Fuller's Earth

Terra Fullonica; Tierra de Fuller.

CAS — 8031-18-3.

Profile

Fuller's earth consists largely of montmorillonite, a native hydrated aluminium silicate, with which very finely divided calcite (calcium carbonate) may be associated. It is an adsorbent and has been used in dusting powders, toilet powders, and lotions. Fuller's earth of high adsorptive capacity has been used in industry as a clarifying and filtering medium.

It has been used in the treatment of paraquat poisoning (p.2047), usually as a 15% suspension given in an initial oral dose of about 100 g, followed by further doses of about 50 g every 2 hours for 3 doses. Purgatives such as magnesium sulfate or mannitol have been given at the same time to promote emptying of the gut, but some suggest they should only be given with the first dose.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Camomila.

Glucagon *(BAN, rINN)*

Gliukagonas; Glucagón; Glucagonum; Glukagon; Glukagoni; HGF. His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp-Ser-Arg-Arg-Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-Met-Asn-Thr.

Глюкагон

$C_{153}H_{225}N_{43}O_{49}S$ = 3482.7.

CAS — 16941-32-5.

ATC — H04AA01.

ATC Vet — QH04AA01.

Pharmacopoeias. In *US*.

USP 31 (Glucagon). A polypeptide hormone obtained from porcine and bovine pancreas glands. A fine, white or faintly coloured, practically odourless, crystalline powder. Soluble in dilute alkali and acid solutions; insoluble in most organic solvents. Store under nitrogen in airtight glass containers at a temperature of 2° to 8°.

Adverse Effects

Nausea and vomiting may occur after use of glucagon. Hypersensitivity reactions, abdominal pain, hypotension, tachycardia, and hypokalaemia have also been reported.

Precautions

Glucagon should generally not be given to patients with phaeochromocytoma since it can cause a release of catecholamines producing marked hypertension. Glucagon should be given with care to patients with insulinoma as it may induce hypoglycaemia due to its insulin-releasing effect. Glucagon was formerly used to diagnose phaeochromocytoma and insulinoma but this use has been largely abandoned. Caution is also required when it is being used as a diagnostic aid in diabetic patients or in elderly patients with heart disease.

Glucagon is not effective in patients with marked depletion of liver glycogen stores, as in starvation, adrenal insufficiency, alcohol-induced hypoglycaemia, or chronic hypoglycaemia. Oral carbohydrates should be given after glucagon to prevent the development of secondary hypoglycaemia.

Interactions

Warfarin. For a report of glucagon enhancing the anticoagulant effect of warfarin, see p.1431.

Pharmacokinetics

Glucagon has a plasma half-life of about 3 to 6 minutes but longer values have been reported in diabetics (see Bioavailability, below). It is inactivated in the liver, kidneys, and plasma.

Bioavailability. In a study[1] in healthy subjects and diabetic patients the bioavailability of glucagon given intranasally was about 30% of that after intramuscular injection. However, the mean value for the apparent half-life after intramuscular injection was 28.6 and 31.4 minutes respectively in the two groups, compared with 6.6 and 11.9 minutes for intravenous infusion, and 5.5 and 13.8 minutes when given intranasally, possibly due to slow release of glucagon from the injection site.

1. Pontiroli AE, *et al.* Pharmacokinetics of intranasal, intramuscular and intravenous glucagon in healthy subjects and diabetic patients. *Eur J Clin Pharmacol* 1993; **45:** 555–8.

Uses and Administration

Glucagon is an endogenous polypeptide hormone that is produced by the alpha cells of the pancreatic islets of Langerhans. It is a hyperglycaemic that mobilises glucose by activating hepatic glycogenolysis. It can to a lesser extent stimulate the secretion of pancreatic insulin. Glucagon for therapeutic use may be derived from animal sources but is now more commonly produced using recombinant DNA techniques. It is given as the hydrochloride, but doses are usually expressed as glucagon (note that 1 unit is equivalent to 1 mg of glucagon).

Glucagon is used in the treatment of severe hypoglycaemic reactions when the patient cannot take glucose by mouth and intravenous glucose is not feasible. It is given by subcutaneous, intramuscular, or intravenous injection in a dose of 1 mg (or 500 micrograms in patients under about 25 kg body-weight). If there is no response within 10 minutes, intravenous glucose should be given, although there is no contra-indication to repeating the dose of glucagon. Once the patient has responded sufficiently to take carbohydrate orally this should be given to restore liver glycogen stores and prevent secondary hypoglycaemia.

