THE COMPARATIVE EFFECTIVENESS OF THREE COMMERCIAL ORAL SOLUTIONS IN CORRECTING FLUID, ELECTROLYTE AND ACID–BASE DISTURBANCES CAUSED BY CALF DIARRHOEA

A. R. MICHELL, H. W. BROOKS, D. G. WHITE and A. J. WAGSTAFF

Department of Large Animal Medicine and Surgery, Royal Veterinary College (University of London), Hawkshead Lane, North Mymms, Hatfield, Herts. AL9 7TA

SUMMARY

Three commercial oral rehydration solutions (Effydral ('E'), Lectade ('L') and Lectade Plus ('LP')) were evaluated in young calves with diarrhoea following the administration of *E. coli*. Twenty calves with non-fatal diarrhoea were included in each group and examined for electrolytes, acidosis (pH, P_{CO_2} and T_{CO_2}), PCV and selected biochemical parameters. Faecal consistency and clinical state were also assessed. Eight calves were examined for plasma and ECF volume. Calves were treated with the appropriate ORS only for 2 days and with ORS plus milk substitute for a further 2 days. No other treatments were given. Solutions E, L and LP were chosen specifically to test the hypothesis that their ability to repair extracellular volume would depend on their sodium content (E>L>LP) and their ability to correct metabolic acidosis would reflect their content of bicarbonate precursor (E>LP>L). Both hypotheses were confirmed as was the fact that the higher sodium content of E helps it to repair ECF volume without predisposing to hypernatraemia. The importance of correcting hyponatraemia as well as ECF volume is emphasized. Direct measurement of such changes proved much more sensitive than traditional clinical parameters such as weight loss, skin elasticity, etc. Although this study was not designed to examine mortality, it is noted that nine treated calves died, none in the E-treated group.

INTRODUCTION

Diarrhoea is common in newborn animals. It has a variety of causes, infective and non-infective, and leads to progressive dehydration, electrolyte loss and metabolic acidosis, which are potentially fatal. A recent study (Groutides & Michell, 1990a) showed that the most important therapeutic targets in reducing mortality due to calf diarrhoea were (1) correction of dehydration, especially the reduction in extracellular fluid volume (ECF) and its associated hyponatraemia; and (2) cor-

rection of metabolic acidosis and its associated hyperkalaemia. Hypoglycaemia did not appear to be an important determinant of mortality.

We therefore investigated the ability of three commercial solutions Effydral (E) (Solvay-Duphar Veterinary), Lectade (L) and Lectade Plus (LP) (SmithKline Beecham) to correct these disturbances under conditions identical to the earlier study. The solutions were selected because they had considerable differences in sodium concentration. Since sodium is the osmotic skeleton of ECF (Michell *et al.*, 1989), it was our view that the ability of these solutions to correct ECF volume would reflect their sodium content. They were also chosen because they differed considerably in their content of bicarbonate precursor and, in particular, one (L) was extremely low in precursor. We therefore doubted its effectiveness in correcting metabolic acidosis except insofar as it improved renal function by repairing ECF volume (plus a minor contribution from the precursor). The solutions, once mixed, had the composition shown in Table I: one of them (E) is about to be marketed, the others (L and LP) are well established.

In view of the rapid proliferation of commercial oral rehydration solutions (ORSs) it is important that clinicians are able to choose between them on the grounds of their demonstrated effectiveness in correcting key pathophysiological disturbances, not just marketing literature or price. Simply recommending 'oral rehydration' in the 1990s is as imprecise as advocating 'antibiotics' in earlier decades (Michell, 1989). Rational therapeutic choices can be made, given the data.

MATERIALS AND METHODS

General design

The basic design of the experiment was as follows. Three treatment groups were formed from calves purchased from their original farms within 24 h of birth and excluding those showing spontaneous diarrhoea following arrival. Diarrhoea was induced using enterotoxigenic *E. coli* as previously described (Groutides &

Table I
Composition of solutions tested (mmol/l)

	L[1]	*LP*[2]	*E*[3]
Na	73	50	120
K	16	20	15
Cl	73	39	55
HCO_3^- precursor[5]	1	29	80
Glucose	114	160	180[4]
Glycine	41	20	30
PO_4	15	5	

[1]L, Lectade (SmithKline Beecham).
[2]LP, Lectade Plus (SmithKline Beecham).
[3]E, Effydral (Solvay-Duphar Veterinary).
[4]Lactose (90 mmol/l≡180 mmol/l glucose).
[5]Citrate: 1 mmol≡3 mmol bicarbonate.
L and LP are presented as sachets of powder for dilution, E as an effervescent tablet.

Michell, 1990a) and each calf was then treated with one of three ORSs. This routine continued throughout the experiment but during phase I calves were used to study changes in fluid spaces and plasma electrolyte concentrations whereas during phase II calves were used to study changes in a range of clinical parameters and biochemical and haematological data. The reason for the separation into two distinct phases was simply a matter of workload; phase I was highly labour-intensive, particularly since samples for the determination of plasma volume could not be stored.

