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Reducing the risk of harm in fluids prescribing: is 0.9% sodium chloride with dextrose superior to 0.45% sodium chloride with dextrose for maintenance? An audit of electrolytes in children following appendicectomy.

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Summary

We retrospectively audited serum electrolytes in a series of children (n=110) whose maintenance fluids were subject to one of two institutional written protocols – the first predominantly featured 0.45% saline with 2.5% glucose and the second was based on 0.9% saline with 5% glucose in line with regional guidance. Both solutions caused a progressive decrease in both urea and potassium. About one quarter of patients subject to the first protocol were hyponatraemic after 36 hours, compared with 4% in the second group. However the majority of those subjected to the second protocol became hyperchloraemiac by the same time. We conclude that neither protocol provided ideal biochemical homeostasis for reasons of continuing hyponatraemia with the 0.45% saline group and the development of hyperchloraemia in a majority of patients receiving 0.9% saline.

There is consensus that the unmonitored use of hyponatraemic maintenance fluids (such as 0.18% sodium chloride with glucose 4%) contributed to hyponatraemia and may have caused deaths. Despite this a recent Association of Paediatric Anaesthetists (APA) survey found that hyponatraemic solutions were still favoured for maintenance by many anaesthetists prescribing for children and that few institutions had developed policy in this area (1).

0.45% sodium chloride with 2.5% glucose became a popular maintenance option in many hospitals caring for children, on the assumption that it would reduce the risk of hyponatraemia associated with 0.18% saline and glucose 4%. Department of Health guidance in Northern Ireland went further still, recommending 0.9% sodium chloride with 5% glucose for use in conditions associated with hyponatraemia (2) and the National Patient Safety Agency (NPSA) guide template reinforces this (3). There remains concern that so much fluids prescribing remains in the realm of custom and practice rather than evidence based practice (4).

Until now 0.9% sodium chloride with 5% glucose has seldom been used for maintenance, but it is licensed, it contains glucose and it would seem unlikely that it could worsen

hyponatraemia. It is by no means an uncontroversial choice; saline at this strength has been shown to be superior to hypotonic saline with dextrose for rehydrating children with gastroenteritis (5) but it has been shown to induce nausea when given by bolus, possibly by induction of hyperchloraemic acidosis (6) and solutions containing 4% glucose have been associated with hyperglycaemia (7).

Following a fatal case of hyponatraemic encephalopathy in our institution, we introduced a written perioperative protocol governing the availability of IV fluid preparations, maintenance rates of administration and serum electrolyte monitoring. Consequently no child in our care may be prescribed intravenous maintenance therapy without prospective 12 hourly electrolyte sampling and adherence to a written policy governing their fluid choice and rate of administration and electrolyte data is continuously monitored by the trust's risk management department. The policy was modified in line with guidance issued in 2006 recommending 0.9% saline with 5% glucose for patients at risk of hyponatraemia.

Aims

This audit aims to assess and compare the effectiveness of two perioperative maintenance fluids protocols in children undergoing appendicectomy, one of many clinical scenarios associated with hyponatraemia (8).

Methods

We retrospectively reviewed data for 110 children consecutively undergoing unscheduled appendicectomy in our institution over a period of two years. For the first twelve months, 57 children had been prescribed maintenance fluids according to a protocol whose major element was 0.45% saline with 2.5% glucose (Protocol H, Appendix 1). Similarly we analysed data for the 53 comparable cases over the following year. These had all received maintenance fluids as per a protocol based on 0.9% saline with 5% glucose (Protocol N, Appendix 2).

Inclusion criteria for review were that children were previously healthy; aged between their 2nd and 14th birthdays; that there was compliance with the fluid protocol pertinent to their time of admission (Protocol H or N); that maintenance fluids were prescribed for at least twelve hours; that surgery was straightforward and additional fluids (resuscitation boluses and replacement prescriptions) had not been not required.

Protocol H (Appendix 1) involved prescribing maintenance fluids at a rate (standard maintenance rate, SMR) determined by the 4,2,1 rule. Initially all children were maintained on 0.45% saline with 2.5% glucose. For 24 hours post operatively the choice of maintenance solution was dictated by the serum sodium such that 0.45% saline with glucose was administered to all children whose serum sodium was greater than 136 mmol/L. Subjects whose initial serum sodium was 135 mmol/L or lower were prescribed Hartmann's solution for twelve hours. All subjects had electrolyte sampling repeated

twelve hourly prior to further prescribing. After the initial post operative 24 hours children were maintained with only 0.45% saline with 2.5% glucose as before.

