).

There are three published RCTs in the haemodialysis population looking at the effects of serum bicarbonate levels on nutritional parameters. Increasing the predialysis serum bicarbonate from 18 to 24 mmol/L (n = 6) and from 19 to 23 mmol/L (n = 46) had beneficial effects in two studies (Graham et al 1997b, Williams et al 1997), as measured by reduction protein turnover and decreasing protein catabolic rate. However, these outcomes measures may not accurately reflect protein catabolism or protein intake. A short-term study by Brady and Jasbargen (1998) over 6 weeks (n = 36) did not show any nutritional benefit in raising the predialysis bicarbonate from 17 to 20 mmol/L.

Two RCTs in patients treated with lactate buffered peritoneal dialysate have shown nutritional benefits from increasing serum bicarbonate from 19 to 26 mmol/L (n = 7) (Graham et al 1996) and from 23 to 27 mmol/L (n = 200) (Stein et al 1997). A controlled study comparing peritoneal dialysate buffered with lactate to one buffered with bicarbonate (both at dialysate concentration of 35 mmol/L ) reported improvements in systemic acidosis and normalised protein catabolic rate in the bicarbonate group (n = 73) (Feriani et al 1998).

Only one RCT reported on hospitalisation rates. Stein et al (1997) found peritoneal dialysis patients with serum bicarbonate of 27 mmol/L had fewer hospital admissions and shorter lengths of stay compared with a cohort with bicarbonate of 23 mmol/L.

The method of correcting the acidosis (eg the oral route versus dialysate) and the type of alkali used may be important. This has not been well studied.

*Haemodialysis*

There is level A evidence of benefit for increasing predialysis serum bicarbonate from < 19 mmol/L up to 23-24 mmol/L.

There are no data for levels between 20 and 23 mmol/L or > 25 mmol/L.

There are no data on appropriate targets for post-dialysis serum $HCO_3$ but post-dialysis alkalosis may be associated with morbidity.

There are no data on the most appropriate method for achieving the target bicarbonate.

*Peritoneal dialysis*

There is level A evidence of benefit for increasing serum bicarbonate from < 23 mmol/L up to 26-27 mmol/L.

There are no data for levels between 23 and 26 mmol/L or > 27 mmol/L.

The following table summarises the current evidence retrieved by a literature search on acidosis in ESRF in humans.

**Acidosis in end-stage renal failure in humans**

| Study | Intervention | Serum bicarbonate (predialysis) | Endpoints | Population | Level of evidence |
|---|---|---|---|---|---|
| Lowrie and Lew 1992 | none | < 10 to > 25 mEq/L | mortality | 13,535 HD patients | Level B |
| Lefebvre et al 1989 | dialysate bicarbonate 33 vs (40 + oral mmol/L | 16 vs 24 mmol/L | bone metabolism and morphology | 21 HD patients | Level A |
| Graham et al 1997a | | | | | Level A |
| Graham et al 1997b | dialysate bicarbonate 35 vs 40 mmol/L | 18 vs 24 mmol/L | protein balance studies | 6 HD patients | Level A |
| Williams et al 1997 | dialysate bicarbonate 30 vs 40 mmol/L | 19 vs 23 mmol/L | nutritional indices | 46 HD patients | Level B |
| Brady and Jasbargen 1998 | dialysate bicarbonate 35 vs (40 + oral) mEq/L | 17 vs 20 mmol/L | serum albumin, PCR, total lymphocyte count | 36 HD patients | Level A |
| Graham et al 1996 | Oral bicarbonate to serum level = 25 mmol/L | 19 vs 26 mmol/L | protient balance studies | 7 CAPD patients | Level A |
| Stein et al 1997 | dialysate lactate 40 vs 35 mmol/L | 23 vs 27 mmol/L | mortality, technique failure, hospitalisation, nutritional indices, bone metabolism | 200 new CAPD patients | Level A |
| Feriani et al 1998 | dialysate lactate 35 vs bicarbonate 34 mmol/L | 21 mmol/L both groups | adequacy, nPCR | 73 CAPD patients | Level A |

PCR – Protein catabolic rate, nPCR – normalised protein catabolic rate

## What do the other guidelines say?

**DOQI:** No recommendation.

**BRA:** Serum bicarbonate should be not less than and not more than 3 mmol/L outside the normal range. In haemodialysis patients, predialysis serum bicarbonate should be in the normal range by 3 months.

**CSN:** No recommendation.

**EDTA-ESN:** No recommendation.

## Implementation and audit

ANZDATA should collect pre-and post-haemodialysis and routine peritoneal dialysis bicarbonate levels at the end of each survey period.

## Suggestions for future research

1. Is serum bicarbonate an independent risk factor for mortality and/or morbidity (as assessed by measures such as hospital days, quality of life)? A multivariate regression analysis of other significant variables such as dialysis dose and nutritional status would be required.

2. What is the best way to achieve target bicarbonate in haemodialysis and peritoneal dialysis?

3. What is the safe upper range of serum bicarbonate, with special attention to post-haemodialysis bicarbonate?

4. Are there risks in correcting acidosis, in regard to arterial calcification, hypertension and cellular function?