West Middlesex University Hospital

Date of Search: 06 Mar 2017
Sources Searched: Medline, Embase, BNF, DynaMed Plus, NICE Evidence Search

Insulin Degludec (Tresiba) in Pregnancy

Summary

There is no evidence derived from either clinical experience or controlled trials to support the use of insulin degludec (Tresiba) in pregnancy. Animal reproduction studies however have not revealed any differences between insulin degludec and human insulin in terms of embryotoxicity and teratogenicity.

According to the BNF evidence for the safety of long-acting insulins in pregnancy is limited. However, where required isophane insulin can be recommended and insulin detemir may also be considered.

Sources:

European Medicine's Agency: Tresiba Product Characteristics
http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002498/WC500138940.pdf [Last Accessed 06/03/2017]

BNF: Insulins: https://www.evidence.nhs.uk/formulary/bnf/current/6-endocrine-system/61-drugs-used-in-diabetes/611-insulins#PHP4039 [Last Accessed 06/03/2017]

1. Insulin use in pregnancy: An update

Author(s): Blum A.K.

Source: Diabetes Spectrum; 2016; vol. 29 (no. 2); p. 92-97

Publication Date: 2016

Publication Type(s): Journal: Article

Available in full text at Diabetes Spectrum - from Free Access Content

Available in full text at Diabetes Spectrum : A Publication of the American Diabetes Association - from National Library of Medicine

Abstract: Insulin remains the standard of care for the treatment of type 1 diabetes, type 2 diabetes, and uncontrolled gestational diabetes. Tight control maintained in the first trimester and throughout pregnancy plays a vital role in decreasing poor fetal outcomes, including structural anomalies, macrosomia, hypoglycemia of the newborn, adolescent and adult obesity, and diabetes. Understanding new insulin formulations and strengths is important in assessing risks, since no data on their use in human pregnancy exist. Copyright © 2016 by the American Diabetes Association.

Database: EMBASE

2. Safety of insulin analogues as compared with human insulin in pregnancy.

Author(s): Toledano, Yoel; Hadar, Eran; Hod, Moshe

Source: Expert opinion on drug safety; Jul 2016; vol. 15 (no. 7); p. 963-973

Publication Date: Jul 2016

Publication Type(s): Comparative Study Journal Article Review

Abstract:INTRODUCTION Diabetes during pregnancy may lead to maternal, fetal and neonatal complications. In order to limit unwarranted outcomes, strict glycemic control is essential. In the past, human insulin was the only insulin formulation administered in pregnancy. However, insulin analogues have also been used for this indication in recent years. AREAS COVEREDThis article reviews the published data regarding the safety of insulin analogue use during pregnancy. We present the qualities, advantages and pitfalls of insulin analogue use in pregnancy compared with human insulin. Insulins lispro, aspart and detemir are safe in pregnant women with type 1 diabetes. Correspondingly, they were reclassified for the treatment of pregnant women with diabetes from category C to category B. For insulin glargine use in pregnancy, most studies are small and retrospective. Yet, no major safety concerns were reported. Insulin glulisine and degludec have not been studied in pregnancy. EXPERT OPINION Insulin analogues are viable therapeutic options for diabetes in pregnancy, specifically lispro, aspart and detemir. Though data in limited, their safety and efficacy are comparable with human insulin. Remarkably, the analogues are superior to human insulin regarding hypoglycaemia risk. More data, specifically for their use in pregnancies complicated by gestational diabetes or type 2 diabetes, is needed.

Database: Medline

3. Insulin analogues in pregnancy and specific congenital anomalies: A literature review

Author(s): de Jong J.; de Jong-van den Berg L.T.W.; Wang H.; Garne E.; Wender-Ozegowska E.; Morgan M.

