

SWISS SOCIETY OF NEONATOLOGY GUIDELINES

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Care of the Newborn Infant \geq 34 0/7 Gestational Weeks with increased risk or occurrence of hypoglycaemia in the Delivery Suite and on the Maternity Ward

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Introduction

The aim of these recommendations is to give guidance in avoiding and treating hypoglycaemia in term and late preterm newborn infants (\geq 34 0/7 weeks gestational age), in the delivery unit and on the maternity ward. Preterm infants of less than 34 weeks of gestation and sick term infants are usually cared for in a neonatal unit as they need specialized care and treatment.

Background information

With the delivery of a newborn infant, several metabolic adaptive processes take place in order to insure the shift from placental glucose provision and foetal glycogen synthesis to proper glucose production and regulation. During delivery, endogenous glucagon and catecholamine levels rise 3 to 5 fold and initiate glycogenolysis, which in turn assures glucose homeostasis during the first hours of life. Growth hormone and cortisol secretion during delivery promote gluconeogenesis, which becomes increasingly important after the first few hours of life. In parallel, insulin levels drop to a low level. In order for glycogenolysis and gluconeogenesis to take place, the involved enzymes and the necessary substrates, such as fat and amino acids, must be available. ^{8,11, 17, 21, 22, 23}

Even during optimal postnatal adaptation, blood sugar levels drop during the first 2 hours of life. Thereafter they rise slowly but steadily until glucose homeostasis is reached. Glucose is the primary substrate for cerebral energy requirements. Newborn infants have high weight-adjusted glucose needs because of the relative important weight of the CNS in relation to total body weight. The CNS can also use ketone bodies as an energy substrate, produced in case of lipolysis. Thus the brain of a newborn infant is not completely dependent on glucose alone. For this reason, routine blood glucose monitoring is not warranted in the healthy term newborn infant. Compared to healthy term infants, preterm infants and small for gestational age infants have reduced glycogen pools and less fat storage, leading to a diminished capacity for lipolysis, which in turn means insufficient energy substrate delivery in form of ketone bodies to the brain. Furthermore, these newborn infants show insufficient gluconeogenetic counter regulation in the presence of low blood glucose levels because of a lack of substrates for gluconeogenesis (such as lactate, pyruvate, alanine and ketone bodies). ^{6, 7, 8, 11, 13, 17, 18, 21, 22, 23, 24}

Early initiation of enteral feeds with breast milk promotes gluconeogenesis by providing the necessary substrates. Ketogenesis is enhanced due to fatty acids in the milk, and insulin secretion is only discretely increased in the presence of lactose in the milk. Administering glucose enterally on the other hand can lead to substantial insulin secretion and diminished glucagon production, thus delaying the necessary gluconeogenic and ketogenic homeostatic processes. For these theoretical reasons, feeding milk is far more advantageous. ^{6, 8, 17, 18, 23}

In the medical literature there is still no consensus as to the definition of hypoglycaemia in the newborn infant. There are 4 concepts for a possible definition: 1. Definition marked by clinical symptoms (so-called symptomatic hypoglycaemia), 2. Definition according to epidemiological data, 3. Definition dependent on acute metabolic, endocrine and neurological findings. 4. Definition according to long term neurological outcome. None of the above mentioned concepts are satisfactory and each one has disadvantages, some of which are significant. ^{1, 3, 4, 5, 6, 8, 9, 19, 23, 24}

Differential diagnosis

Hypoglycaemia of the newborn infant is not a homogeneous disease pattern. It is far more expression of a perturbed postnatal metabolic adaptive process, or a non specific symptom of various diseases (i.e. infection, asphyxia, polyglobuly). Hypoglycaemia is especially frequent in premature and small for gestational age infants. (see Recommendation: [Care of Premature Infants 34 0/7 to 36 6/7 Weeks Gestational Age](#)). In most cases, the history and clinical exam will help elucidate the aetiology of the hypoglycaemia (i.e. prematurity, intrauterine growth restriction, diabetic foetopathy). In case of persistent or recurrent hypoglycaemia despite adequate glucose supply, the newborn infant should be transferred to a neonatal unit for further work up (i.e. for hyperinsulinism, metabolic disorders or endocrinopathy).

