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Indication of Alkali Treatment in Connection with Neonatal Exchange Transfusion

By

D. Boda, L. Murányi, Gy. Tóth and Erna Eck

Department of Paediatrics, University Medical School, Szeged

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It has been shown [10, 2] that most cases of neonatal hyperbilirubinaemia are accompanied by metabolic acidosis which may become critical if ACD blood, a preparation of low pH, is used for exchange transfusion. This observation has been corroborated by several authors [1, 6, 9]. Acidosis occurring in the course of blood exchange is considered a potential danger and several methods for its prevention have been worked out. Barrie [1] first recommended to administer sodium bicarbonate during transfusion, but now pretreats ACD blood with bicarbonate, while Oliver [9] with tris buffer. We are giving preference to bicarbonate. Investigations made so far do not, however, suffice for drawing conclusions in this respect. According to Varga and Hutás [12], alkali treatment is justified only exceptionally. Calladine and Gardner [3] have pointed out that the citrate given with blood soon causes the acid-base balance to shift toward alkaline values and this is then further increased by sodium bicarbonate treatment. Again, Frenzel and Rogner [5] observed no acidosis; on the contrary, they found the acid-balance to have shifted towards alkalosis immediately after blood exchange. To prevent it, they recommended heparinized blood for the exchange.

The present study has been undertaken in order to settle this problem and, in particular, to study the correlation between bicarbonate infusion and alkalosis arising after the intervention.

Material and Method

The material consisted of 84 newborn babies who needed blood exchange on account of simple bilirubinaemia or blood-group incompatibility. Repeated transfusions were performed in 7 cases. While 38 of the babies had had no treatment before the intervention, the rest received 50 ml/kg of 1/6 molar sodium bicarbonate solution infused in 2 hours immediately before the blood exchange. Exchange transfusion of about 200 ml/kg of blood was invariably made through the umbilical vein. The intervention lasted 2 to 2 1/2 hrs. Blood samples were collected before the infusion, before, and 24, 48 and 72 hrs. after the blood exchange. Blood samples before and after the transfusion were obtained from the umbilical vein, after flushing the dead space of the catheter with the patient's blood, while the other samples were from arterialized capillary blood of the finger tip. The pH and standard bicarbonate were determined according to Astrup.

TABLE I

Acid-base balance in newborn infants after exchange transfusion

1.	2.	3.	4.	5.	6.	I.	II.	III.	IV.	V.	i.	ii.	iii.	iv.	v.
H. E.	3100	6	650	HB	29.6	7.37	7.28	7.35	7.46	7.37	21.8	19.5	23.9	24.9	22.3
B. M.	1450	6	280	HB	25.0	7.37	7.20	7.35	7.38	7.43	19.1	15.1	23.1	21.8	21.5
S. M.	2100	3	380	RH	18.7	7.39	7.36				21.1	20.5			
		7	380		28.5	7.38	7.37	7.47	7.43	7.44	26.5	24.3	27.0	28.8	25.4
R. M.	3000	1	630	RH	13.2	7.47	7.43	7.47			26.6	23.8	30.8		
		2	630		18.1	7.47	7.41	7.49	7.52	7.46	30.3	28.6	31.3	30.1	25.9
T. I.	4000	1	730	AB0	18.2	7.30	7.39	7.53	7.45	7.45	17.4	23.5	29.2	27.3	24.2
B. M.	2700	1	550	AB0	19.5	7.38	7.36	7.52	7.49	7.47	19.2	20.3	31.5	23.3	25.6
T. T.	3740	4	800	HB	18.0	7.37	7.42	7.50	7.46	7.49	16.9	20.6	21.6	23.9	25.5
S. A.	1000	5	180	HB	21.6	7.29	7.29	7.48	7.42	7.39	18.8	15.6	24.5	22.7	27.6
N. E.	2450	4	500	HB	24.6	7.27	7.23	7.33	7.48	7.45	19.0	18.5	19.2	21.5	23.0
Sz S.	3280	1	680	RH	15.8	7.37	7.38	7.25	7.42	7.32	18.9	19.0	19.9	22.1	21.1
D. M.	2200	4	500	AB0	40.0	7.40	7.31	7.42	7.34	7.48	20.0	19.4	25.1	26.0	25.0
K. G.	1500	7	280	HB	18.4	7.18	7.14	7.22	7.26	—	18.0	16.4	23.0	20.1	—
M. S.	2450	5	550	HB	31.5	7.31	7.25	7.36	7.39	7.40	18.4	16.5	21.0	20.8	20.9
L. J.	3200	1	670	AB0	13.9	7.33	7.31	7.36	7.37	—	17.1	16.8	22.2	23.2	—
M. S.	2350	5	430	RH	29.1	7.35	7.27	7.36			19.1	17.5	21.6		
		6	450		28.6	7.38	7.27	7.32	7.40	7.42	25.0	24.0	24.4	27.3	23.5
M. E.	2100	8	375	AB0	47.5	7.25	7.40				15.7	21.4			
		9	450		28.2	7.44	7.34	7.42	7.38	7.34	26.2	17.4	27.1	22.5	21.5
H. I.	3240	2	560	RH	23.8	7.39	7.42	7.44	7.39	7.43	23.5	18.8	22.7	22.0	24.0
K. H.	1950	7	370	HB	29.7	7.37	7.27	7.41	7.38	7.36	23.1	20.0	24.5	23.9	20.1
T. E.	2540	3	530	HB	26.4	7.40	7.30	7.43	7.41	7.43	23.2	20.5	25.7	23.8	21.1