Source of calves studied

Dairy and dairy-cross calves were purchased from their farms of origin within 24 h of birth. They were weighed on arrival (day A) and individually penned on wood chips. The calves were offered warm milk substitute (Volac Easimix) twice daily (08:00 and 16:00), starting on the evening of day A. They were encouraged to drink from the bucket as soon as possible, either with or without a teat.

Calves were observed twice daily at feeding times from the morning of day B and faecal consistency was scored (see below). There was a qualifying period covering three observations. Many calves had transient (once or twice) high scores (3 or 4) as meconium was eliminated and as diet changed to skimmed milk powder but most had normal faeces by the morning of day C. Calves with a cumulative faecal score (FS) above 5 by the morning of day C were withdrawn from the trial.

Induction of diarrhoea

On days C and D, prior to feeding, each qualifying calf was drenched with 4 g of sodium bicarbonate in 60 ml water to overcome the protective effects of abomasal acidity. Calves were then dosed with 10^{10} enterotoxigenic *E. coli* (ETEC) (09:K30:K99) in 10 ml sterile brain/heart infusion broth culture (a modification by Bywater, 1977). Aliquots from stock culture of ETEC were stored at −20°C. These samples were then used to seed 10 ml broth cultures, which were incubated at 39°C for 16 and 24 h respectively.

Formation of treatment groups

On day C, blood samples were taken from calves to obtain baseline values of the plasma parameters to be monitored during treatment and to assess the transfer of colostral immunoglobulin to each calf using the zinc sulphate turbidity (ZST) test (McEwan *et al.*, 1970).

Twice daily faecal scoring continued as described below; treatment began after a total FS of:

- 10 by the afternoon of day D, i.e. third observation after first inoculation; or
- 11 by the morning of day E; or
- 12 by the afternoon of day E; or
- 13 by the morning of day F.

The calves were assigned to three groups (E, L and LP) as they qualified for oral rehydration therapy (ORT) to start. Assignment was initially by random ballot but

as the trial progressed, care was taken to keep the three treatment groups evenly matched for (1) breed, and (2) ZST status.

Treatment with one of the three ORSs (E, L or LP; Table I) started at the afternoon feed after the qualifying faecal score was achieved (the first day of treatment becoming day V for that calf). Milk powder at this, and the next three feeds, was replaced by the relevant ORT dissolved in 2 l lukewarm water. Calves were stomach-tubed if drinking was not voluntary. From the afternoon of day X, the calves were offered 2 l of 50% ORT–milk substitute for four feeds. From the afternoon of day Z the calves returned to milk powder feeds.

Before and during therapy the calves were studied according to the following protocols. Phase I of the trial ended when there were eight calves completing treatment in each group. Phase II continued until 20 calves completed treatment in each group.

Phase I: determination of fluid volumes

Equal volumes of 10% sodium thiocyanate (NaSCN) and 1% Evans blue dye (EB) were mixed and sterilized in 100 ml volumes.

At 14:00 on day C, before the afternoon feed, an i.v. cannula (Critikon IV Cannula, Critikon Ltd, 18G) was inserted into the jugular vein of the calf and a 10 ml heparinized blood sample (Monovette Li-Heparin LH/10, Sarstedt) was collected. Immediately after this a standard 5 ml volume of the NaSCN and EB mixture was given via the cannula. The cannula was flushed two or three times by aspiration and reinjection of blood. A digital stopwatch was started and the cannula was removed.

Sampling. Serial blood samples were taken via single-use hypodermic needles (Monoject, 19G×1 inch) and heparinized syringes (as before) after 15, 30, 60 and 120 min. This procedure was repeated on days V, W, X and Y. Samples were centrifuged (with 1 ml Serasieve; Hughes & Hughes Ltd) at 3500 r.p.m. for 15 min, within 60 min of collection. A single blood sample was taken on day Z to measure plasma sodium concentration; aliquots of plasma were frozen for this.

Analyses. (1) *Plasma volume determination using Evans blue dye method.* The optical density (*D*) of plasma from samples I–IV was read immediately (SP 30 Spectrophotometer, Pye Unicam) against a water blank, at 620 nm. The *D*s were compared with a standard aliquot of the injection solution diluted 1:1000 in 5% albumin, giving a final Evans blue concentration of 5 mg/l.

$$5\ (D\ \text{Unknown}/D\ \text{Standard}) = \text{concentration (mg/l)}$$

The pre-injection concentration was subtracted from each post-injection concentration. From a time versus log concentration plot of these values, the apparent concentration at time of injection was extrapolated and used in the following formula:

$$\text{Plasma volume (l)} = \text{Initial dose (50 mg)} / \text{concentration (mg/l)}$$

(2) *ECF volume using NaSCN method.* A volume of 0.5 ml plasma was mixed with

0.5 ml 20% trichloroacetic acid, the mixture shaken well and centrifuged (3000 r.p.m., 10 min). A sample of 100 μl of the supernatant was mixed with 400 μl of 16% ferric nitrate made up in *N* nitric acid; *D* was read immediately at 460 nm. The procedure was carried out on a Gilford selective batch analyser (SBA 300). The standard and calculations were analagous to those for Evans blue (see above).