Protocol N (Appendix 2) involved prescribing 0.9% saline at a rate determined by serum sodium so that patients whose serum sodium exceeded 132 mmol/L received 0.9% saline with 5% glucose at SMR or 70% SMR for those whose serum sodium was 131 mmol/L or lower. Electrolytes were sampled twelve hourly as before. Unlike Protocol H, this protocol covered the entire time from admission to discontinuance of fluids, so that 0.9% saline with 5% glucose was the only maintenance solution used.

No account was taken of intraoperative administration of fluids because Hartmann's solution had been administered intraoperatively as per in our institutional operating department policy, and this was unchanged for both years.

Electrolyte results were obtained for each subject at presentation and for twelve hourly time periods whilst receiving maintenance fluids. An initial sample taken prior to the administration of any fluids was recorded together with all subsequent samples at approximately 12 hourly intervals up to a maximum of 48 hours. The data were entered into a spreadsheet (Microsoft Excel) for interpretation and comparison.

Values were recorded for major ion concentrations (sodium, chloride, potassium and urea) and glucose. We tabulated mean values, maximum and minimum values, interquartile ranges, and percentage of patients above and below their reference ranges.

Results

The data obtained are shown in Tables 1 and 2. Mean age and gender mix in both groups were broadly similar. 68.8% of patients in the first group (Protocol H) had histologically inflamed appendixes, compared with 66% of appendixes in the Protocol N group. Only 9 of the original 53 patients in group N remained on maintenance fluids forty eight hours after their commencement, compared with 22 of 53 in protocol H.

High levels of biochemical hyponatraemia were observed at presentation, before the administration of any fluid. At 21.1% this was more prevalent in Protocol H than the 13.2% in Protocol N, despite similar mean values (137 mmol/L versus 136.6 mmol/L repectively) and ranges (130 – 142 mmol/L, Protocol H versus 130 – 140 mmol/L Protocol N).

Of the twelve Protocol H patients who were hyponatraemic initially, eleven were hyponatraemic at twelve hours and nine were hyponatraemic at 24 hours, and all of those had sodiums which were the same or lower than at the start of their maintenance period. Five patients with previously normal sodium, became hyponatreamic. Overall the trend in mean sodium decreased across the 48 hour period. The lowest sodium values were found in Protocol H patients (figure 2).

Progressively fewer subjects maintained with Protocol N became hyponatraemic so that none (of 9) were hyponatraemic at 48 hours (Figure 1). By contrast, 27% (6 of 22) of Protocol H patients remained hyponatraemic by 48 hours and 3 of these were more hyponatraemic than when previously sampled.

We found no explanation for the higher proportion of children who were hyponatraemic in the Protocol H group at presentation. It was noted that sodium means, proportion with inflamed appendixes and demographic data were broadly similar in both groups. This may be a function of small study size or the heterogeneity of this population. We found no signs that initial samples were taken after fluids started.

There was an increase in serum chloride over time in subjects maintained in Protocol N patients. By the fourth sampling interval 56% (15 of 27) were biochemically hyperchloraemic with a discernible increase in the mean of and a peak values of (highest 113 mmol/L). This compared with 5.7% in Protocol H with a peak chloride of 109 mmol/L (Figures 3 & 4).

There was a downward trend in potassium in both groups. Mean levels were comparable under each protocol but the lowest values were recorded in Protocol H at the 36 hour and 48 hour samples. No patients received parenteral supplementary potassium.

Mean glucose levels ranged from 5.2 mmol/L to 5.5 mmol/L in Protocol H, and 5.2 mmol/L to 5.9 mmol/L in Protocol N. Between 4% and 9% of Protocol H Patients were hypoglycaemic (compared with between 2% and 6%, Protocol N). Protocol N had greater numbers of hyperglycaemic patients (8% to 21% compared with between 7% and 11.4% in Protocol H). There was greater variation in glucose values in Protocol H patients (Figure 5).

Discussion

The current regional recommendation of 0.9% saline with glucose 5% for patients at risk of hyponatraemia (9) owes much to the fact that it is a one of a few glucose-containing saline preparations unlikely to worsen hyponatraemia (3). In fact, one of the working group's recommendations, Hartmann's Solution with pre-added glucose, was rejected because it does not have a UK license.

As much of the guidance in this area focuses on the potential for maintenance regimes to worsen or cause hyponatraemia, the NPSA material published in March 2007 ("Alert 22 Reducing the risk of harm when administering intravenous fluids to children") similarly featured 0.9% saline with dextrose 5% prominently. Any concerns expressed about 0.9% saline have been in the setting of large volumes and bolus use (6), rather than as a maintenance fluid, where presumably fewer problems were anticipated.