K. I.	2300	5	420	HB	25.2	7.30	7.27	7.36	—	7.33	18.3	17.3	21.5	—	21.0
V. S.	3650	4	630	HB	27.1	7.34	7.33	7.45	7.33	7.36	16.5	21.5	23.5	20.7	21.1
N. G.	1250	4	240	HB	27.6	7.32	7.31	7.46	7.45	7.42	19.5	19.5	25.0	23.5	23.6
P. S.	3000	4	600	AB0	29.0	7.11	7.17	7.40	7.45	7.44	14.0	15.1	24.1	19.6	20.0
D. Zs.	2800	1	560	RH	16.6	7.36	7.34	7.52	7.49		17.4	18.5	25.5	24.9	
		2	560		23.3	7.47	7.35	7.46	7.38	7.47	23.5	23.0	27.5	25.0	27.0
V. I.	2860	7	600	RH	26.1	7.29	7.13	7.39	7.40	7.43	26.1	8.7	15.2	15.3	17.0
O. I.	2850	2	560	AB0	30.9	7.43	7.41	7.48			19.0	21.5	26.1		
		3	560		21.5	7.41	7.40	—	—	7.47	24.9	26.0	—	—	24.0
M. I.	2670	5	580	HB	25.5	7.42	7.31	7.40	7.39	7.41	20.7	19.3	21.0	23.4	24.0
Sz. S.	2050	5	420	HB	24.0	7.32	7.28	7.39	7.39	7.31	20.6	17.2	25.5	27.7	26.0
H. L.	3640	3	750	AB0	24.0	7.30	7.26	7.40	7.44	7.45	20.0	19.2	27.2	23.5	19.7
L. J.	3100	2	650	AB0	27.2	7.20	7.25	7.43	7.42	7.43	15.7	18.0	29.0	33.0	21.7
F. A.	1950	3	400	AB0	35.2	7.24	7.27	7.44			20.5	15.5	25.0		
		4	400		25.2	7.41	7.27	7.24	7.25	7.34	26.0	21.7	19.7	19.2	20.1
S. L.	2100	2	460	RH	27.8	7.35	7.23	7.42			21.2	17.1	27.5		
		3	460		22.1	7.38	7.23	7.40	7.40	7.49	21.0	17.5	25.7	21.7	25.4
D. J.	2700	5	550	AB0	27.8	7.37	7.24	7.45	7.47	7.51	18.5	17.1	24.7	21.0	21.5
A. A.	3470	5	790	AB0	29.9	7.30	7.36	7.39	7.40	7.42	17.9	21.8	26.2	26.1	25.0
T. T.	2650	5	560	AB0	32.8	7.20	7.11	7.34	7.31	7.34	17.9	15.8	26.3	25.5	23.4
T. E.	2100	4	450	HB	23.2	7.22	7.32	7.42	7.45	7.42	15.3	19.2	23.8	24.2	21.2
T. G.	2950	4	650	HB	24.9	7.26	7.19	7.44	7.44	7.38	20.0	18.8	29.5	27.4	24.7
S. R.	2550	1	400	RH	15.0	7.22	7.19				13.1	12.6			
		2	400		28.8	7.23	7.18				18.3	15.4			
		3	400		26.8	7.35	7.38	7.39	7.44	7.39	23.4	22.7	26.9	24.7	24.2
Mean						7.32	7.29	7.40		7.41	18.9	18.6	24.0		22.5
Standard deviation ±						0.07	0.09	0.08		0.10	3.1	2.7	5.2		2.3