Diagnostics / Testing methods

Requirements for testing devices are high when glucose levels need to be determined in a newborn infant: the results must be readily available, the results must be precise in the low range, analysis should require a minimal amount of blood, and the method should be cost-effective. The gold standard is enzymatic determination via the hexokinase method in the laboratory. For practical reasons, the bed side determination method using portable devices has become established during these past years. Many devices have been examined for their efficiency of measuring hypoglycaemia.^{10,12,14,15,16,20} In conclusion one can state that, as a rule, most devices overestimate the actual blood glucose level. Depending on the device used, deviations can be between 0.2 and 0.6 mmol/L when blood glucose levels are measured between 2.0 and 2.5 mmol/L. On occasion, measured blood glucose values with the bedside method have been falsely low. Since this bedside method has become an established means to measure blood glucose, these measurement errors must be taken into consideration. Regular calibration (quality control) of the devices used should be insured. Before introducing a new device into neonatology, calibration with the hexokinase-method is warranted.

Assessment of Hypoglycaemia

Although hypoglycaemia should ideally be defined individually (and depending on the clinical situation), for pragmatic reasons, a pre-determined cut-off value is in every day clinical use. The literature describes an increasing risk of neurological sequelae in the presence of glycaemic values below 2.0 to 2.2 mmol/L (determined according to the hexokinase-method). Although certain newborn infants without increased risk of neurological sequelae will be treated unnecessarily (over-treatment), cautious risk assessment seems to justify this glucose threshold. Since many clinics use these portable bed-side devices, the issue of measurement error must always be taken into consideration. For this reason, a potential overestimation of the actual blood glucose level of 0.2 to 0.6 mmol/L using the bed-side device must be incorporated into the clinical evaluation:

A blood glucose level of < 2.5 mmol/L in an infant of \geq 34 0/7 weeks gestation determined by a bed-side device is considered hypoglycaemic.

Pathway for Follow-Up and Treatment with Increased Risk of Hypoglycaemia

Figure 1 depicts the necessary preventive measures (early and additional feeds), blood glucose determinations, and the possible therapeutic measures in newborn infants with increased risk of developing hypoglycaemia. Additionally, extra glucose consumption should be reduced to a minimum by optimizing thermoregulation (see Recommendation: [Care of Premature Infants 34 0/7 to 36 6/7 Weeks Gestational Age](#)).

