UHL NNU guideline: The Use of Human Soluble Insulin on the Neonatal Unit

University Hospitals of Leicester NHS Trust

C25/2006

Contents

1. Introduction and Who Guideline applies to

This guideline is aimed at all health care professionals involved in the care of infants within the Neonatal Service.

Human Soluble Insulin (Actrapid) is a pancreatic hormone involved in the regulation of blood glucose concentration.

Indications for use

- Control of high blood glucose levels (as defined in the **Neonatal Hyperglycaemia Guideline Trust ref: C26/2006**.
- Control of hyperkalaemia (glucose-insulin infusion).

Key Points:

- Blood glucose levels may be very unstable and close monitoring is essential
- Use the blood gas machine for measuring blood glucose levels – if unavailable use an alternative glucose oxidase method
- Always use an **INSULIN SYRINGE** (marked in units) to draw up insulin.
- When adjusting insulin infusion rates consider previous response and trends in blood glucose levels rather than single levels in isolation

Related UHL documents:

Neonatal Hyperglycaemia Neonatal Guideline Trust ref: C26/2006.

Hyperkalaemia Neonatal Guideline Trust ref: C39/2010

Prevention and Management of Symptomatic or Significant Hypoglycaemia
Neonatal Guideline Trust ref: C22/2008

2. Preparation (single strength* infusions)

- 100 units in 1 ml human soluble insulin
- Vial contains 10 ml =1000 units insulin
- **Use an INSULIN SYRINGE to draw up 10 units of insulin. A 0.3ml insulin syringe should be used, marked in UNITS of insulin NOT mls (0.01 ml= 1 unit of insulin)**

- *Prior to administration*: Dilute 10 units of the 100 unit/ml solution in 9.9 ml glucose 5% or 0.9 % sodium chloride to give a working solution of 1 unit in 1 ml. Stable when diluted for 24 hours.

- *For an infusion via syringe and extension tubing*: Add (5 x weight in kg) units of insulin to 50 mL of glucose 5%. This produces a solution, which if given at 1 mL/hr will provide a dose of 0.1unit insulin/kg/hr.

To reduce fluctuations in insulin concentration due to adsorption* by plastics[1]:

- Prime the extension tubing (and the T piece) with insulin solution, wait for 30 minutes.

- The line should be flushed with a volume at least as great as the volume of the giving set before attaching to the baby so a 'fresh' solution is administered

- Insert the syringe to the pump and perform a mechanical purge (using syringe driver to get rid of the slack) to purge up to the point of delivery before connecting to the infant at patient hub

The infusion must be attached as close to the infusion site as possible and dead space minimized

*For information on insulin adsorption, the rationale for using single strength insulin, and situations where double or quadruple strength may be considered, refer to Appendix 2

3. Administration of continuous IV insulin infusion[2, 3]

3.1 For hyperglycaemia

- Aim for a target blood glucose 5-8 mmol/l

- Co-infuse the insulin infusion with the glucose source (maintenance fluids or aqueous PN bag). The benefit of co-infusion of insulin with the glucose source is that in the event the line extravasates or is displaced, both the glucose and insulin infusion will be interrupted at the same time, reducing the likelihood of hypoglycaemia or worsening hyperglycaemia

- Before co-infusing with other drug infusions check for incompatibilities in the IV monograph and/or contact the neonatal pharmacist for advice

- Do not flush a line that contains or has contained insulin once connected to a patient, however be attentive to signs of extravasation or infiltration injury

- Insulin infusions should not be filtered

- The insulin infusion should not normally be included in the total fluid volume calculation. However it would be appropriate to discuss with the medical team whether the volume should be included if the infusion rate exceeds 20mls/kg/day

- The infusion line should be labelled near the connection point to ensure the insulin infusion is not mistakenly clamped off or disconnected

Guidance for starting insulin:

- Commence insulin when indicated by the neonatal guideline on management of hyperglycaemia

- Commence infusion at 0.05 unit/kg/hr (=0.5 ml/hr if single strength insulin diluted as above)

- Check blood glucose on neonatal unit within 1 hour of starting insulin infusion.

- Refer to Appendix 1 for guidance on titrating insulin in response to blood glucose **trends** and rate of change.