Fluid spaces obtained by these techniques are extremely similar in calves to those obtained by the use of radiolabelled sodium or albumin respectively (Wagstaff *et al.*, 1992).

(3) *Plasma sodium and potassium concentration determination.* Concentrations of plasma sodium [Na] and potassium [K] were determined simultaneously with an integrating flame photometer (Radiometer FLM3) using our usual quality controls (Groutides & Michell, 1990a).

Phase II: biochemical and clinical observations

Sampling and data recording. Faecal scores were assessed twice daily as before, using the following classification:

1=Normal
2=Semi-solid
3=Liquid
4=Very liquid and copious.

At the same time, clinical condition was scored as follows:

Demeanour, N (normal), D (dull but standing), R (sternally recumbent), C (comatose/collapsed);
Enophthalmus, N (normal), S (sunken);
Mucous membranes, N (normal), D (dry);
Extremity temperature, W (warm), C (cool), V (very cold);
Skin elasticity, N (rapid return to normal after 'tenting'), S (slow), V (very slow).

The scoring system was specified on all data sheets to maintain consistency and accuracy.

The calves were re-weighed at the end of treatment and 7 days later.

Heparinized blood samples taken anaerobically on days C, V, W, X, Y and Z were placed on ice until they reached the laboratory (within 1 h) for analysis (pH, Pco_2, Tco_2, Corning 158 Blood Gas Analyser; PVC, microhaematocrit centrifuge). Plasma was separated as in phase I and stored deep frozen (–20°C). A sample of 1 ml whole blood was added to sodium fluoride, centrifuged and stored for glucose analysis.

Analyses and statistical evaluations. Measurement of ZST, Na and K was undertaken as in phase I. The following analysis was carried out on a Gilford selective batch analyser (SBA 300): total protein (biuret), albumin (bromcresol green), calcium (cresolphthalein), magnesium (calmagnite), phosphorus (molybdate), urea (urease, GLDH kinetic), creatinine (Jaffe), glucose (GDH).

The plasma parameters and fluid spaces were subjected to statistical analysis (Student's *t*-test) using mean absolute values between treatment groups (E versus

L; L versus LP; E versus LP). Means of individual changes from prediarrhoeic (day C) samples and of individual changes from pretreatment (day V) samples were also compared (paired t-test). In addition, the ECF volume data were also evaluated by analysis of covariance. The weight gains or losses for each ORS group during the treatment period of 7 days post-treatment were also compared. The frequency of each grade of the various clinical observations for treatment groups E, L and LP was tabulated for days V–Z (see Table II) and subjected to the chi-squared test. In all cases results were regarded as statistically nonsignificant between treatments.

RESULTS

In examining the results, we lay greatest emphasis on the changes detected by sample day X, i.e. the last sample before the partial reintroduction of milk replacer. The reason is twofold: (1) changes only evident after this cannot be attributed specifically to the ORS; (2) changes beyond this point would be affected by the nature of the milk replacer, as well as the ORS, in any other calves, whether experimental or clinical. Any disparity between results at this point (2 days of

Table II
Clinical parameter scores

	E						*LP*						*L*				
	V	*W*	*X*	*Y*	*Z*		*V*	*W*	*X*	*Y*	*Z*		*V*	*W*	*X*	*Y*	*Z*
Demeanour																	
N	10	15	18	17	20	N	15	15	20	19	19	N	9	17	19	19	20
D	6	5	1	3	0	D	3	4	0	1	1	D	7	2	1	1	0
R	4	0	1	0	0	R	2	1	0	0	0	R	4	1	0	0	0
C	0	0	0	0	0	C	0	0	0	0	0	C	0	0	0	0	0
Enopthalmus																	
N	16	19	19	20	19	N	16	17	19	19	19	N	16	17	20	20	20
S	4	1	1	0	1	S	4	3	1	1	1	S	4	3	0	0	0
Mucous membranes—dryness																	
N	11	17	17	19	19	N	14	15	19	19	18	N	11	16	19	20	20
D	9	3	3	1	1	D	6	5	1	1	2	D	9	4	1	0	0
Extremity temperature																	
W	14	16	16	16	20	W	13	13	18	19	20	W	15	16	18	18	20
C	6	4	4	4	0	C	7	7	2	1	0	C	5	4	2	2	0
V	0	0	0	0	0	V	0	0	0	0	0	V	0	0	0	0	0
Skin elasticity																	
N	10	15	17	19	19	N	12	14	18	17	19	N	11	14	17	20	19
S	9	5	3	1	1	S	8	6	2	3	1	S	9	6	3	0	1
V	1	0	0	0	0	V	0	0	0	0	0	V	0	0	0	0	0
Faecal score																	
1	0	3	4	6	5	1	0	1	3	7	8	1	0	0	3	8	8
2	2	6	9	5	7	2	0	4	10	8	6	2	4	10	7	6	5
3	10	10	6	8	7	3	12	12	7	5	5	3	7	8	10	5	7
4	8	1	1	1	1	4	8	3	0	0	1	4	9	2	0	1	0

See text for definition of symbols.

treatment) and completion (4 days of treatment, two of them with 50:50 ORS+milk replacer) is, however, noted.