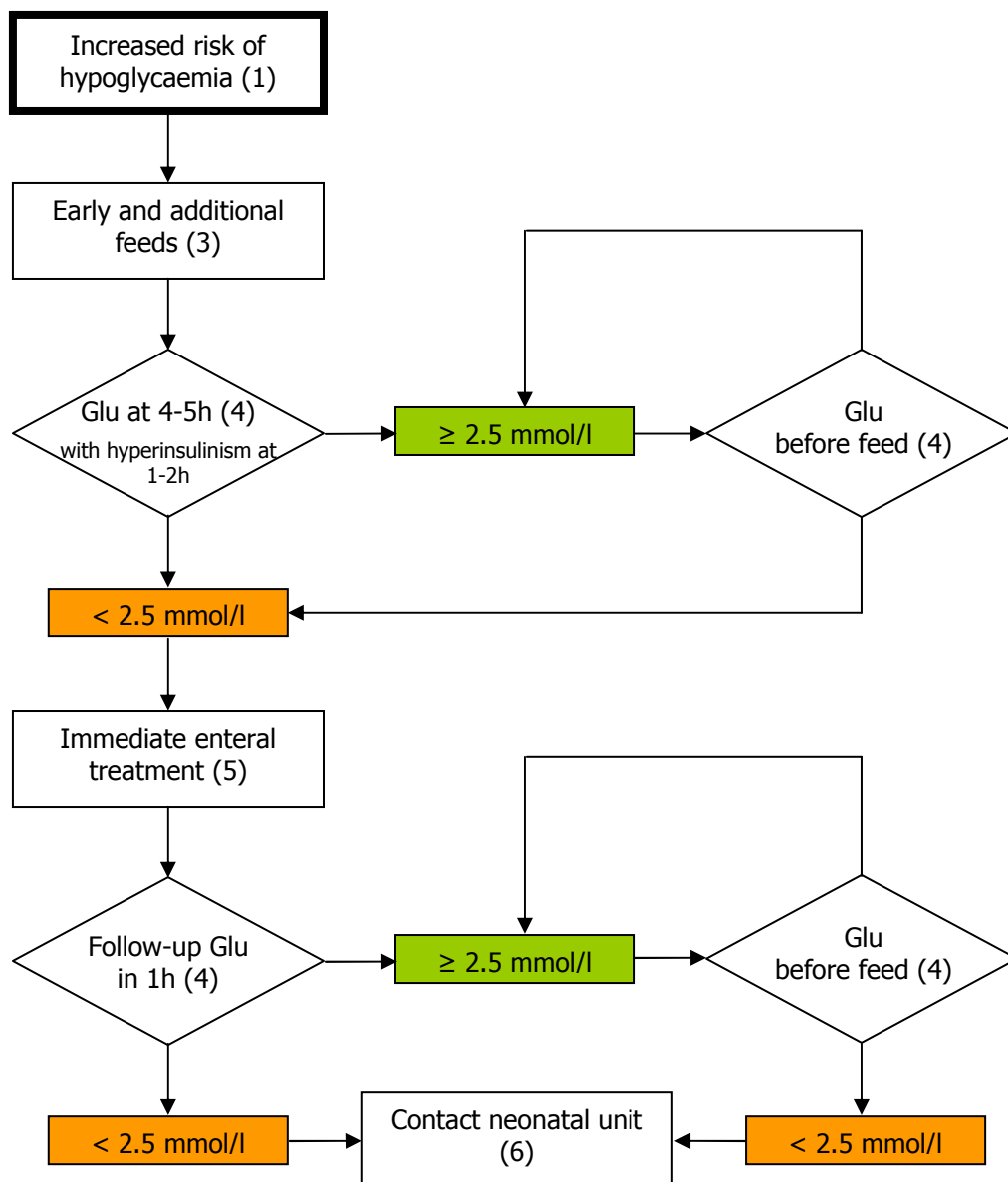


Figure 1: See page 5 for footnotes with definitions (Glu = blood glucose levels)

Pathway for Follow-Up and Treatment with Suspected Hypoglycaemia

Figure 2 shows the necessary blood glucose determinations and possible therapeutic measures for newborn infants with suggestive symptoms for hypoglycaemia.

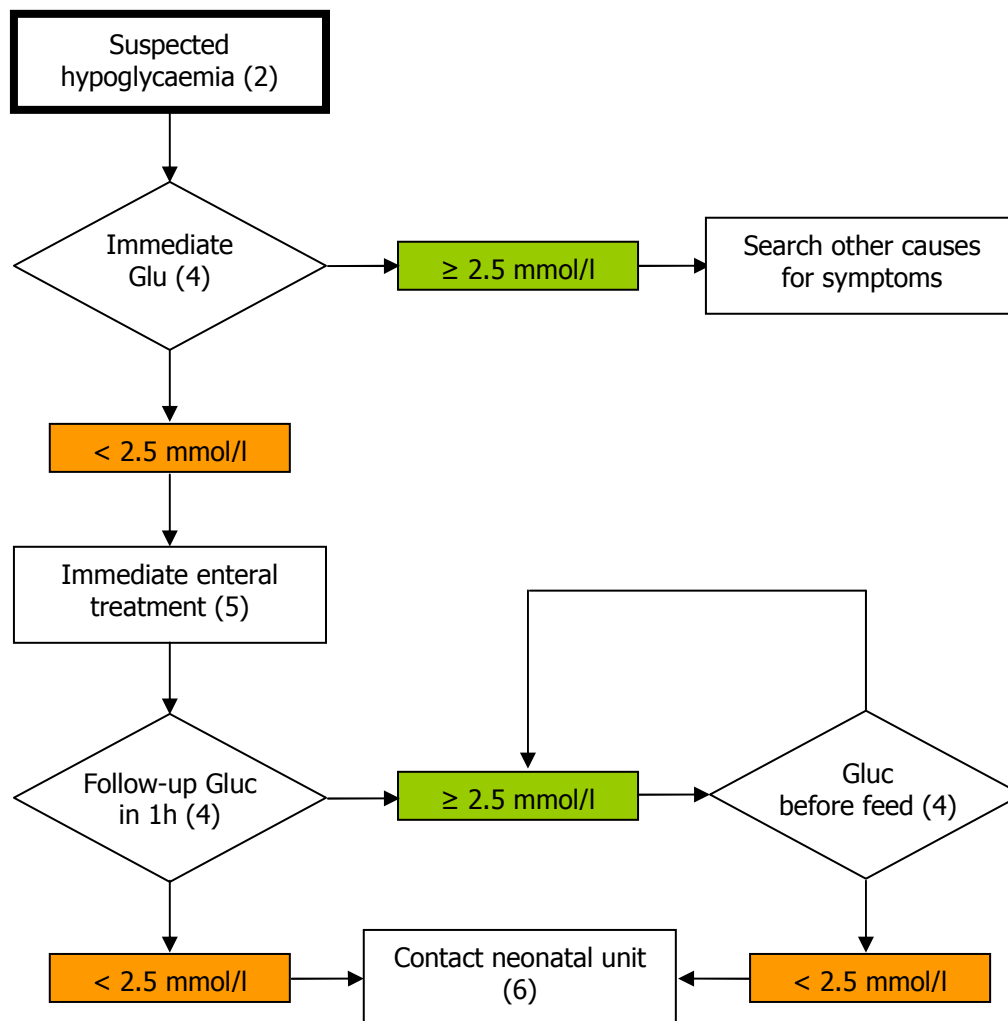


Figure 2: See Page 5 for footnotes with definitions (Glu = blood glucose level)