Symbols to Table I
1. Initials
2. Birth weight
3. Age, days, at exchange transfusion
4. Volume of transfused blood, ml
5. Diagnosis. HB: Hyperbilirubinaemia
   AB0 : AB0 incompatibility
   RH : RH incompatibility
6. Serum bilirubin level before exchange transfusion

I. Blood pH before exchange transfusion
II. Blood pH at termination of exchange transfusion
III. Blood pH 24 hrs after exchange transfusion
IV. Blood pH 48 hrs after exchange transfusion
V. Blood pH 72 hrs after exchange transfusion
i. = Standard bicarbonate (mEq/litre) before exchange transfusion
ii. = Standard bicarbonate (mEq/litre) at termination of blood exchange transfusion
iii. = Standard bicarbonate (mEq/litre) 24 hrs after exchange transfusion
iv. = Standard bicarbonate (mEq/litre) 48 hrs after exchange transfusion
v. = Standard bicarbonate (mEq/litre) 72 hrs after exchange transfusion

* Computed from values at first exchange.

Results

Results without bicarbonate pretreatment are shown in Table I; those with bicarbonate pretreatment, in Table II.

Most hyperbilirubinaemic babies were acidotic; mean blood pH amounted to 7.32 in the group without pretreatment, and to 7.30 and even less in 16 of the 38 cases. Mean pH was likewise 7.32 before the infusion of sodium bicarbonate in the pretreated group, and in 16 instances were values of 7.30 or less registered. On bicarbonate infusion the situation improved considerably, but the increase in pH and in the plasma bicarbonate value was slight; it corresponded, on the average, to the normal level (pH = 7.37; standard bicarbonate = 22.5 mEq/litre). The initial acidosis was further increased after blood exchange without pretreatment, a phenomenon agreeing well with earlier observations (mean pH = 7.291; standard bicarbonate = 18.6 mEq/litre). Compared with pre-transfusion values, the difference was not considerable and in some cases even of opposed sign, but — as presented in Fig. 1 — grave acidosis usually developed precisely in newborns with initially low pH-values so that their further decrease following the exchange transfusion would have been especially dangerous. This could be prevented by sodium bicarbonate pretreatment (Table II; Fig. 1). Changes in standard bicarbonate showed the same regularity as the pH-values did. It is evident from Table I and II that, in agreement with the original observations of Calladine et al. [3], the exchange transfusion was followed by a shift of the pH to alkaline values. The change was mainly metabolic, it was rather the standard bicarbonate value which had risen. Although the alkalosis was usually moderate, the pH of blood exceeded 7.50 and the standard bicarbonate increased to

above 30 mEq/litre in exceptional cases. Post-exchange alkalosis occurred fairly regularly in the non-pretreated group as well, but became still more pronounced after alkali pretreatment, so much so that — although less marked than in the non-pretreated group — it was still demonstrable 72 hrs after the intervention. No correlation was observed between the pre-transfusion acid-base balance and the subsequent alkalosis so that it was not possible to foretell the degree of post-transfusion alkalosis on the evidence of the blood samples obtained before the exchange.

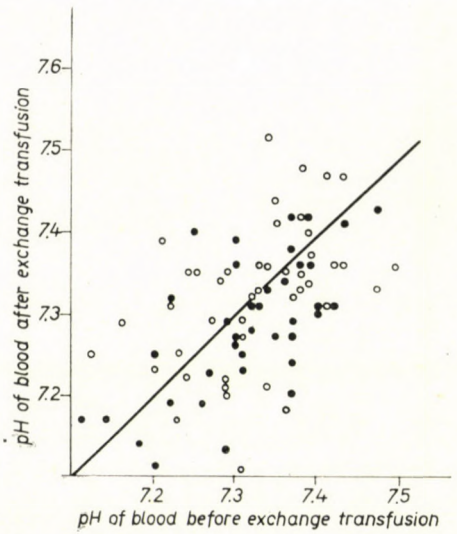

FIG. 1. Blood pH before and after exchange transfusion, with (○) and without (●) preceding sodium bicarbonate infusion

DISCUSSION

The possibility of fatal consequences of the use of ACD blood for exchange transfusion was clearly shown by the case of G. K. (See Table I), a premature baby who died a few days after the intervention. Death in this case was due to another complication, but there can be no doubt that a control of the acidosis before the blood exchange and the prevention of its aggravation after the intervention would have helped in coping with the situation. It is surprising that the grave acidosis should have caused no clinical symptoms either in the present series or in earlier observations.