All data were initially checked to confirm that statistically significant differences were absent before the onset of diarrhoea, i.e. that the allocation of calves produced uniform groups. Statistically significant differences between groups did not appear until after the start of treatment, although inevitably not all changes were identical in all groups before treatment, e.g. group LP had the greatest fall in ECF and plasma volume.

Fluid spaces, electrolytes and acid–base

These are the crucial changes since most of the other systemic effects either of the disease or the ORS are secondary to them.

The only solution to improve ECF volume before reintroduction of milk replacer was E (Fig. 1) and analysis of covariance showed that the advantage over LP was statistically significant ($P<0.01$). On the other hand, the best improvement in circulating volume was with LP (Fig. 2), thus during the 48 h of treatment with ORS alone, LP raised plasma volume by 0.25±0.09 l, whereas with L it fell by 0.14± 0.11 l; this difference was significant. None of the solutions fully restored either fluid compartment within 4 days.

In order to compare the effects in calves with more severe volume depletion, those with a fall in plasma volume or ECF exceeding 0.25 or 0.5 l respectively were selected. This comprised about half the E and L calves but all the LP calves. These changes (Table III) show that only E improved ECF in 48 h (mean±SEM 0.4±0.4 l)

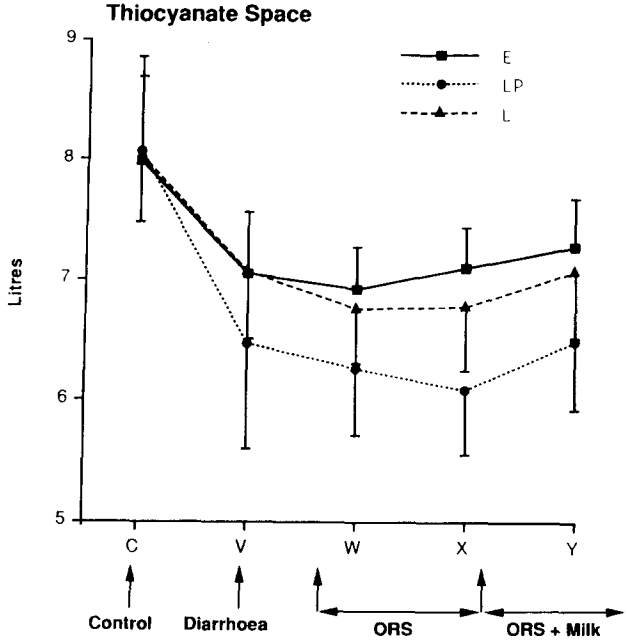

Fig. 1. ECF volume (thiocyanate space) before induction of diarrhoea (day C), after onset of diarrhoea (pretreatment: day V) and during treatment with ORS (days W, X, Y); means±SEM for 8 calves. Solutions E, LP and L as in Table I.

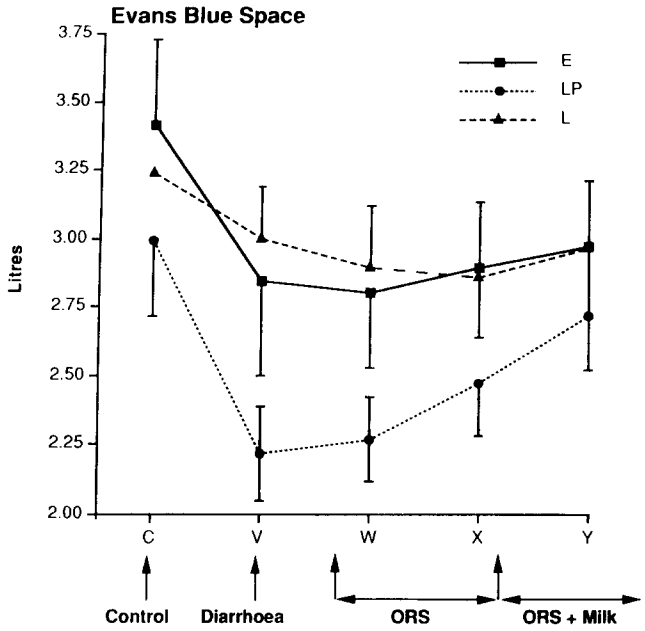

Fig. 2. Plasma volume (Evans blue space): other details as Fig. 1.

Table III
Changes in fluid compartments during the first 48 hours of therapy in calves with more severe depletion (exceeding 0.25 l plasma, 0.5 l ECF)

	Increase in volume (l)	
	ECF	*Plasma*
E	+0.41±0.39	+0.33±0.08
LP	−0.39±0.44	+0.31±0.08
L	−0.13±0.43	+0.15±0.02

whereas it remained depressed in L and LP treated calves (by 0.1±0.4 and 0.4± 0.4 l). With such small numbers these differences are statistically insignificant but for a 37.3 kg calf with 250 ml/kg of ECF, the difference between losing or gaining 0.4 l is close to 9% of ECF volume. The plasma volume in calves with severe volume depletion improved least with solution L (0.15±0.02 l) and most with E (0.33 ±0.08 l) and LP (0.31±0.08 l). The most consistent difference, therefore, at 48 h was the ability of E to correct ECF volume, even in the more severely dehydrated calves.