The following situations must be avoided or, in case of occurrence, rapidly and resolutely addressed as they are associated with an increased risk of neurological sequelae. Contact with a neonatal unit should be sought immediately and the necessary steps in treatment introduced without delay:

- **low hypoglycaemic value < 1.5 mmol/l**
- **symptomatic hypoglycaemia**
- **prolonged hypoglycaemia > 4 hours**
- **recurrent hypoglycaemia**

1. Increased risk of hypoglycaemia

- Preterm infants < 37⁰/₇ weeks gestation
- Birth weight < 2500 g or < 3rd percentile
- Maternal diabetes and newborn infant with clinical signs of diabetic foetopathy (birth weight > 4500 g or > 97th percentile, cushingoid habitus, plethoric, hepatomegaly, hypertrichosis of earlobe).
- Ill newborn infant (i.e. asphyxia, sepsis, respiratory distress syndrome, haemolysis)
- Hypothermia

2. Suspected hypoglycaemia

Symptoms suggestive of hypoglycaemia are jitteriness, muscular hypotonia, apnoeas, hypothermia, seizures, hyperexcitability, or apathy. If hypoglycaemia leads to cerebral symptoms, one must assume that the brain is not receiving sufficient glucose and that sufficient alternate energy sources are not available. For this reason, rapid and efficient treatment must be initiated. The described symptoms of hypoglycaemia are non-specific. Therefore, other diagnoses must be considered if symptoms persist despite adequate treatment.

3. Early and additional feeds

Newborn infants at increased risk of hypoglycaemia should be offered early feeds. These should be given soon after delivery, but within 2 hours of birth at the latest. During the first 2 to 3 days of life, the infant should be breast fed every 3 to 4 hours. Immediately after breast feeds the infant should be offered supplemental feeds with the corresponding infant formula milk until sufficient breast milk is available. Dextromaltose solution can be offered as an alternative to formula milk.* Glucose solutions are not at all recommended for oral feeds (i.e. Glucose 10%).

4. Blood Glucose determinations

Blood glucose levels may be determined by means of bed-side tests. In case of an asymptomatic newborn infant with increased risk of developing hypoglycaemia, the first blood glucose level should be determined at the age of 4-5 hours of life just before his second feed. The exception is for the infant with increased risk of hyperinsulinism, in which case the blood glucose level should be determined 1-2 hours postpartum, because these children can manifest severe hypoglycaemia within a very short time. In case of a documented hypoglycaemia, the blood glucose level should be determined again within 1 hour so as to assess the treatment effect. If the blood sugar level is ≥ 2.5 mmol/L, further blood glucose determinations can be done before the next feeds. If 3 consecutive levels are normal, further blood draws are not needed. In case of symptoms suggestive of hypoglycaemia, the blood glucose level must be immediately determined.

5. Enteral treatment

Diagnosis of hypoglycaemia should lead to therapeutic consequences without delay. The enteral treatment consists of giving breast milk or adequate infant formula milk (10-15 ml/kg body weight). Thereafter, the infant receives additional feeds every 3 (- 4) hours (possibly more frequently) after every breast feed during the first 2 to 3 days of life (for a total of 10-15 ml/kg/feed). Dextromaltose can be offered as an alternative to formula milk. It is not recommended to give glucose solutions orally (i.e. Glucose 10%). In case of feeding difficulties or even refusing feeds, milk should be applied via a feeding tube or advice sought from the neonatologist/ paediatrician.

* Offering milk formula or dextromaltose is controversial. Advantages of formula milk are based on theoretical considerations (preferred gluconeogenic and ketogenic processes); disadvantageous is exposing normally exclusively breast fed infants to formula milk.

6. Contacting the neonatologist

If hypoglycaemia cannot be corrected with enteral feeds, glucose should be administered parenterally. This treatment usually is accomplished in a neonatal unit. In case of severe or symptomatic hypoglycaemia and/ or prolonged and/ or recurrent hypoglycaemia, contact the closest neonatal unit to discuss further measures.

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