- Persistent hyperglycaemia early in insulin use may be due to insulin adsorption by plastics (see Appendix 2). As a result, higher doses of insulin may be required in the first few hours of an insulin infusion through a new line, followed by reduced rates to avoid hypoglycaemia once insulin adsorption reaches equilibrium.

- Where symptomatic hyperglycaemia is refractory to insulin dose adjustments made following the guidance in Appendix 1, discuss with consultant for review and planning of bespoke management strategies

Guidance for ongoing treatment and monitoring[4]:

Refer to Appendix 1 for guidance on titrating insulin in response to blood glucose trends and rate of change.

When adjusting insulin infusion rates consider patient-specific trends in response rather than absolute blood glucose values in isolation.

3.2 For hyperkalaemia[5]

- Recommended dose is 0.5 units/kg IV over 1 hour (glucose 20%-insulin infusion).
- Please refer to the hyperkalaemia guideline and insulin in hyperkalemia neonatal IV monograph for further information

Route
Intravenous

Side Effects
Hypoglycaemia, Hypokalaemia, Local reaction

Contra-indications
None known

For details of compatible and incompatible drugs for co-infusion, stability and storage refer to neonatal insulin IV monograph.

4. Education and Training

Annual neonatal insulin training via HELM for all neonatal nursing and medical staff

5. Audit criteria

Insulin to be drawn up in an insulin syringe marked in units (100%).

6. References

1. Knopp L, Bishop K, Lerios T & Chase G (2021). *Capacity of Infusion Lines for Insulin Adsorption: Effect of Flow Rate on Total Adsorption.* Journal of Diabetes Science and Technology. 15(1) 109-120.
2. Neonatal Formulary, 8th Edition, 2020. Blackwell Publishing, Oxford.
3. Evelina London Paediatric Formulary accessed 17/06/2020 at http://cms.ubqo.com/public/d2595446-ce3c-47ff-9dcc-63167d9f4b80/content/2976ba81-627e-4bd0-a8c2-7d855b2f7589
4. NHSGGC guidelines. Hyperglycaemia in the neonate accessed 02/03/2021 at https://www.clinicalguidelines.scot.nhs.uk/nhsggc-paediatric-clinical-guidelines/nhsggc-guidelines/neonatology/hyperglycemia-in-the-neonate/
5. UHL Management of Hyperkalaemia on the neonatal unit 2019

7. Key Words

Actrapid, Blood glucose concentration

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

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Contact and review details			
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Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
Dec 2005	**1**		Original guideline
Oct 2011	**2**	Guidelines Meeting	
Oct 2015 - Jan 2016	**3**	Reviewed by author (VK) Neonatal Guidelines Meeting Neonatal Governance Meeting	No significant changes required
Mar 2016	**4**	Neonatal guidelines lead (REM)	Minor editorial changes
Jun 2016	**5**	Lucy Stachow	Clarify preparation information
Dec 2018	**6**	Lucy Stachow Neonatal Guidelines Meeting Neonatal Governance Meeting	Amendments required
Jan 2022 - Mar 2022	**7**	AK & LS Neonatal Guidelines Meeting Neonatal Governance Meeting	Amendment to insulin titration, use of double and quadruple strength insulin, additional safety information on co-infusion of glucose source, flushing, adsorption. Hyperkalaemia dose updated to reflect current hyperkalaemia guideline.
Mar 2025	**8**	AK & LS Neonatal Guidelines Meeting Neonatal Governance Meeting	Minor amendment , Co infusion of insulin infusion with the glucose source

Appendix 1 - Adjusting insulin rates in response to blood glucose trends

All adjustments in insulin rates should be made with consideration of the individual patient's blood glucose trends and their previous responses to insulin rate changes. Where symptomatic hyperglycaemia is refractory to insulin dose adjustments made following the table below, discuss with consultant for review and planning of bespoke management strategies.