The changes in plasma sodium are shown in Fig. 3. The highest sodium concentration recorded in the control readings (prediarrhoea) was 144 mmol/l and the only higher reading in a diarrhoeic calf (145 mmol/l) occurred prior to therapy; there was thus no evidence of hypernatraemia. Diarrhoea caused hyponatraemia (plasma sodium below 130 mmol/l) in about 15% of each group: during treat-

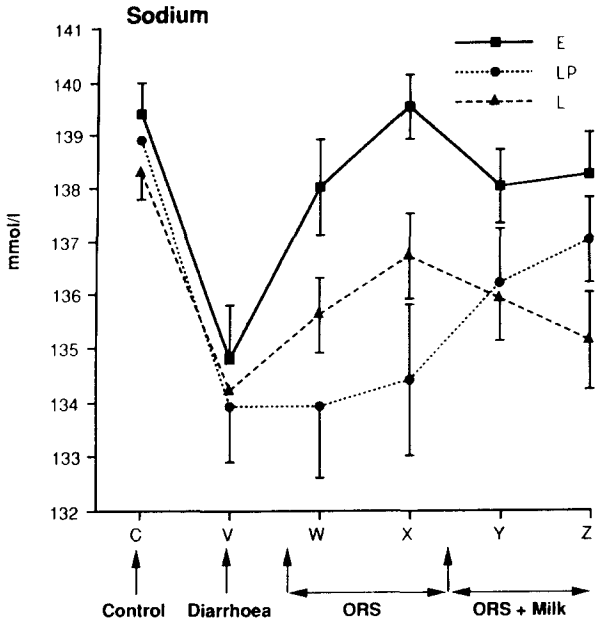

Fig. 3. Plasma sodium concentration: other details as Fig. 1 but treatment extends to day 2 of ORS+milk replacer. Means±SEM for 20 calves.

ment the percentage fell to 0 with E, 5% with L and with LP it rose to 30%. Within 48 h, E (unlike L or LP) had restored plasma sodium concentration; the difference from L or LP is statistically significant ($P<0.01$). All the solutions improved the hyperkalaemia caused by the diarrhoea (Fig. 4) and there was little to choose between them.

The difference between solutions in improving acidosis was, however, obvious (Figs 5 and 6). After 48 h, plasma bicarbonate (Tco_2) had virtually returned to normal with E whereas the rise with LP was only about 40% as great (from 27.8 to 30.8 mmol/l) and with L, Tco_2 had actually fallen during the first 48 h of treatment (30.1 to 29.0 mmol/l). The difference between Tco_2 with solution E at 48 h and with other solutions was statistically significant in both cases ($P<0.001$). Very similar trends are reflected in pH and again the differences between E and other solutions are statistically significant (P 0.01 versus LP, 0.001 versus L), bearing in mind the limitations of such comparisons with logarithmic data.

The measurements of ECF space and plasma Na allow extracellular sodium (mmol) to be calculated (Table IV). In the 48 h when ORS was the sole fluid, only E increased ECF Na (by 4%). With L and LP it remained below the level at onset of diarrhoea (by 2% and 6%). The average fall in ECF Na caused by diarrhoea prior to treatment was 17% but it was greatest (23%) in the group subsequently receiving LP.

Changes associated with dehydration

PCV increased sharply with diarrhoea (Fig. 7a) and only recovered partially dur-

ing treatment. Changes in albumin concentration (Fig. 7b) were essentially similar but less marked and with recovery by the second (L) or fourth day of treatment (LP and E). Total protein, on the other hand, did not reflect changes in hydration and fell throughout the experiment with all three solutions (as it does during untreated diarrhoea; Groutides & Michell, 1990a). PCV was thus the best reflection of the underlying changes in ECF volume.

Urea and creatinine concentration both rose during dehydration (Fig 8a,b) with urea increasing more, as expected with pre-renal failure (Groutides & Michell, 1990a). During the first 48 h, LP and L clearly reduced urea and LP had the greatest effect on creatinine; E did not reduce either until mixed with milk replacer.