From the results of this audit together with other published data, we consider 0.45% saline with 2.5% dextrose to be an unsafe maintenance fluid owing to the continuing high incidence of hyponatraemia. Our data suggests also that those patients maintained with it required maintenance fluids for longer. At least one systematic review has already called into question the widespread use of dilute solutions like this in paediatric practice (10). Taking all these things together, surely the popularity of this solution is an area for concern?

0.9% saline with dextrose 5% appeared to effectively eliminate hyponatraemia in our patients, and this much is reassuring. This was to be expected given that a controlled randomised study had already demonstrated its benefits with relation to natraemic status (5). However it was surprising that so many patients maintained on 0.9% sodium chloride with 5% glucose became hyperchloraemic.

Even allowing for the small size of this audit, the finding that over half of patients were biochemically hyperchloraemic within 36 hours concerns us sufficiently that we are reconsidering the routine use of 0.9% saline with 5% glucose also. The fact that hyperchloraemia appears to have been well tolerated is not reassuring – after all hyponatraemia was widely considered tolerable for some years.

While there may be debate about the exact nature of hyperchloraemic acidosis (11), it makes sense that it should probably be avoided. Several groups have examined the effects of intravenous 0.9% sodium choride compared with crystalloids such as Plasmalyte 148 and Hartmann's solution (12-14). All of these have indicated that 0.9% sodium chloride strongly promotes hyperchloraemic acidosis and that this in turn has been associated with important clinical effects such as reduced splanchnic perfusion and reduced renal function (15).

Concerns that hypertonic solutions could have a detrimental effect on hydration, were not upheld by our findings. These data suggest that 0.9% saline with 5% glucose, a hypertonic preparation, provided hydration comparable to that achieved with a solution of

half its tonicity. Indeed if serum urea can be taken as a guide to hydration, it would appear that the established "4,2,1" method (16) which is widely used may well provide a minor degree of over-hydration.

It had been reported that solutions containing 4% glucose were associated with hyperglycaemia (5) so it was unsurprising that 5% glucose seemed to bring some recipients into double figures. It has been shown that as little as 0.9% glucose may be sufficient to prevent ketosis and hypoglycaemia (17). Considering the relative proportions of patients in either group developing either hypoglycaemia or hyperglycaemia, then it would appear from this study that for our purposes the ideal glucose concentration may be somewhere between 2.5% and 5%.

Electrolyte behaviour in this audit appears to have been predictable with respect to fluids administered, and this is consistent with the published literature. Therefore we have already implemented a hospital protocol based on Hartmann's solution with pre-added 3% dextrose for these patients, and we have made our data available to the relevant authorities. We feel strongly that a glucose-containing alternative should be included when the guidance is next reviewed and this should not be limited only to licensed products.

There will not be a single solution for all patients in every circumstance. Clearly a more holistic approach needs to be fostered if we are to avoid replacing one problem with another and this means a wider consideration of "isoplasmic" solutions rather than a reflex action dictated by the last major problem. As large randomized trials are not anticipated in this field, it would seem that there is now a need for regional or national audits in developing coherent practice in fluids prescribing for children.

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Table 1 Gender, age and diagnoses per group.

	% Male	Mean age (IQR)	Youngest	Oldest	Acute appendicitis	No (t = 0hrs)	No (t= 48hrs)
Protocol H	56%	10y 1m (4y 9m)	2y 11m	13y 10m	68.8%	57	22
Protocol N	64%	10y 9m (2y 9m)	3y 4m	13y 11m	66.0%	53	9

Table 2.
Electrolyte profiles of patients form Protocol N and Protocol H.

