For Best Practices in Health
CDBPS-H
Pour des Bonnes Pratiques en Santé

WORLD DIABETES DAY, 14th NOVEMBER 2017

World Diabetes Day is celebrated every year on November 14th. This date was chosen because it is the birthday of Frederick Banting, who with Charles Best, first developed the theory of insulin discovery in 1992.
Diabetes prevalence has been rising more rapidly in middle- and low-income countries.
Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.
In 2015, an estimated 1.6 million deaths were directly caused by diabetes. Another 2.2 million deaths were attributable to high blood glucose in 2012. WHO projects that diabetes will be the seventh leading cause of death in 2030.
The Centre for Development of Best Practices in Health (CDBPH) provides to readers, this booklet illustrating summaries in English and French, of Cochrane systematic reviews on prevention and management of diabetes.

JOURNEE MONDIALE CONTRE LE DIABETE, le 14 NOVEMBRE 2017

La Journée Mondiale du Diabète est célébrée le 14 Novembre. Cette date a été choisie car c'est l'anniversaire de Frederick Banting, qui avec Charles Best, a développé la théorie de la découverte de l'insuline en 1992.
La prévalence du diabète a augmenté plus rapidement dans les pays à revenu faible ou intermédiaire. Le diabète est une cause majeure de cécité, d'insuffisance rénale, d'accidents cardiaques, d'accidents vasculaires cérébraux et d'amputation des membres inférieurs. En 2015, on a estimé que 1,6 million de décès étaient directement dus au diabète et que 2,2 millions de décès supplémentaires devaient être attribués à l'hyperglycémie en 2012. L'OMS prévoit qu'en 2030, le diabète sera la 7e cause de décès dans le monde.
De concert avec la communauté internationale, le Centre pour le Développement des Bonnes Pratiques en Santé (CDBPS-H) met à la disposition des lecteurs, cette brochure illustrant des résumés en Anglais et en Français, de revues systématiques Cochrane sur la prévention et la prise en charge du diabète.

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1. Combinations of insulin and oral glucose-lowering drugs for people with type 2 diabetes on insulin treatment

Introduction

Many guidelines on type 2 diabetes recommend a glycosylated haemoglobin A1c (HbA1c) level below 7%. HbA1c levels in the blood express glucose or glycaemic control over a longer time period (two to three months). During the course of type 2 diabetes it will get more difficult to reach these levels with 'lifestyle' modification (diet, exercise or both) and oral glucose-lowering agents alone. Finally, a substantial number of people will need insulin therapy for better glycaemic control. Insulin therapy can be initiated as insulin alone, called monotherapy (which means that oral glucose-lowering medication will be stopped) or in combination with oral glucose-lowering agents. In the former case, oral blood glucose-lowering agents can be added at a later stage, if insulin monotherapy fails to achieve a good HbA1c level. Hypoglycaemia and weight gain are the most common and well known side effects of insulin therapy. Adding oral agents to insulin could reduce the required insulin dose and thus decrease these insulin-related side effects. However, there could be other side effects specific to the various oral blood glucose-lowering drugs.

Review question

To assess the effects of insulin monotherapy and the addition of an oral antidiabetic drug in people with type 2 diabetes already treated with insulin but not having good glycaemic control.

Background

It is unclear whether people with type 2 diabetes mellitus on insulin alone who do not achieve good glucose levels should continue with insulin alone or can benefit from adding an oral antidiabetic drug to their insulin therapy.

Study characteristics

All 37 included studies were randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups). Their duration ranged from 2 to 12 months. The total number of participants was 3227. Several types of insulin monotherapy (once-daily long- or intermediate-acting insulin, twice-daily premixed insulin, multiple injection therapy with short-acting insulin) were compared with different types of additional antidiabetic tablets: sulphonylureas (such as glibenclamide/glyburide), metformin, alpha-glucosidase inhibitors (such as acarbose), pioglitazone and DPP-4 inhibitors (such as saxagliptin).