Other plasma changes

Plasma glucose concentration fell from 6.7 to 5.1 mmol/l with the onset of diarrhoea; the nadir was after 24 h of treatment (4.4 mmol/l) but by 48 h recovery had started with glucose concentration significantly higher ($P<0.05$) in calves treated with LP than those treated with E or L (5.2±0.3 mmol/l, versus 4.5±0.2, 4.3±0.2 mmol/l). During the first 48 h of treatment, however, the change in glucose concentration was not significantly different in all three groups (−0.31±0.45, −0.35±0.24, −0.61±0.29 mmol/l). The effect of diarrhoea on inorganic phosphate was variable, thus the effect of treatment was difficult to assess: however, plasma phosphate fell during treatment in most calves. Plasma calcium concentration fell during diarrhoea (from 2.7 to 2.5 mmol/l) and the fall continued during the first

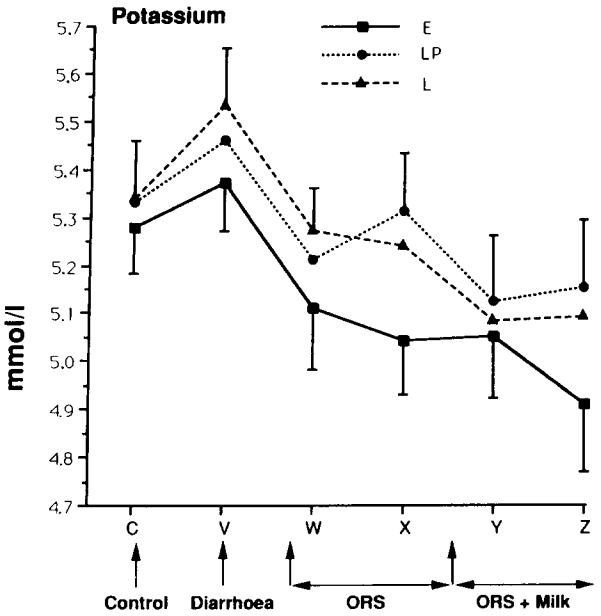

Fig. 4. Plasma potassium concentration: other details as Fig. 3.

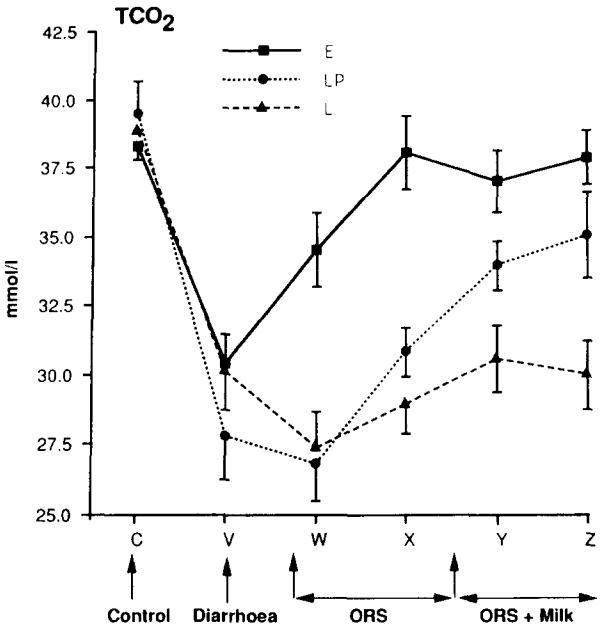

Fig. 5. Total CO_2 concentration (an index of plasma bicarbonate): other details as Fig. 3.

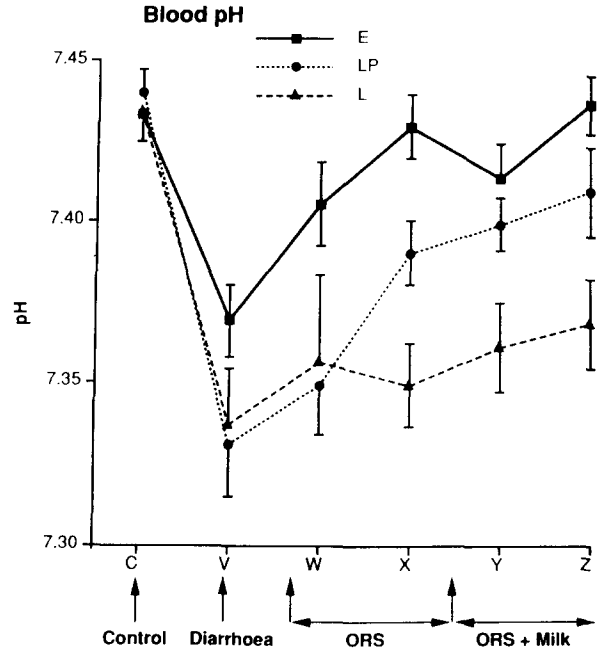

Fig. 6. Blood pH: other details as Fig. 3.

Table IV
Changes in total extracellular sodium produced by combined effects of changes in ECF volume and plasma sodium concentration

	Extracellular sodium (mmol)		
	E	*LP*	*L*
Prediarrhoea	1112	1121	1112
Pretreatment	949	865	946
48-h treatment	989	816	925