Protocol		N	H	N	H	N	H	N	H	N	H
Time (hours)		0		12		24		36		48	
Number in group		53	57	52	50	44	46	27	35	9	22
Sodium (135 – 145 mmol/L)	means	137	136.6	138.2	135.6	138.8	135.5	139.0	136.0	139.1	135.4
	IQR	3.0	2.8	3.0	3.0	2.8	4.3	2.8	3.5	2.8	2.8
	% < 135mmol/L	13.2	21.1	9.6	32.0	4.5	28.3	3.7	25.7	0.0	27.3
	Highest	140	142	143	141	144	140	144	141	143	140
	Lowest	130.0	130.0	133.0	130.0	131.0	129.0	131.0	130.0	135.0	129.0
Potassium (3.5-5.1 mmol/L)	means	4.0	4.0	3.9	4.0	3.8	3.9	3.7	3.8	3.6	3.8
	IQR	0.5	0.4	1.3	1.0	0.4	0.4	0.3	0.5	0.3	0.4
	Highest	5.3	5.8	5.1	4.8	4.7	5.1	4.7	4.9	4.4	5.0
	Lowest	3.1	3.2	3.4	3.1	3.1	3.3	3.1	3.2	3.3	3.0
	% below	5.7	5.3	1.9	4.1	14.0	11.4	33.3	13.6	33.3	13.3
Chloride (94-110 mmol/L)	means	104.0	103.3	106.5	103.6	107.5	103.8	107.7	103.7	106.8	103.4
	IQR	3.3	5.0	3.0	3.0	4.0	4.0	4.0	3.5	4.0	3.5
	Highest	110.0	109.0	114.0	109.0	112.0	110.0	114.0	108.0	113.0	108.0
	Lowest	94.0	95.0	100.0	98.0	100.0	99.0	100.0	98.0	102.0	97.0
	% high	9.4	0.0	34.6	8.0	54.5	10.9	55.6	5.7	55.6	9.1
Urea (2.5-6.4 mmol/L)	means	4.2	5.7	3.9	4.0	3.5	3.8	3.2	3.7	3.0	3.6
	IQR	1.2	1.6	2.0	1.7	1.9	1.3	1.7	1.3	1.6	1.6
	Highest	8.3	104.0	6.2	10.5	7.0	9.8	5.4	9.1	4.6	9.4
	Lowest	2.4	1.7	2.0	1.7	1.9	1.3	1.7	1.3	1.6	1.6
Glucose (3.9-6.7 mmol/L)	means	5.3	5.2	5.9	5.4	5.8	5.2	5.3	5.4	5.5	5.5
	IQR	1.3	1.0	1.5	1.2	1.3	1.2	1.5	1.2	1.0	1.2
	% High	9.6	7.0	21.2	10.0	20.5	6.5	7.7	11.4	11.1	9.1
	% Low	5.7	7.0	1.9	4.0	4.5	8.7	3.8	11.4	0.0	9.1
	Highest	8.8	8.0	10.3	8.7	10.2	9.7	7.8	8.7	7.9	11.0
	Lowest	2.7	3.5	3.7	3.3	3.7	3.0	3.7	3.4	2.0	3.6

Figure 1 Percentage of patients hyponatraemic.

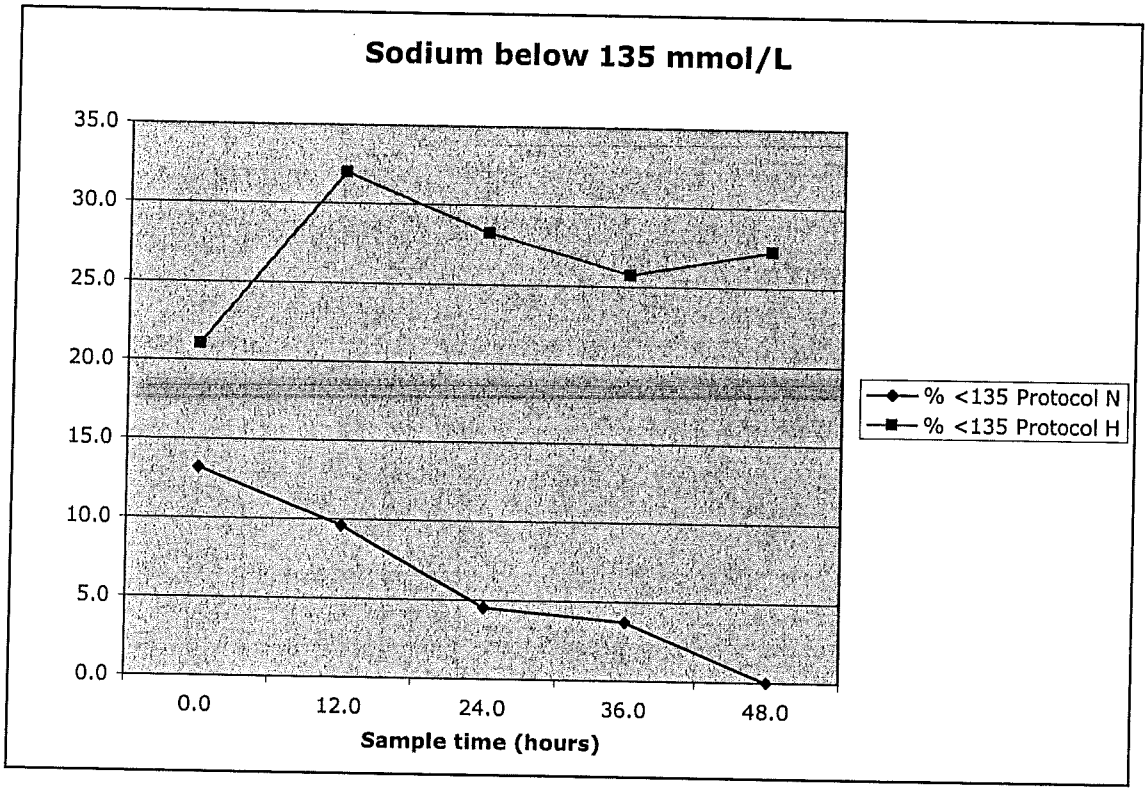


Figure 2 Serum sodium (means & troughs) measured in each protocol.