It is clear from the present results that the decrease of the mean values for pH and standard bicarbonate was not considerable since it resulted from opposed deviations. Therefore, mean values did not present a true picture in this case, and this is why individual results have been registered. It is the rare but sometimes critical cases of acidosis which are the real danger; instead of a deviation of the mean, they only manifest themselves with a wider scattering of values.

ODELL's [7, 8] investigations have stressed the significance of acidosis in the sequelae of jaundice. Bilirubin encephalopathy is well known to arise after the bilirubin binding capacity of serum proteins has been exhausted. This capacity depends, among others, on the pH, and bilirubin binding decreases considerably in acidosis. DIAMOND's [4] recent animal experiments have shown that metabolic acidosis promotes the binding of bilirubin to the nervous system. The

TABLE II

Acid-base balance in newborn infants after exchange transfusion with preceding sodium bicarbonate infusion

1.	2.	3.	4.	5.	6.	I.	II.	III.	IV.	V.	VI.	i.	ii.	iii.	iv.	v.	vi.
T. R.	3420	3	690	AB0	24.7	7.39	7.47	7.34	7.52	7.41	7.52	18.7	25.2	24.8	27.4	23.0	25.6
P. P.	2570	3	250	AB0	21.0	7.43	7.52	7.47	7.54	7.43	7.46	20.7	28.2	31.6	27.4	25.2	25.2
K. E.	3400	3	680	AB0	19.9	7.38	7.45	7.42	7.50	7.44	7.46	21.8	23.0	24.2	27.2	23.3	23.3
R. P.	4100	5	790	AB0	24.4	7.35	7.46	7.46	7.36	7.42	7.33	21.3	27.2	26.8	24.2	25.9	21.8
B. A.	3500	4	720	HB	29.5	7.38	7.46	7.49	7.40	7.45	7.43	19.5	22.6	25.4	23.5	22.5	25.8
J. E.	2180	5	400	HB	25.1	7.41	7.32	7.31	7.36	7.38	7.41	20.9	19.4	20.8	21.5	23.9	23.8
Sz. E.	3550	3	700	AB0	23.5	7.41	7.42	—	7.44	7.49	7.43	20.8	22.0	—	29.8	27.8	25.1
P. Zs.	3400	1	700	AB0	12.6	7.29	7.32	7.22	7.38	7.43	—	18.4	23.8	19.2	28.2	23.4	—
K. N.	2900	1	570	AB0	25.4	7.36	7.41	7.18	7.46	7.43	7.41	19.8	31.2	18.2	26.8	29.2	24.8
K. A.	3100	4	650	AB0	33.7	7.49	7.40	7.38	7.44	7.50	7.51	22.2	24.8	22.8	29.2	30.2	27.8
R. E.	3110	1	620	AB0	14.5	7.34	7.43	7.52	7.51	7.45	7.45	19.8	25.8	26.8	32.0	26.9	25.0
S. E.	2250	4	380	HB	21.1	7.33	7.44	7.36	7.39	7.35	7.50	17.9	22.8	23.8	25.9	23.8	25.9
K. T.	3100	4	630	HB	26.1	7.43	7.43	7.36	7.48	7.43	7.41	21.8	23.8	22.3	25.3	29.8	23.8
R. E.	2700	4	500	HB	22.9	7.25	7.42	7.35	7.56	7.42	7.46	20.3	27.0	27.1	33.2	30.8	26.2
J. E.	2800	3	560	AB0	25.7	7.12	—	7.25	7.46	7.40	7.48	15.8	—	16.8	32.1	29.2	27.8
B. J.	2900	3	610	AB0	26.5	7.35	7.24	7.41	7.39	7.41	7.42	23.0	21.8	24.2	32.8	26.9	24.3
H. K.	3500	5	630	AB0	30.0	7.41	7.44	7.47	7.50	7.42	7.47	23.8	29.6	29.2	33.2	27.2	28.2
N. A.	3100	4	640	HB	22.8	7.29	7.38	7.35	7.44	7.40	—	19.7	20.4	20.2	27.8	24.2	—
K. T.	2540	4	400	HB	29.4	7.27	7.25	7.29	7.39	7.37	7.39	16.7	18.3	18.9	21.6	21.7	19.4
K. A.	2000	3	420	HB	28.7	7.36	7.41	7.35	7.44			19.7	19.7	20.2	24.7		
		5	430		30.5	—	7.47	7.27	7.39	7.38	7.45		23.8	20.3	25.6	24.0	23.8
B· A.	2750	4	550	HB	27.8	7.23	7.35	7.25	7.41	7.45	7.33	17.4	20.7	17.8	26.2	26.8	24.5
V. L.	1750	3	320	HB	29.5	—	7.30	7.35	7.43	7.44	7.42	—	17.3	21.2	20.9	23.6	23.6