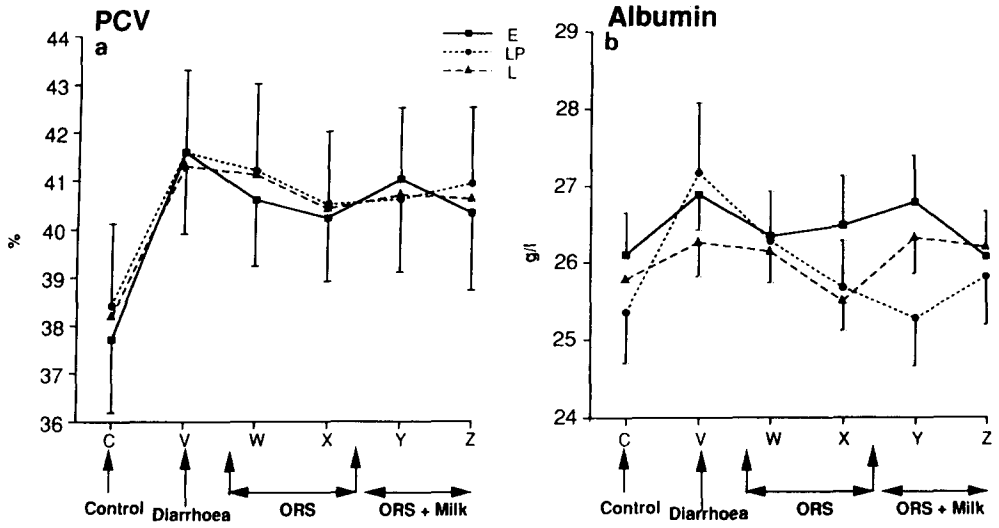

Fig. 7. Haematocrit (PCV) (a) and plasma albumin (b) concentration: other details as Fig. 3.

48 h of treatment (to 2.3 mmol/l) but improved with reintroduction of milk replacer. Magnesium changed little during diarrhoea but fell substantially during 48 h of ORS (from 0.95 to 0.82 mmol/l) with recovery beginning in most calves when milk replacer was reintroduced.

Direct observation of the calves

The initial weights of all three groups of calves were very similar (E 37.4±1.7 kg; LP 36.8±2.3, L 37.5±2.3). At the start of treatment, only 17% of calves were recumbent and 57% were normal in demeanour. Only 20% had sunken eyes, 30% cold extremities, 40% dry mucous membranes and 45% reduced skin elasticity. These all suggest weight losses in the range 5–10% (Michell *et al.*, 1989; Tremblay, 1990). Indeed, Groutides & Michell (1990a), using the same calf model, showed that even in dying calves, average weight loss was only 13%, sometimes as little as 6%. With calves in which the diarrhoea was more severe at the start of treatment (Groutides & Michell, 1990b), i.e. the PCV had risen by more than 5 and the pH had fallen below 7.3, weight loss was only 5%.

By the end of treatment, L-treated calves were still 4.2% below their initial body

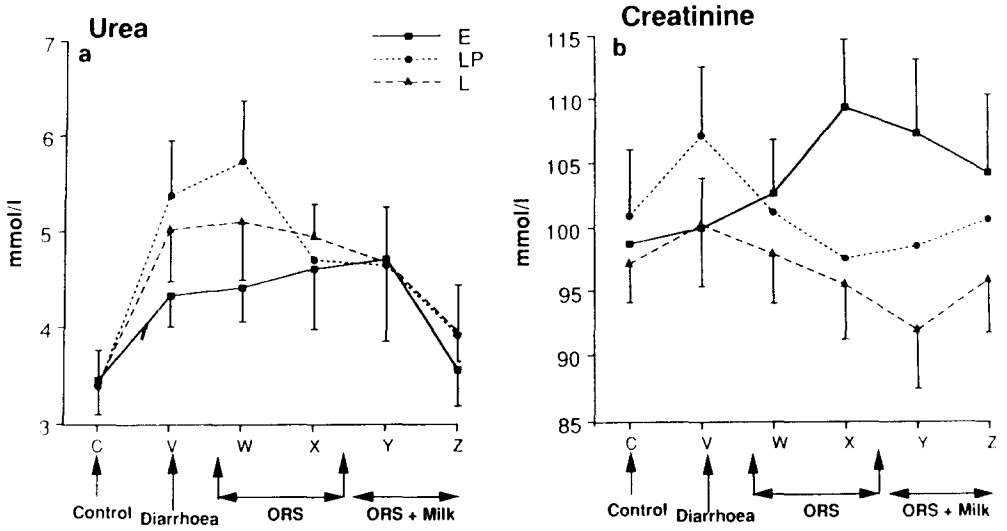

Fig. 8. Plasma urea (a) and creatinine (b) concentration: other details as Fig. 3.

weight, E-treated calves 1.7%, but LP-treated calves regained their initial weight (0.5% above). A week after the end of treatment, both E- and LP-treated calves gained 0.4±0.4, 0.1±0.4 kg compared with the end of treatment and were within 0.3±0.6 kg of their prediarrhoeic weight. L-treated calves remained within 0.2 kg of their weight at the end of treatment and 1.7±0.7 kg below their prediarrhoeic weight. Clinical criteria (demeanour, enophthalmus, mucous membrane dryness, extremity temperature, skin elasticity and faecal score) all improved during therapy without differences between solutions. Thus at the start of treatment, 90% of calves had faecal scores of 3–4 whereas by the last day this had fallen to 35%.