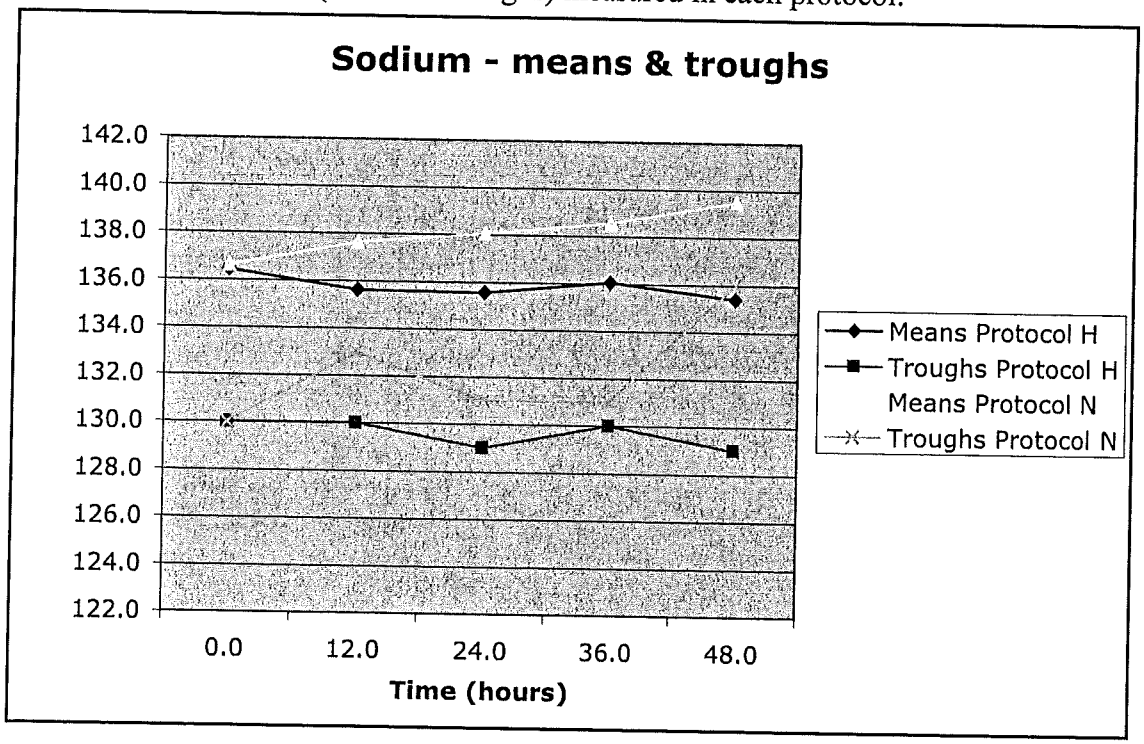


Figure 3. Percentages of patients developing hyperchloraemia.