T. I.	1500	5	340	HB	26.9	7.31	7.35	7.27	7.44	7.46	7.47	17.0	20.7	16.9	24.2	27.2	25.4
F. T.	2370	6	465	HB	25.3	7.39	7.42	7.37	7.48	7.37	7.42	20.2	25.2	22.2	26.9	21.0	20.3
L. Á.	2675	5	620	HB	26.2	7.24	7.34	7.22	7.45	7.53	—	18.3	21.3	19.0	29.3	29.7	—
T. Sz.	1700	4	320	HB	26.4	7.29	7.43	7.20	7.43	7.46	7.41	19.6	21.6	22.6	29.0	26.0	23.3
		8	330		26.5	7.38	7.41	7.33	7.45	7.27	7.31	23.6	25.4	22.0	27.2	23.2	21.5
T. J.	3320	1	700	RH	13.8	7.34	7.40	7.36	7.43	7.43	7.40	20.7	25.3	24.0	28.7	30.2	25.0
H. G.	2980	1	660	AB0	18.4	7.34	7.39	7.21				17.9	20.2	14.7			
		3	670		21.3	—	7.46	7.36	7.49	7.49	—	—	29.1	21.2	30.0	30.4	—
B. F.	2400	5	400	HB	23.4	7.16	7.35	7.29	7.51	7.47	7.39	13.7	22.8	23.2	26.8	24.7	22.2
L. Z.	3150	1	800	AB0	9.0	—	7.30	7.27	7.39	7.48	—	—	21.8	21.2	26.9	22.7	—
Cs. É.	3120	5	730	HB	29.3	7.31	7.36	7.29	7.53	7.48		17.9	21.8	21.4	28.5	29.2	
		7	750		24.7	—	7.37	7.30	—	—	7.33	—	20.7	18.2	—	—	23.9
N. I.	3200	2	680	HB	19.0	7.29	7.34	7.21	7.35	—	7.33	20.2	21.8	18.8	26.0	—	25.6
R. K.	3100	1	650	AB0	17.5	7.22	7.35	7.31	7.51	7.31	7.46	17.1	18.3	18.8	28.7	20.3	22.7
L. L.	2600	3	730	AB0	22.0	7.28	7.38	7.34	7.49	—	—	19.4	22.6	20.2	21.7	—	—
C. G.	3920	3	920	AB0	32.3	7.23	7.29	7.17	7.29			15.8	21.8	20.0	26.7		
		4	750		27.5	—	7.39	7.25	7.48	7.49	7.44	—	24.7	22.8	31.7	31.2	27.9
S. J.	3030	4	660	HB	23.7	7.20	7.27	7.23	7.39	7.44	—	15.4	20.2	17.8	23.8	29.4	—
B. J.	2950	4	850	AB0	24.5	7.42	7.39	7.36	7.45	—	—	20.3	24.5	22.1	29.9	—	—
		5	650		22.0	—	7.42	7.36	7.42	7.37	7.47	—	24.8	23.2	29.4	23.4	28.1
B. K.	1800	3	315	HB	22.8	7.38	7.34	7.36	7.40	7.42	7.48	21.2	20.7	21.7	26.2	25.3	25.8
K. A.	1300	4	280	HB	23.9	7.33	7.37	7.33	7.38	7.43	7.32	18.9	21.7	18.2	24.8	25.7	24.1
S. E.	3100	4	650	AB0	22.5	7.21	7.33	7.39	7.43	7.44	7.44	18.7	21.9	23.7	31.9	29.2	25.7
V. Gy.	3360	3	700	AB0	26.1	7.33	7.36	7.10	7.46			20.7	20.4	12.2	27.5		
		5	640		25.2	—	7.43	7.43	7.49	7.47	7.39	—	24.8	24.7	30.2	27.5	26.1
Sz. R.	3350	4	690	HB	26.8	7.39	7.42	7.40	7.51	7.50	7.44	21.4	25.6	24.9	29.3	29.2	28.3
L. E.	3260	2	730	HB	32.2	7.37	7.30	7.32	7.45	7.51	—	20.4	23.3	23.9	29.9	32.0	—

