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# A&I

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## Infantile neuroaxonal dystrophy

## Insulinoma

orphanaesthesia

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

## SUPPLEMENT NR. 19 | 2020

## OrphanAnesthesia –

### ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patienten mit seltenen Erkrankungen. Damit will Orphan Anesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesisten damit keine Erfahrungen gesammelt haben, so dass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

**Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:**

**www.ai-online.info/Orphsuppl**
**www.orphananesthesia.eu**

## OrphanAnesthesia –

### a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommenations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

**Find a survey of the recommendations published until now on:**

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orphananesthesia

# Anaesthesia recommendations for

# Insulinoma

**Disease name:** Insulinoma

**ICD 10:** D13.7 (benign), C25.4 (malignant), D37.8 (uncertain behaviour)

**Synonyms:** –

**Disease summary:** Insulinoma is a rare neuroendocrine tumour of the pancreas, which is usually small, solitary and benign. It may be part of multiple endocrine neoplasia type-1 syndrome. It is characterised by hypoglycaemic episodes as a result of inappropriate secretion of insulin from the pancreatic adenoma cells. Whipple's triad is pathognomic of insulinoma, which includes: 1) symptoms of neuroglycopaenia, 2) documented hypoglycaemia (plasma glucose level less than 50 mg/dl) and 3) relief of symptoms (often within 5–10 min) following glucose administration. Documented hyperinsulinism in presence of hypoglycaemia warrants further investigations to confirm the diagnosis. Gold standard for the diagnosis is a 72 h-fasting test, demonstration of Whipple's triad. The localisation of the tumour is a challenge for the clinicians. Surgical resection is the curative treatment with a high success rate. Intraoperative ultrasound and surgical palpation confirm the site of the tumour. There may be severe hypoglycaemia during surgical handling of the tumour, symptoms of which may be masked when the patient is under anaesthesia. So the main anaesthetic concern is to maintain an optimum plasma glucose level. Glucose infusion and frequent plasma glucose monitoring to maintain glucose level more than 60 mg/dl is found to be helpful.

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

**Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net**

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## Typical surgery

Surgical excision of insulinoma, Laparoscopic resection of insulinoma, enucleation of insulinoma, distal pancreatectomy.

## Type of anaesthesia

Regarding anaesthetic agents, no specific recommendations are available. Combination of general anaesthesia with propofol, epidural block and opioid as part of multimodal anaesthesia is a useful choice of anaesthesia for the removal of insulinoma. The anaesthetic technique should include drugs that decrease the cerebral metabolic rate for oxygen ($CMRO_2$). Both thiopentone sodium and propofol reduce $CMRO_2$. Propofol has an advantage over thiopentone sodium, as the latter one can cause severe hypotension in patients receiving diazoxide therapy because both are protein-bound drugs. Moreover, propofol has no effect on the release of insulin and glucose regulation. Although enflurane and halothane are not much in use now, they inhibit pancreatic insulin release, resulting into hyperglycaemia.

## Necessary additional pre-operative testing (beside standard care)

In addition to standard care, it is important to confirm the diagnosis of insulinoma.

The 72 h-fasting test is a demonstration of Whipple's triad of symptoms, which is considered as the gold standard for the diagnosis. Insulinoma is diagnosed when the following criteria are fulfilled:

1. Blood glucose less than 50 mg/dl with hypoglycaemic symptoms
2. Relief of symptoms after meals
3. Elevated C-peptide (>200 pmol/l)
4. Absence of plasma sulfonylurea
5. Increased serum insulin level (>5–10 µU/ml)
6. Increased proinsulin level (≥25% or ≥22 pmol)

Other tests include: Intravenous secretin test of insulinoma, C-peptide inhibition test etc., and can be used to diagnose insulinoma.

The localisation of the tumour may be a challenge, as it is a very small and intrapancreatic tumour. The success rate of non-invasive modalities is poor, as has been shown in different studies. In case of transabdominal ultrasound, it is 9–66%, in computed tomography (CT) 50–80%, in magnetic resonance imaging (MRI) 40–70%, and in somatostatin receptor scintigraphy 17%.

The overall success rate of all these modalities together is around 80%. CT and MRI are helpful to detect metastatic disease. The use of endoscopic ultrasound (EUS) has increased recently. The sensitivity of EUS is reported as 40–93%. Invasive modalities like pancreatic



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arteriography, which was considered as the “gold standard”, is now not much in use. Transhepatic portal venous sampling (THPVS) was also considered as one of the most accurate tools for localisation. The intra-arterial calcium stimulation test or arterial stimulation and venous sampling (ASVS) has almost replaced THPVS now. Intraoperative ultrasound (IOUS) is a very useful tool of localising the insulinoma, especially when it is small and not easily palpable. IOUS can localise insulinoma in almost 86–90% of the cases.