As glucagon reduces the motility of the gastrointestinal tract it is used as a diagnostic aid in gastrointestinal examinations. The route of administration and dose is dependent upon the diagnostic procedure. A dose of 1 to 2 mg intramuscularly has an onset of action of 4 to 15 minutes and a duration of effect of 10 to 40 minutes; 0.2 to 2 mg intravenously produces an effect within 1 minute that lasts for 5 to 25 minutes.

Glucagon possesses positive cardiac inotropic activity but is not generally considered suitable for heart failure. However, as it can bypass blocked beta receptors, it is used in the treatment of beta-blocker overdosage, see Cardiovascular Effects, below.

Intranasal preparations have been studied.

Cardiovascular effects. Glucagon has chronotropic and inotropic effects due to its ability to raise cyclic AMP concentrations independently of a response to catecholamines.[1] It is used in the management of beta-blocker overdosage (p.1227), although evidence of benefit is mainly anecdotal;[2] doses of 2 to 10 mg (or 50 to 150 micrograms/kg in children) by intravenous injection, followed by an infusion of 50 micrograms/kg per hour, have been suggested.

Glucagon may also have a role in anaphylactic shock (see under Adrenaline, p.1205), particularly in patients receiving beta blockers, in whom adrenaline may be less effective. A dramatic improvement in refractory hypotension during an anaphylactic reaction to contrast media was described in a 75-year-old man receiving beta blockers after intravenous glucagon.[3]

There has also been a report[4] of benefit with intravenous glucagon following calcium-channel blocker overdosage, but evidence from controlled studies is not available[2] and glucagon is not generally regarded as standard treatment for such patients.

1. White CM. A review of potential cardiovascular uses of intravenous glucagon administration. *J Clin Pharmacol* 1999; **39:** 442–7.
2. Bailey B. Glucagon in β-blocker and calcium channel blocker overdoses: a systematic review. *J Toxicol Clin Toxicol* 2003; **41:** 595–602.
3. Zaloga GP, *et al.* Glucagon reversal of hypotension in a case of anaphylactic shock. *Ann Intern Med* 1986; **105:** 65–6.
4. Walter FG, *et al.* Amelioration of nifedipine poisoning associated with glucagon therapy. *Ann Emerg Med* 1993; **22:** 1234–7.

Diagnosis and testing. Glucagon stimulates secretion of growth hormone and cortisol (hydrocortisone) and has been used as a test of pituitary function in adults,[1-3] and in children.[4,5] It may be particularly suitable when first-line tests such as the insulin-tolerance test are contra-indicated.[3] The glucagon stimulation test should be used with caution in young children;[5] severe secondary hypoglycaemia and death has been reported[6] in a 2-year-old child after a glucagon test for growth hormone secretion.

1. Gómez JM, *et al.* Growth hormone release after glucagon as a reliable test of growth hormone assessment in adults. *Clin Endocrinol (Oxf)* 2002; **56:** 329–34.
2. Abs R. Update on the diagnosis of GH deficiency in adults. *Eur J Endocrinol* 2003; **148:** S3–S8.
3. Ho KKY. Consensus guidelines for the diagnosis and treatment of adults with GH deficiency II: a statement of the GH Research Society in association with the European Society for Pediatric Endocrinology, Lawson Wilkins Society, European Society of Endocrinology, Japan Endocrine Society, and Endocrine Society of Australia. *Eur J Endocrinol* 2007; **157:** 695–700. Also available at: http://www.ghresearchsociety.org/files/2007_Consensus_AGHD.pdf (accessed 18/07/08)
4. Hindmarsh PC, Swift PGF. An assessment of growth hormone provocation tests. *Arch Dis Child* 1995; **72:** 362–8.
5. GH Research Society. Consensus guidelines for the diagnosis and treatment of growth hormone (GH) deficiency in childhood and adolescence: summary statement of the GH Research Society. *J Clin Endocrinol Metab* 2000; **85:** 3990–3. Also available at: http://www.ghresearchsociety.org/files/Eilat.pdf (accessed 04/10/05)
6. Shah A, *et al.* Hazards of pharmacologic tests of growth hormone secretion in childhood. *BMJ* 1992; **304:** 173–4.

Gastrointestinal disorders. The relaxant effect of glucagon on smooth muscle has been used to facilitate passage of swallowed foreign bodies[1] and impacted food boluses[2] that have become lodged in the lower oesophagus. However, a controlled trial[3] in children with impacted oesophageal coins found that glucagon was not effective.

1. Cooke MW, Glucksman EE. Swallowed coins. *BMJ* 1991; **302:** 1607.
2. Farrugia M, *et al.* Radiological treatment of acute oesophageal food impaction. *Br J Hosp Med* 1995; **54:** 410–11.
3. Mehta D, *et al.* Glucagon use for esophageal coin dislodgment in children: a prospective, double-blind, placebo-controlled trial. *Acad Emerg Med* 2001; **8:** 200–3.

