BIMDG
British Inherited Metabolic Disease Group

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MANAGEMENT OF SURGERY IN CHILDREN WITH UREA CYCLE DISORDERS

Patients with urea cycle disorders who are usually well controlled can easily decompensate during surgery, particularly if catabolism is precipitated by fasting and surgery. Elective surgery in these patients is usually best done at the hospital with the regional metabolic unit. It is important to follow an appropriate protocol, minimising catabolism by providing adequate amounts of carbohydrate. This protocol should be used in conjunction with the emergency regimens on the BIMDG website.

The following instructions apply to patients with:

- **Ornithine carbamyl transferase (OCT or OTC) deficiency**
- **Citrullinaemia (Argininosuccinic acid synthase deficiency)**
- **Argininosuccinic aciduria (ASA, Argininosuccinic acid lyase deficiency)**
- **Arginase deficiency**
- **Carbamyl phosphate synthase deficiency**
- **N-acetylglutamate synthetase deficiency**

1. PRE-OPERATIVE MANAGEMENT

If this is a routine procedure, check that the child is healthy. If he is not, postpone the operation. Emergency operations and major procedures (lasting longer than about 30 minutes) require special consideration: seek specialist advice.

On admission, check the plasma ammonia and quantitative amino acids. If the ammonia is >100 μmol/l and the child is unwell, cancel any elective procedure & contact the metabolic team. If the ammonia is >100 μmol/l and the child seems well, seek specialist advice as it may still be safe to proceed. Plasma amino acids will not be available pre-operatively but serve as a useful baseline if there are problems later.

Check the usual feeding regimen & dosages of medicines with the parents & the metabolic team. The drugs are likely to include sodium benzoate, sodium phenylbutyrate and arginine (or citrulline). If the child is scheduled to have his operation early on the list, ask the parents whether the child is likely to take their medicines early in the morning, accompanied only by a drink of clear fluids (glucose polymer[§], Ribena[®] or a carbonated drink).

INTRAVENOUS THERAPY

By the time the operation starts the child will need to be receiving intravenous 10% glucose/ 0.45% saline (for instructions to make this solution click here). at the rate given by the formula given below.

It is simplest if the operation is first on an afternoon list. The anaesthetist will probably then allow them to follow their usual overnight management, with an early breakfast & a drink containing glucose polymer 3-4 hours pre-op (concentration and volume as in their emergency regimen). Otherwise it may be safest to start the intravenous infusion at the beginning of the pre-operative fast. If the surgery is first thing in the morning, it may be necessary to start the infusion the previous night: discuss with the metabolic consultant.

Formula for calculating for peri-operative intravenous therapy
Fluid/24 hours = 100ml/kg for 1st 10kg then 50 ml/kg for next 10kg then 20ml/kg thereafter.

- If the child is receiving sodium benzoate and or sodium phenyl butyrate use 10% glucose

- If the child is NOT receiving either sodium benzoate or sodium phenylbutyrate use 10% Glucose/0.45% sodium chloride. (for instructions to make this solution click here).

- Potassium should be added to this solution 10 mmol in 500 ml.

If cannulation is difficult or the child is likely to pull out the cannula before getting to theatre, it may be possible to postpone insertion of the cannula until after induction of anaesthesia. However, this depends on the child being able to fast for at least as long as the anaesthetist's minimum pre-operative fasting interval. This is likely to be true for most metabolic disorders but a few cannot tolerate this. This management strategy is easiest if the operation is towards the end of the morning list as this allows the usual overnight/morning routine to be followed. If the child is scheduled to have the operation early on the list, the parents would have to persuade the child to take a drink containing glucose polymer in the early hours of the morning. Moreover, it will still be necessary to start the infusion before anaesthesia if the surgery is delayed.

Is the child is late enough on the list to have their usual morning medicines ?
Oral drugs can be given up till 3-6 hrs pre-operatively (as determined by the anaesthetist). Giving medicines for a urea cycle disorder a few hrs early will cause no problems but children may be too sleepy to take them before 6 a.m. (unless they are given down a nasogastric tube).