## Particular preparation for airway management

Usually, insulinoma does not affect the airway and therefore no particular preparation is required.

## Particular preparation for transfusion or administration of blood products

As the surgery is either laparotomy and resection of the tumour or lapraroscopic enucleation of the tumour, the preparation for the transfusion of blood products is similar to any other major laparotomy or laparoscopic procedure.

## Particular preparation for anticoagulation

There is no evidence to support the need of anticoagulation. But the patients with malignant insulinoma as a part of MEN1 syndrome may have a higher risk of postoperative thrombosis.

## Particular precautions for positioning, transportation and mobilisation

Not reported.

## Interactions of chronic disease and anaesthesia medications

These patients are often on diazoxide, which reduces insulin secretion. Thiopentone sodium can cause severe hypotension as both of these drugs are protein-bound drugs. Enflurane and halothane inhibit pancreatic insulin release, which results in hyperglycaemia. This inhibitory effect is higher with enflurane than with sevoflurane and desflurane.

## Anaesthetic procedure

The patient should get admitted 1 day prior to the scheduled surgery. Intravenous infusion of 10% dextrose should be started for the fasting period. Frequent glucose monitoring is important to prevent plasma glucose level to fall below 40–50 mg/dl at any time. Diazoxide and somatostatin analogues are continued in the morning of surgery to reduce insulin secretion intraoperatively while handling of the tumour.



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General anaesthesia with epidural block is a preferred technique of anaesthesia. Thiopentone sodium is to be avoided for induction. Among inhalational agents, enflurane and halothane should be avoided.

## Particular or additional monitoring

The main concern of anaesthetic management is to prevent hypoglycaemia until tumour resection and the control of rebound hyperglycaemia soon after resection. Various approaches have been described, including the use of “artificial pancreas”, which continuously monitors plasma glucose and delivers glucose or insulin to maintain a predetermined glucose level, but it is not much in use due to its costs and complexity. Another suggested approach is continuous infusion of 10% glucose and every 15 minutes monitoring of blood glucose levels to maintain plasma glucose in the range of 100–150 mg/dl. This method helps to detect sudden hypo- or hyperglycaemia. Other groups recommended this frequency of sampling every 30 minutes. Some surgical groups prefer to maintain moderate hypoglycaemia so that post-resection increase in plasma glucose concentration can be used as an indication of successful tumour removal. But this technique can lead to severe hypoglycaemia intraoperatively, and hyperglycaemic rebound is not adequately reliable as there are reports of both false-positive and false-negative responses. Therefore, this large swing in plasma glucose during handling of the tumour should be carefully monitored and maintained.

## Possible complications

Hypoglycaemia until tumour resection and rebound hyperglycaemia after resection.

## Post-operative care

Usually, the blood glucose rapidly comes back to the normal level after resection of insulinoma, but it may take several hours to several days. During the postoperative period, support by glucose infusion along with strict monitoring helps to maintain optimum level of blood glucose. In this process, the blood glucose level may rise up to 180–230 mg/dl, which may require small doses of insulin. It is recommended to measure the blood glucose level frequently during hospitalisation and once daily after discharge.

## Disease-related acute problems and effect on anaesthesia and recovery

A disease related acute problem is severe hypoglycaemia and associated problems. There may be neurological damage due to a previous hypoglycaemic episode, which should be documented.

Adequate NPO may not be achieved as patients may become symptomatic even after a few hours of fasting and due to poor patient compliance. Hence the risk of aspiration must be considered while inducing these patients and adequate care must be taken.

Rebound hyperglycaemia and associated problems may be a concern during recovery.



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### Ambulatory anaesthesia

The management should be the same.

### Obstetrical anaesthesia

As far as the maintenance of the mother-foetus binomial and a safe clinical treatment are concerned, the use of diet supervised by specialist and the use of drugs such as diazoxide, beta blockers, calcium channel blockers, and octreotide should be taken into consideration.

Regarding anaesthetic management in these patients, the main goal is the same as in non-pregnant patients, i.e. prevention of hypoglycaemia and controlling the hyperglycaemic rebound after resection. Therefore, perioperative and postoperative monitoring and control to prevent major changes in blood glucose levels is recommended.



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