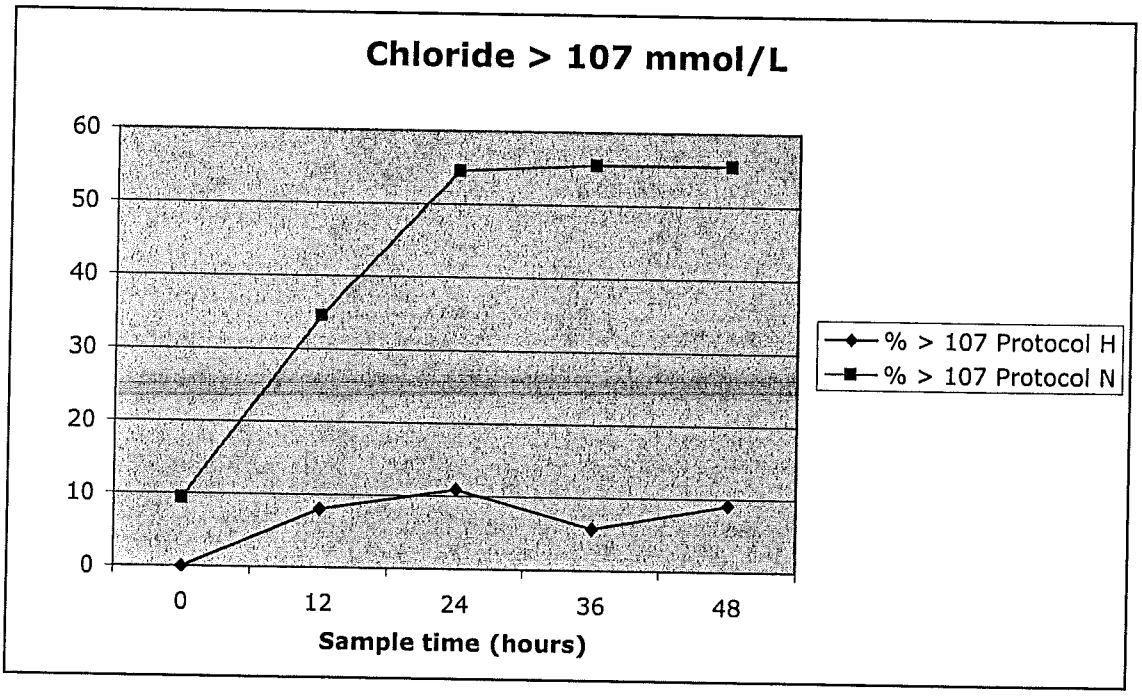


Figure 4. Mean and maximum chloride levels.