Hypoglycaemia. Hypoglycaemia most commonly occurs in diabetic patients, particularly those receiving insulin therapy. Other rare causes include alcohol ingestion and tumours such as insulinomas. Neonatal hypoglycaemia occurs in small-for-gestational-age infants or infants of diabetic mothers. Persistent or recurrent hypoglycaemia in neonates is usually due to an endocrine or metabolic disorder, such as nesidioblastosis.

Glucose is the treatment of choice for **acute** hypoglycaemia since it corrects the problem at source. In patients who are unconscious or unable to take glucose orally, it may need to be given intravenously. Glucagon is an alternative in such situations, and first-line use has been suggested[1] since it is more convenient and easier to give than parenteral glucose, particularly in emergency situations. However, glucagon has a slower onset and may not always be effective, particularly where hepatic glycogen stores are depleted, such as in patients with alcohol-induced hypoglycaemia or with insulinoma. Low doses of glucagon have also been given prophylactically[2] in diabetic children at risk of developing hypoglycaemia due to gastrointestinal disorders or reduced oral intake.

Hypoglycaemia in neonates is usually managed by adjusting the enteral feeds or by giving parenteral glucose in symptomatic infants. Glucagon may be used if parenteral glucose is not effective or cannot be given.[3,4] In infants with persistent hyperinsulinaemic hypoglycaemia,[5] continuous infusion of glucagon has been used, although oral treatments such as diazoxide or chlorothiazide are usually preferred.

Intractable hypoglycaemia (such as that resulting from excessive endogenous insulin production from islet cell tumours or hyperplasia) is usually treated with diazoxide, but continuous infusion of glucagon has been used in patients with tumour-associated hypoglycaemia.[6,7]

1. Gibbins RL. Treating hypoglycaemia in general practice. *BMJ* 1993; **306:** 600–1.
2. Haymond MW, Schreiner B. Mini-dose glucagon rescue for hypoglycemia in children with type 1 diabetes. *Diabetes Care* 2001; **24:** 643–5.
3. Carter PE, *et al.* Glucagon for hypoglycaemia in infants small for gestational age. *Arch Dis Child* 1988; **63:** 1264.
4. Williams AF. Hypoglycaemia of the newborn: a review. *Bull WHO* 1997; **75:** 261–90.
5. Aynsley-Green A, *et al.* Practical management of hyperinsulinism in infancy. *Arch Dis Child Fetal Neonatal Ed* 2000; **82:** F98–F107.
6. Samaan NA, *et al.* Successful treatment of hypoglycemia using glucagon in a patient with an extrapancreatic tumor. *Ann Intern Med* 1990; **113:** 404–6.
7. Hoff AO, Vassilopoulou-Sellin R. The role of glucagon administration in the diagnosis and treatment of patients with tumor hypoglycemia. *Cancer* 1998; **82:** 1585–92.

Liver disorders. For references to the use of glucagon with insulin in the treatment of liver disorders, see under Insulin, p.452.

Preparations

USP 31: Glucagon for Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: GlucaGen; ***Austral.:*** GlucaGen; ***Austria:*** GlucaGen; ***Belg.:*** GlucaGen; ***Braz.:*** GlucaGen; ***Cz.:*** GlucaGen; ***Denm.:*** GlucaGen; ***Fin.:*** GlucaGen; ***Fr.:*** GlucaGen; ***Ger.:*** GlucaGen; ***Gr.:*** GlucaGen; ***Hong Kong:*** GlucaGen; ***Hung.:*** GlucaGen; ***India:*** GlucaGen; ***Irl.:*** GlucaGen; ***Israel:*** GlucaGen; ***Ital.:*** GlucaGen; ***Malaysia:*** GlucaGen; ***Neth.:*** GlucaGen; ***NZ:*** GlucaGen; ***Pol.:*** GlucaGen; ***Port.:*** GlucaGen; ***Rus.:*** GlucaGen (Глюкаген); ***S.Afr.:*** GlucaGen; ***Singapore:*** GlucaGen; ***Spain:*** GlucaGen; ***Switz.:*** GlucaGen; ***Turk.:*** GlucaGen; ***UK:*** GlucaGen; ***USA:*** GlucaGen.

Glucarpidase *(rINN)*

Carboxypeptidase G_2; Glucarpidasa; Glucarpidasum.

Глюкарпидаз

CAS — 9074-87-7.

ATC — V03AF09.

ATC Vet — QV03AF09.