Source: Diabetes/Metabolism Research and Reviews; May 2016; vol. 32 (no. 4); p. 366-375

Publication Date: May 2016

Publication Type(s): Journal: Article

Available in full text at Diabetes/Metabolism Research and Reviews - from John Wiley and Sons

Abstract: Insulin analogues are commonly used in pregnant women with diabetes. It is not known if the use of insulin analogues in pregnancy is associated with any higher risk of congenital anomalies in the offspring compared with use of human insulin. We performed a literature search for studies of pregnant women with pregestational diabetes using insulin analogues in the first trimester and information on congenital anomalies. The studies were analysed to compare the congenital anomaly rate among foetuses of mothers using insulin analogues with foetuses of mothers using human insulin. Of 29 studies, we included 1286 foetuses of mothers using short-acting insulin analogues with 1089 references of mothers using human insulin and 768 foetuses of mothers using long-acting insulin analogues with 685 references of mothers using long-acting human insulin (Neutral Protamine Hagedorn). The congenital anomaly rate was 4.84% and 4.29% among the foetuses of mothers using lispro and aspart. For glargine and detemir, the congenital anomaly rate was 2.86% and 3.47%, respectively. No studies on the use of insulin glulisine and degludec in pregnancy were found. There was no statistically significant difference in the congenital anomaly rate among foetuses exposed to insulin analogues (lispro, aspart, glargine or detemir) compared with those exposed to human insulin or Neutral Protamine Hagedorn insulin. The total prevalence of congenital anomalies was not increased for foetuses exposed to insulin analogues. The small samples in the included studies provided insufficient statistical power to identify a moderate increased risk of specific congenital anomalies. Copyright © 2016 John Wiley & Sons, Ltd.

Database: EMBASE

4. Insulin degludec (Tresiba) - a new long-acting insulin for diabetes

Author(s): anonymous

Source: Medical Letter on Drugs and Therapeutics; Dec 2015; vol. 57 (no. 1483); p. 163-164

Publication Date: Dec 2015

Publication Type(s): Journal: Article

Available in full text at Medical Letter on Drugs and Therapeutics, The - from ProQuest

Database: EMBASE

5. Insulin degludec (New Drug)

Author(s): anonymous

Source: Prescrire International; Jun 2014; vol. 23 (no. 150); p. 149

Publication Date: Jun 2014

Publication Type(s): Journal: Article

Abstract:* Insulin isophane (NPH) is the standard long-acting human insulin for patients with type 1 and type 2 diabetes. Long-acting human insulin analogues are also available: insulin glargine and insulin detemir. Uncertainties remain concerning their long-term adverse effects. * Insulin degludec (Tresibadegree , Novo Nordisk) is another long-acting human insulin analogue, also approved in the EU for patients with type 1 and type 2 diabetes. It was authorised at a concentration of 100 units per ml, like other insulins, and also at a concentration of 200 units per ml. * There are no comparative data on insulin degludec 200 units per ml in patients using high doses of insulin. * Insulin degludec has mainly been evaluated in ten randomised, unblinded, "non-inferiority" trials lasting 26 to 52 weeks, nine versus insulin glargine and one versus insulin detemir . Insulin degludec was administered at a fixed time each evening, or in either the morning or evening on alternate days, at varying intervals of 8 to 40 hours between doses. Efficacy in terms of HbA1c control was similar to that of the other insulin analogues administered once a day. * The frequency of severe hypo - glycaemia was similar in the groups treated with insulin degludec and those treated with the other insulins (10% to 12% among patients with type 1 diabetes and less than 5% in patients with type 2 diabetes). * Deaths and other serious adverse events were similarly frequent in the different groups. A meta-analysis of clinical trials, carried out by the US Food and Drug Administration, suggested an increase of about 60% in the incidence of cardiovascular complications, based on a composite endpoint combining myocardial infarction, stroke and cardiovascular death. * Other adverse effects observed in these trials were already known to occur with human insulin and its analogues, including weight gain, hypersensitivity reactions, reactions at the injection site, etc. The trials were too short in duration to assess long-term harms, particularly cancer. * Clinical experience with insulin degludec in pregnant women is very limited. It is therefore best to avoid using this analogue during pregnancy. * In France, the concentration of all other insulins injected with a syringe or prefilled pen is 100 units per ml. The new concentration of 200 units per ml contained in insulin degludec prefilled pens creates a risk of confusion and overdose. * In practice, there is already a relatively wide range of options available for patients with type 1 or type 2 diabetes who require insulin therapy. As insulin degludec has no proven advantages, it is better to avoid using it, at least pending further data on the risk of cardiovascular events. Insulin isophane remains the first-choice long-acting insulin, while insulin glargine is most appropriate for some patients with type 1 diabetes. ©Prescrire.