Blood glucose mmol/l	Falling	Stable e.g. fluctuating by no more than 1.5mmol/l between measurements	Rising
<2.6	• **STOP all insulin** • Medical review • Check all lines • Follow UHL Prevention and management of symptomatic or significant hypoglycaemia in neonates guideline		
2.6-4.9	• **STOP all insulin** • Check all lines • Increase glucose infusion rate (using glucose infusion or PN)	• **STOP all insulin** • Check all lines • Consider increased glucose infusion rate (using glucose infusion or PN)	
5-8 Target	• Stop insulin OR reduce to half rate *depending on rate of blood glucose fall* (you must look at blood glucose trends and previous response to insulin rate changes)	• No change to insulin rate	• No change to insulin rate
8.1-12.0	• Consider stopping insulin OR reducing to half rate *depending on rate of blood glucose fall* (you must look at blood glucose trends and previous response to insulin rate changes)	• Wean off any additional glucose infusion (in preference to PN) if previously added, then if BG still ≥8mmol/l • RE-Start insulin at 0.05 units/kg/hour or increase insulin rate by 50% UNLESS within one hour of newly started insulin infusion	• Wean off any additional glucose infusion (in preference to PN) if previously added, then if BG still ≥8mmol/l • RE-Start insulin at 0.05 units/kg/hour or increase insulin rate by 50% UNLESS within one hour of newly started insulin infusion
>12.0	• No change to insulin rate unless blood glucose is falling rapidly (>4mmol/l/hr) when you should • reducing to half rate	• Wean off any additional glucose infusion if previously added, then • Start or RE-start insulin at 0.05 units/kg/hour or increase insulin rate by 50% UNLESS within one hour of newly started insulin infusion	• Wean off any additional glucose infusion if previously added, then • Start or RE-start insulin at 0.05 units/kg/hour or increase insulin rate by 50% UNLESS within one hour of newly started insulin infusion

Frequency of blood glucose testing

- For blood glucose <2.6mmol/l refer to UHL Prevention and management of symptomatic or significant hypoglycaemia in neonates guideline for frequency of blood glucose monitoring and management of hypoglycaemia on the neonatal unit.
- For blood glucose in 2.6-4.9 mmol/l range, check blood glucose levels hourly.
- Check blood glucose within an hour of starting insulin and every hour for the first four hours of treatment. Thereafter check blood glucose within an hour of every insulin dose change or change in glucose infusion rate.
- Once rate of insulin infusion and blood glucose is stable in 5-8 mmol/l range blood glucose monitoring can be reduced to 2-3 hourly.

Check serum potassium every 12-24 hours.

Appendix 2 – Effect of insulin adsorption on initial response to treatment and choice of insulin infusion strength

Insulin Adsorption

Insulin adsorption describes the binding of insulin molecules to the surfaces of materials that are used in syringes and administration sets. This binding results in under-delivery of insulin to the patient. Initial insulin concentration and flow rate of insulin are two of the factors that affect the extent of adsorption[4].

When a new syringe of insulin is prepared, or a new giving set attached, there is a period when adsorption occurs until equilibrium is reached. This results in a reduced concentration of insulin reaching the patient early in use.

Persistent hyperglycaemia early in insulin use may be caused by insulin adsorption that occurs maximally in the first one to two hours of infusion. As a result, higher doses of insulin may be required in the first few hours of an insulin infusion through a new line, followed by reduced rates to avoid hypoglycaemia once insulin adsorption reaches equilibrium.

Reduced adsorption can be achieved by the “priming” described in the preparation section above but adsorption is still significant at the lower concentrations and lower flow rates commonly used in neonates.

Choice of insulin strength – single versus double or quadruple

Single strength insulin is the preferred starting strength to allow the fine titration of insulin rates that are required to achieve control of hyperglycaemia whilst minimizing the risk of hypoglycaemia.

There may also be benefits in terms of reducing the effect of insulin adsorption which is more significant at lower flow rates[4].

Where neonates require high volumes of single strength insulin to achieve normoglycaemia, and this negatively affects fluid management or nutritional input, double or quadruple strength insulin infusion should be considered if the infant has stable insulin requirements (e.g. at least 2 consecutive blood glucose measurements without requiring insulin titration). **Where this is the case, there must be clear documentation that the infusion is either ‘double’ or ‘quadruple’ the standard infusion concentration**.

Double or quadruple strength insulin is not appropriate where the infant is sensitive to small changes in insulin dose and where insulin rates are being weaned with the intention of discontinuation.