The data only concern calves surviving to the end of treatment and dying calves were replaced; it is noted that apart from eight calves completing the fluid space measurements in each group and 20 completing the entire experiment in each group, nine calves died after treatment began, none in the E-treated group.

The main changes are summarized in Table V.

DISCUSSION

Among the essential attributes of an ORS (Michell, 1988, 1989), it should yield sufficient bicarbonate to correct acidosis and sufficient sodium, at an appropriate ratio to glucose, to be absorbed, along with water, and thus improve ECF volume. The importance of these attributes is amply borne out in these results; the ability to repair acidosis and ECF volume reflects the concentration of precursor and sodium in the three solutions. Thus L was least able to repair acidosis, LP to repair ECF volume and E was best able to repair both.

L, and especially LP, were both below the sodium concentration of the solution which became the prototype for oral rehydration therapy, notably the WHO

Table V
Summary of results

	Lectade	*Lectade Plus*	*Effydral*
Restoration of ECF volume	Poor	Poor**	Good**
Restoration of plasma volume	Poor*	Good*	Fair
Correction of hyponatraemia	Poor**	Poor**	Good**
Correction of acidosis	Poor***	Fair***	Good***
Restoration of PCV	Good	Good	Good
Correction of uraemia	Fair	Good	Poor
Restoration of blood glucose	Poor*	Good*	Poor*
Restoration of body weight	Poor	Good	Fair

Eight calves per group were used to assess restoration of fluid volume, 20 calves per group were used to assess other changes.
*Significantly different at $P<0.05$.
**Significantly different at $P<0.01$.
***Significantly different at $P<0.001$.

solution for the treatment of cholera (Michell, 1988); E, in contrast, contained more. Its performance reinforces the view (Michell, 1988, 1989) that within a suitable range, the higher the sodium content of an ORS, the more likely it is to correct ECF volume; hypernatraemia is a problem caused by water loss, perhaps secondary to the addition of excess sugar to an ORS (Michell, 1988) rather than an excessive sodium content.

Perhaps the most important conclusion to emerge from this study is that practitioners are unlikely to be able to evaluate such solutions satisfactorily for themselves. Even if they have large groups of calves with comparable diarrhoea, traditional criteria such as weight loss and skin elasticity give little guidance in comparing solutions, all of which are likely to be effective, but not equally effective. Direct assessment of the improvements in ECF volume, pH and electrolytes is essential. This is clearly illustrated by the fact that by the time treatment began, both ECF and plasma volume were about 15% down, yet body weight had probably changed by less than 10%. This is not surprising since (1) excess fluid pooled within the gut does not yet reduce body weight but does reduce ECF volume, and (2) the dilution of ECF revealed by hyponatraemia implies that intracellular fluid is equally diluted, i.e. by further subtraction of fluid from ECF (Michell *et al.*, 1989).

The latter point is extremely important. Hyponatraemia to the extent of 5 mmol/l may be statistically significant but remains within the normal range and certainly is only about a third of the fall likely to cause neurological symptoms. Nevertheless, the dilution of intracellular fluid required to allow ECF sodium con-

centration to fall from 138.9 to 134.3 mmol/l is approximately 8.7 ml/250 ml. Since ECF volume is 250 ml/kg and total ICF volume is probably around 400 ml/kg, dilution of intracellular fluid would require 14 ml/250 ml of ECF. This would therefore, in itself, diminish ECF volume, in the absence of external losses, by 510 ml, about 45% of the observed fall in ECF volume prior to therapy. The benefit of improving plasma sodium with ORSs, therefore, is not simply the effect on hyponatraemia which may appear modest, but the substantial gain in ECF volume when restoration of a normal sodium concentration allows water to return to ECF from cells.

In its effect on renal function, as far as this is indirectly indicated by measurements of plasma urea and creatinine, rather than clearance, LP was the best solution. Paradoxically (in view of its effect on ECF volume), it also had the best effect on plasma volume but was no better than E in calves with severe dehydration. It was, however, less effective than L or E in restoring ECF volume and in this respect, and its ability to correct acidosis, E was superior to both L and LP; L had the least effect on acidosis, as anticipated from its composition.

None of the solutions prevented a fall in both calcium and magnesium during the first 48 h of therapy, recovery occurring with admixture of milk replacer. Perhaps the divalent cation content deserves more attention in the design of an ORS for diarrhoeic calves.

It should be noted that by chance the calves treated with LP were those with the greatest fall in ECF and plasma volume prior to treatment; those subsequently treated with L had the least prior fall in plasma volume. Although this study was not designed to examine mortality (which would require larger groups) it is also worth noting that nine treated calves died, none in the E-treated group.

In conclusion, E was the most and LP the least effective solution in correcting ECF volume and sodium concentration; E was also the most and L the least effective solution in correcting acidosis. This was consistent with their compositions, i.e. with sodium concentrations of 120, 73, 50 mmol/l (E, L, LP) and with bicarbonate or precursor concentrations (expressed as mmol/l bicarbonate or potential bicarbonate) of 80, 1, 29 respectively. Veterinary surgeons should examine critically the final composition (i.e. received by the calf) of oral rehydration solutions which they intend to use or advocate.

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