Database: EMBASE

6. The use of insulin analogues in pregnancy

Author(s): Lambert K.; Holt R.I.G.

Source: Diabetes, Obesity and Metabolism; Oct 2013; vol. 15 (no. 10); p. 888-900

Publication Date: Oct 2013

Publication Type(s): Journal: Review

Available in full text at Diabetes, Obesity and Metabolism - from John Wiley and Sons

Abstract: Excellent glycaemic control is essential in pregnancy to optimise maternal and foetal outcomes. The aim of this review is to assess the efficacy and safety of insulin analogues in pregnancy. Insulin lispro and insulin aspart are safe in pregnancy and may improve post-prandial

glycaemic control in women with type 1 diabetes. However, a lack of data indicating improved foetal outcomes would suggest that there is no imperative to switch to a short-acting analogue where the woman's diabetes is well controlled with human insulin. There are no reports of the use of insulin glulisine in pregnancy and so its use cannot be recommended. Most studies of insulin glargine in pregnancy are small, retrospective and include women with pre-existing diabetes and gestational diabetes. There appear to be no major safety concerns and so it seems reasonable to continue insulin glargine if required to achieve excellent glycaemic control. A head-to-head comparison between insulin detemir and NPH insulin in women with type 1 diabetes showed that while foetal outcomes did not differ, fasting plasma glucose improved with insulin detemir without an increased incidence of hypoglycaemia. The greater evidence base supports the use of insulin detemir as the first line long-acting analogue in pregnancy but the lack of definitive foetal benefits means that there is no strong need to switch a woman who is well controlled on NPH insulin. There seems little justification in using long acting insulin analogues in women with gestational diabetes or type 2 diabetes where the risk of hypoglycaemia is low. © 2013 John Wiley & Sons Ltd.

Database: EMBASE

DISCLAIMER: Results of database and or Internet searches are subject to the limitations of both the database(s) searched, and by your search request. It is the responsibility of the requestor to determine the accuracy, validity and interpretation of the results.

Strategy 151347

#	Database	Search term	Results
1	EMBASE	*"INSULIN DEGLUDEC"/	527
2	EMBASE	("Insulin degludec").ti,ab	652
3	EMBASE	(Tresiba).ti,ab	23
4	EMBASE	(1 OR 2 OR 3)	699
5	EMBASE	(pregn*).ti,ab	542724
6	EMBASE	exp PREGNANCY/	722248
7	EMBASE	exp "PREGNANCY IN DIABETICS"/	28254
8	EMBASE	(5 OR 6 OR 7)	870373
9	EMBASE	(4 AND 8)	6
10	EMBASE	("long acting insulin*").ti,ab	1419
11	EMBASE	*"LONG ACTING INSULIN"/	548
12	EMBASE	(10 OR 11)	1672
13	EMBASE	(8 AND 12)	85
14	EMBASE	exp "INSULIN DEGLUDEC"/	885
15	EMBASE	(8 AND 14)	22
16	Medline	("Insulin degludec").ti,ab	243
17	Medline	(Tresiba).ti,ab	11
18	Medline	(16 OR 17)	245
19	Medline	(pregn*).ti,ab	392284
20	Medline	exp PREGNANCY/	803297

21	Medline	exp "DIABETES, GESTATIONAL"/	9070
22	Medline	(19 OR 20 OR 21)	884456
23	Medline	(18 AND 22)	1
24	PubMed	("Insulin degludec").ti,ab	281
25	PubMed	(Tresiba).ti,ab	11
26	PubMed	(24 OR 25)	283
27	PubMed	(pregn*).ti,ab	903660
28		(26 AND 27)	2
29	Medline	(degludec).ti,ab	270
30	Medline	(22 AND 29)	3
31	PubMed	(degludec).ti,ab	304
32	PubMed	(27 AND 31)	4
33	EMBASE	(degludec).ti,ab	701
34	EMBASE	(8 AND 33)	8