1.	2.	3.	4.	5.	6.	I.	II.	III.	IV.	V.	VI.	i.	ii.	iii.	iv.	v.	vi.
D. H.	2900	4	600	HB	26.7	7.47	7.44	7.33	7.44	7.46	7.44	28.2	26.5	21.7	32.5	30.0	26.5
D. R.	1850	4	400	HB	20.9	7.32	7.35	7.32	7.49	7.41	—	20.7	23.2	18.2	32.0	28.7	—
P. L.	2100	5	400	HB	28.0	7.24	7.28	7.35	7.40	7.39	7.38	18.4	19.5	21.7	28.2	23.2	22.7
Mean						7.32	7.37	7.32	7.44		7.42	19.3	22.5	21.9	26.5		24.5
Standard deviation ±						0.08	0.07	0.09	0.04		0.06	2.3	3.2	3.6	3.2		3.3

Symbols to Table II.
Columns 1 to 6 as in Table I
I. = Blood pH before infusion
II. = Blood pH after infusion, before exchange transfusion
III. = Blood pH at termination of exchange transfusion
IV. = Blood pH 24 hrs after exchange transfusion
V. = Blood pH 48 hrs after exchange transfusion
VI. = Blood pH 72 hrs after exchange transfusion
i. = Standard bicarbonate (mEq/litre) before infusion
ii. = Standard bicarbonate (mEq/litre) after infusion
iii. = Standard bicarbonate (mEq/litre) after blood exchange
iv. = Standard bicarbonate (mEq/litre) 24 hrs after blood exchange
v. = Standard bicarbonate (mEq/litre) 48 hrs after blood exchange
vi. = Standard bicarbonate (mEq/litre) 72 hrs after blood exchange

favourable effect of alkali treatment on bilirubin transport is a further proof of the necessity of preventing and controlling acidosis. Moderate metabolic alkalosis following exchange transfusion even without alkali pretreatment is, thus, rather beneficial, and it is perhaps also for this reason that blood exchange usually ensures favourable results.

Although the post-exchange alkalosis caused no clinical symptoms in the present series, the fairly regularly observed shift towards the alkaline side shows that alkali pretreatment is not always necessary, and its systematic use in every case must be condemned. It was shown in an earlier paper [2] why the use of other preparations (e.g. heparinized blood) is not advisable. Alkali treatment preceding exchange transfusion is only justified in reliably verified cases of already existing acidosis since even a slight aggravation of this may lead to dangerous situations. Acidosis delays the expected metabolization of citrate, and it is only natural that acidosis lasts longer and is more serious in such cases. The acid-base balance should therefore, be examined before exchange transfusion and bicarbonate should be given if the pH is less than 7.30 and standard bicarbonate below 18.0 mEq/litre. Considering that even without bicarbonate pretreatment, post-exchange acidosis usually ceases after the first day, the acidifying effect of ACD blood might be counteracted in the future by improved methods of transfusion, e. g. by performing it at a slow rate.

Summary

In connection with exchange transfusions performed for different reasons, the acid-base balance has been examined in 84 newborn infants, before, immediately after, and for three days following the intervention.

Forty-six babies were pretreated with 50 ml/kg of 1/6 M sodium bicarbonate. Most infants in need of blood exchange showed signs of metabolic acidosis which was sometimes critically aggravated by the transfused ACD blood. On the other hand, metabolic alkalosis develops as a rule during the days following the intervention. Pretreatment of newborn infants with sodium bicarbonate mitigates acidosis during blood exchange but promotes subsequent alkalosis.

It is therefore suggested that exchange transfusions should be preceded by an examination of the acid-base balance, and sodium bicarbonate infusion should be given if the pH is less than 7.30 and the standard bicarbonate below 18 mEq/litre.

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Prof. D. Boda
Gyermekklinika
Szeged, Hungary