Is the child is late enough on the list to allow breakfast ?
Generally a light breakfast is given to children >6 hrs before their minor operations. Thus, children whose operations are scheduled for 12.00 or later will generally be given breakfast, but a parent may tell you that their child is very unlikely to take breakfast before a certain hour, which should be taken into consideration.

Pre-operative glucose polymer
Provided the anaesthetist agrees, a drink of glucose polymer should be given to patients 3 hrs pre-operatively unless an infusion of 10% glucose has already been started. Suitable volumes and

concentrations are given in the table below. Contact your local dietitian for these solutions – details can also be found here. Ask the child's carer how they normally take glucose polymer in his emergency regimen: they may take it with flavouring or via a nasogastric tube. If the child appears unwell, cannot be persuaded to take the glucose polymer or it is vomited or if the operation is delayed, such that the anaesthetic will start more than 4 hrs after the glucose polymer, an intravenous 10% glucose infusion must be started before the anaesthetic.

Table 1: Pre-operative drinks: Suitable doses & concentrations of glucose polymer

Age (yrs)	Concentration (%)	Volume
0-1	10	14 ml/kg
1-2	15	8 ml/kg
2-6	20	100 ml
6-10	20	150 ml
>10	25	180 ml

DELAYED OPERATIONS

If the operation is delayed, the glucose infusion should be started at the time the operation was due to begin. If the operation is delayed more than 3 hours the medicines should be given intravenously (see instruction below paragraph 5). Intravenous medications will also be needed if oral drugs are vomited.

EXTRA INTRA-OPERATIVE INSTRUCTIONS

Does the child have regular nasogastric tube feeds (eg for overnight feeding)?
If so, make sure that the surgeons leave one in situ at the end of the operation, particularly if this was an ENT procedure.

5. POST-OPERATIVE PROCEDURE

Following the operation, the child should be given a dose of medicines orally as soon as it is safe and then continue to have his medicines according to his usual routine.

Intravenous medicines will be needed if recovery is slow, complicated by vomiting oor cannot be given orally. The usual dose should be given as a continuous infusion for however long is required (i.e. 1/4 of daily dose over 6 hrs etc.). For standard doses see table 2. Monitor biochemical status, as indicated, by measuring plasma ammonia.

Table 2: Medicines

The same dose is given orally or intravenously. If oral, give daily dose in 4 divided doses.
If given intravenously give continuously.

Patients having minor surgery (lasting less than 30 minutes)

Medicines - total daily dose	Minor surgery	
	Citrullinaemia/ASA	Other defects
Sodium benzoate	250 mg/kg/day	250 mg/kg/day
Sodium phenylbutyrate	(250 mg/kg/day)*	250 mg/kg/day
Arginine	600 mg/kg/day	

* to be given if on this medication routinely

Patients who are emergency and/or having major surgery (lasting more than 30 minutes)
It is essential to seek specialist help if major surgery is necessary

Drug	Major surgery	
	Citrullinaemia/ASA	Other defects
Sodium benzoate	250 mg /kg/day	500 mg/kg/day
Sodium phenylbutyrate	250 mg/kg/day	500 mg/kg/day
Arginine	600 mg/kg/day	150 mg/kg/d

For more information about the medication please click here.

Discuss doses of medication with metabolic specialist.

Sodium Benzoate and Sodium Phenylbutyrate can be mixed together in 10% glucose (maximum concentration 2.5g of each in 50mls) and given in a syringe pump piggy-backed into the main 10% glucose infusion. Arginine should be diluted separately (maximum 2.5g in 50 ml 10% glucose, given via a syringe pump piggy-backed into the main glucose infusion). For more details please refer to the emergency protocols for urea cycle disorders - please see the BIMDG website and **Use these calculators** (click this link) **for volumes and rates of infusions.**

6. Feed the child at the time you would feed any other child following an equivalent procedure. Discontinue the intravenous infusion ONLY after the child has been seen to tolerate food. Remove the cannula ONLY when there is no chance of the child vomiting. Seek specialist help if there are any problems.

7. Discharge the child ONLY when absolutely sure they have fully recovered and they have been discussed with the metabolic team. This will often be the following day.

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