Key results

The addition of oral agents to insulin monotherapy reduced HbA1c by 0.4% to 1%. Most combinations of oral antidiabetic agents with insulin resulted in a reduction in the necessary insulin dose per day whereas the insulin dose per day had to be increased or remained stable in participants with insulin monotherapy. In studies reporting hypoglycaemic episodes severe events were rare and mild to moderate hypoglycaemia was observed in similar numbers when comparing insulin monotherapy to the addition of oral antidiabetic agents to insulin. However, most studies adding sulphonylureas to insulin reported more hypoglycaemic episodes. Moreover, the addition of sulphonylureas to insulin resulted in an additional weight gain of 0.4

kg to 1.9 kg compared with -0.8 kg to 2.1 kg in the insulin monotherapy groups. Pioglitazone insulin combination therapy caused on average an increase in weight of 3.8 kg compared with insulin monotherapy. The difference in average weight gain with metformin insulin combination therapy compared with insulin monotherapy was 2.1 kg less in favour of the combination therapy. Gastro-intestinal side effects such as flatulence and diarrhoea were mostly reported with metformin and alpha-glucosidase inhibitors. Addition of pioglitazone to insulin compared with insulin monotherapy resulted in more cases of oedema (fluid retention in the body) and heart failure. Only one study assessed participants' treatment satisfaction and showed no substantial differences between the addition of glimepiride or metformin and glimepiride to insulin compared with insulin monotherapy. No study assessed all-cause mortality, diabetes-related morbidity or health-related quality of life.

This evidence is up to date as of November 2015.

Quality of the evidence

Almost a third of the studies had 30 or fewer participants. A lot of studies seemed to be underpowered and thus were probably not able to answer their own research question. This could mean that potentially important differences between intervention and control groups were not detected. Only five studies had a follow-up of 12 months.

Combinaison de l'insuline et de médicaments hypoglycémiants oraux chez les patients atteints de diabète de type 2 sous insulinothérapie

Introduction

De nombreuses directives sur le diabète de type 2 préconisent le maintien du taux d'hémoglobine glycosylée (ou glyquée) A1c (HbA1c) en dessous de 7 %. Le taux sanguin d'HbA1c est un marqueur du contrôle de la glycémie sur une longue durée (deux à trois mois). Au cours de l'évolution d'un diabète de type 2, il devient plus difficile d'atteindre ce taux par les modifications du mode de vie (régime alimentaire, activité physique ou les deux) et en prenant seulement des hypoglycémiants oraux. Beaucoup de sujets diabétiques finissent par avoir besoin d'une insulinothérapie pour obtenir un meilleur contrôle de la glycémie. L'insulinothérapie peut être mise en place en utilisant seulement de l'insuline, en monothérapie (ce qui suppose d'arrêter les hypoglycémiants oraux), ou en la combinant à des hypoglycémiants oraux. Dans le premier cas, des hypoglycémiants oraux pourront être ajoutés par la suite si l'insuline en monothérapie ne permet pas d'atteindre un bon taux d'HbA1c. L'hypoglycémie et la prise de poids sont les effets secondaires les plus courants et les mieux connus de l'insulinothérapie. L'ajout de médicaments oraux à l'insuline pourrait réduire la dose d'insuline nécessaire et limiter ainsi ces effets secondaires. Il pourrait toutefois y avoir alors d'autres effets secondaires spécifiques des différents médicaments hypoglycémiants pris par voie orale.

Question de la revue

Évaluer les effets de l'insuline en monothérapie et de l'ajout d'un médicament antidiabétique oral chez les patients atteints de diabète de type 2 déjà traités avec de l'insuline mais dont la glycémie est mal contrôlée.

Contexte

Le bénéfice relatif du maintien sous insuline seule et de l'ajout d'un antidiabétique oral à l'insulinothérapie chez les diabétiques de type 2 dont la glycémie répond mal à l'insuline seule n'est pas précisément établi.