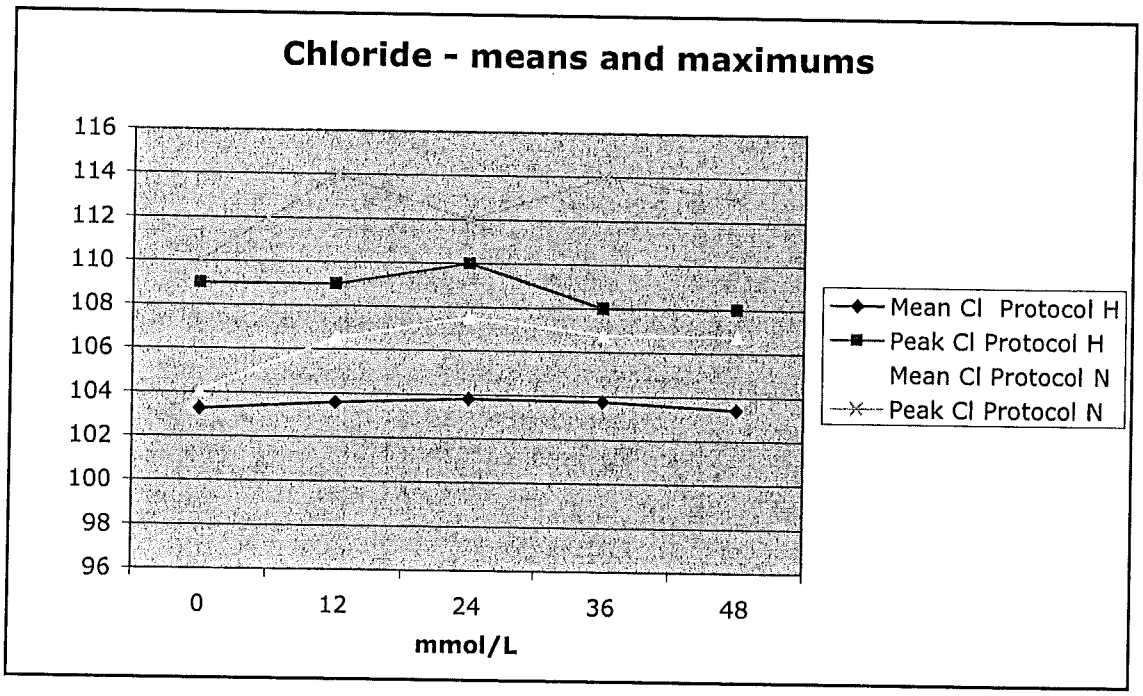
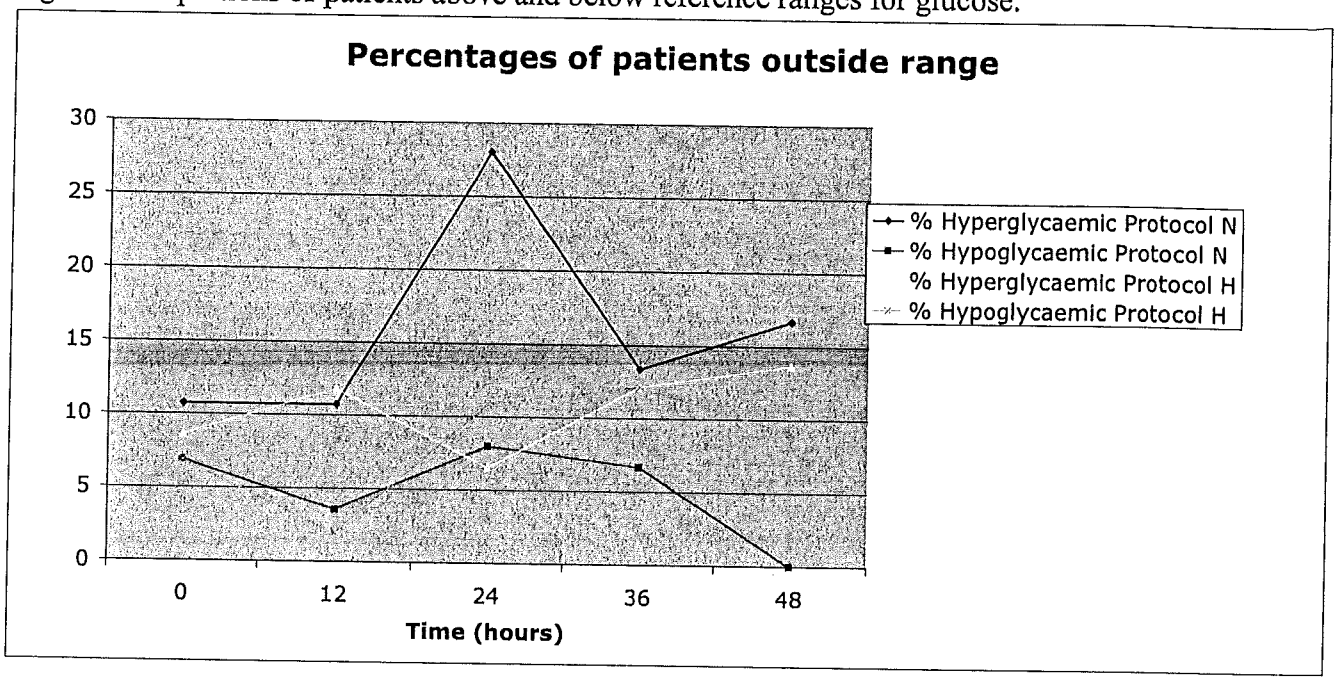
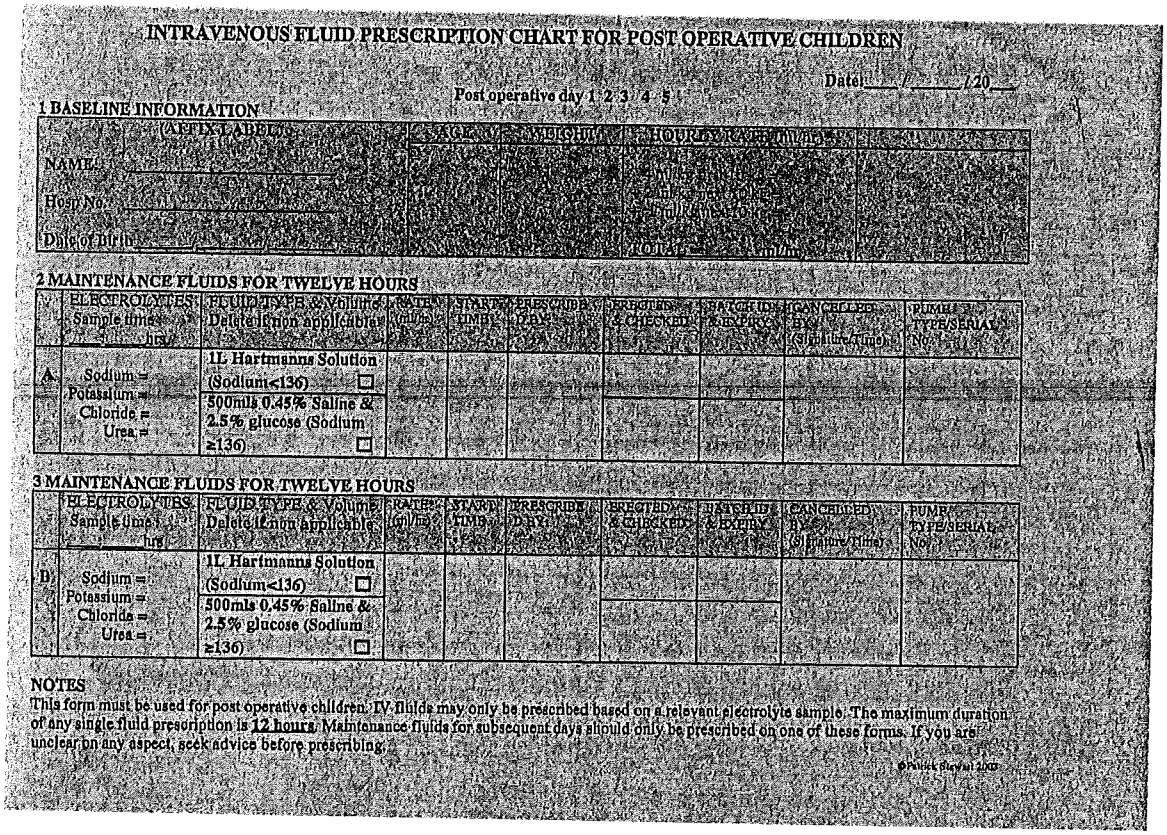


Figure 5. Proportions of patients above and below reference ranges for glucose.



Appendix 1- Protocol H



INTRAVENOUS FLUID PRESCRIPTION CHART FOR POST OPERATIVE CHILDREN

Post operative day 1 2 3 4 5 Date: ____/____/20__

1 BASELINE INFORMATION

AFFIX LABEL

NAME:

Hosp No.:

Date of birth:

AGE WEIGHT HOURLY RATE (ml/hr) TOTAL = ml/day

2 MAINTENANCE FLUIDS FOR TWELVE HOURS

	ELECTROLYTES Sample times hrs	FLUID TYPE & Volume Delete if non applicable	RATE (ml/hr)	START TIME	PRESCRIBED DAY	PRESCRIBED & CHECKED	BATCH ID & EXPIRY	CANCELLED BY (Signature/Time)	PUMP TYPE/SERIAL No.
A	Sodium = Potassium = Chloride = Urea =	1L Hartmanns Solution (Sodium<136) ☐							
		500mls 0.45% Saline & 2.5% glucose (Sodium ≥136) ☐							

3 MAINTENANCE FLUIDS FOR TWELVE HOURS

	ELECTROLYTES Sample times hrs	FLUID TYPE & Volume Delete if non applicable	RATE (ml/hr)	START TIME	PRESCRIBED DAY	PRESCRIBED & CHECKED	BATCH ID & EXPIRY	CANCELLED BY (Signature/Time)	PUMP TYPE/SERIAL No.
B	Sodium = Potassium = Chloride = Urea =	1L Hartmanns Solution (Sodium<136) ☐							
		500mls 0.45% Saline & 2.5% glucose (Sodium ≥136) ☐							

NOTES

This form must be used for post operative children. IV fluids may only be prescribed based on a relevant electrolyte sample. The maximum duration of any single fluid prescription is **12 hours**. Maintenance fluids for subsequent days should only be prescribed on one of these forms. If you are unclear on any aspect, seek advice before prescribing.

Appendix 2 – Protocol N

INTRAVENOUS FLUID SCHEDULE FOR PRE & POST OPERATIVE CHILDREN

1 BASELINE INFORMATION

Date: / / 20

(AFFIX LABEL)	AGE	WEIGHT (Kg)	HOURLY RATE (ml/hr)*
NAME: _____ Hosp No. _____ Date of Birth / /			4 ml/kg first 10 kg = + 2 ml/kg next 10 kg = + 1 ml/kg next 10 kg = 100% Maintenance = ____ mls/hr* 70% Maintenance = ____ mls/hr*

2 MAINTENANCE FLUID PRESCRIPTION (12 hours only)

	Sample time: ___ : ___ hrs	FLUID TYPE & Volume	HOURLY RATE* (ml/hr)	ERECTED & CHECKED	BATCH ID & EXPIRY	PUMP TYPE/ SERIAL No	CANCELLED BY (Signature/Time)
Prescriber: _____ Indication: _____	Sodium = ____ Potassium = ____ Chloride = ____ Urea = ____ Glucose = ____	1L 0.9% Saline with 5% Glucose	100% (Na 132 or higher) ml/hr 70% (Na 132 or lower) ml/hr				

3 MAINTENANCE FLUID PRESCRIPTION (next 12 hours)

Reviewed by:	Sample time: ___ : ___ hrs	FLUID TYPE & Volume	HOURLY RATE* (ml/hr)	ERECTED & CHECKED	BATCH ID & EXPIRY	PUMP TYPE/ SERIAL No	CANCELLED BY (Signature/Time)
Prescriber: _____ Indication: _____	Sodium = ____ Potassium = ____ Chloride = ____ Urea = ____ Glucose = ____	1L 0.9% Saline with 5% Glucose	100% (Na 132 or higher) ml/hr 70% (Na 132 or lower) ml/hr				

*** Use this schedule for routine IV maintenance fluids for children who are pre or post op. Monitor serum electrolytes 12 hourly. If you are unsure of any aspect of this schedule ask a senior colleague. If serum Na is 132mmol/L or less then sample electrolytes 6 hourly and reduce rate to 70% of full maintenance rate.**