Caractéristiques de l'étude

Toutes les 37 études incluses étaient des essais contrôlés randomisés (études cliniques où les gens sont assignés de façon aléatoire dans un des deux ou plusieurs groupes de traitement), d'une durée de 2 à 12 mois et totalisant 3227 participants. Plusieurs types d'insuline en monothérapie (insuline à durée d'action longue ou moyenne une fois par jour, insuline prémélangée deux fois par jour, traitement par injections multiples d'insuline à courte durée d'action) ont été comparés avec différents types d'antidiabétiques supplémentaires en comprimés : sulfonylurées (par ex. glibenclamide/glyburide), metformine, inhibiteurs de l'alpha-glucosidase (par ex. acarbose), pioglitazone et inhibiteurs de la DPP-4 (par ex. saxagliptine).

Principaux résultats

L'ajout d'agents oraux à l'insuline en monothérapie a réduit l'HbA1c de 0,4 % à 1 %. La plupart des combinaisons d'antidiabétiques oraux avec de l'insuline ont permis une réduction de la dose d'insuline nécessaire par jour, tandis que cette dose a dû être augmentée ou est restée stable chez les participants prenant de l'insuline en monothérapie. Dans les études rapportant des épisodes d'hypoglycémie, les événements graves ont été rares et un nombre comparable d'hypoglycémies légères à modérées a été observé avec l'insuline en monothérapie et l'association d'antidiabétiques oraux à l'insuline. Cependant, la plupart des études ont rapporté davantage d'épisodes d'hypoglycémie avec l'ajout de sulfonylurées à l'insuline. En outre, l'ajout de sulfonylurées à l'insuline a entraîné une prise de poids supplémentaire de 0,4 kg à 1,9 kg contre -0,8 kg à 2,1 kg dans les groupes sous insuline en monothérapie. Le traitement combiné par la pioglitazone et l'insuline a entraîné une prise de poids supplémentaire moyenne de 3,8 kg par rapport à l'insuline en monothérapie. La différence de prise de poids moyenne sous metformine et insuline par rapport à l'insuline en monothérapie était inférieure de 2,1 kg avec le traitement combiné. Des effets secondaires gastro-intestinaux tels que flatulences et diarrhées ont été rapportés essentiellement avec la metformine et les inhibiteurs de l'alpha-glucosidase. L'ajout de la pioglitazone à l'insuline a entraîné davantage de cas d'œdème (rétention de liquides dans les tissus) et d'insuffisance cardiaque que l'insuline en monothérapie. Une seule étude a évalué la satisfaction des participants envers le traitement et n'a montré aucune différence substantielle entre l'ajout de glimépiride ou de metformine et de glimépiride à l'insuline et l'insuline en monothérapie. Aucune étude n'a évalué la mortalité toutes causes confondues, la morbidité liée au diabète ou la qualité de vie liée à la santé.

Les données sont à jour à la date de novembre 2015.

Qualité des données probantes

Près d'un tiers des études comptaient 30 participants ou moins. De nombreuses études avaient apparemment une puissance insuffisante et n'étaient donc probablement pas en mesure de répondre à leur propre problématique de recherche. Cela pourrait signifier que des différences potentiellement importantes entre les groupes d'intervention et témoin n'ont pas été détectées. Seules cinq études présentaient un suivi de 12 mois.

Citation: Citation: Vos RC, van Avendonk MJP, Jansen H, Goudswaard AN, van den Donk M, Gorter K, Kerssen A, Rutten GEHM. Insulin monotherapy compared with the addition of oral glucose-lowering agents to insulin for people with type 2 diabetes already on insulin therapy and inadequate glycaemic control. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD006992. DOI: 10.1002/14651858.CD006992.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006992.pub2/epdf

2. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes

Pregnancy profoundly affects the management of diabetes and having diabetes can lead to complications in pregnancy. The most common complications are early births, large babies, difficult births and the need for caesarean section. Increased risks for the infants at birth include bleeding in the brain (intracranial haemorrhage), the baby's shoulder becomes stuck (shoulder dystocia), neonatal low blood sugar levels (hypoglycaemia), jaundice and respiratory distress. The babies are more likely to be admitted to an intensive care unit, and the growing child has an increased risk of having diabetes. Women with existing diabetes that is not well controlled at the time of conception and in the first trimester are at increased risk of miscarriage, having a baby with malformations or a stillbirth. It is important that women's blood glucose levels are very carefully monitored during pregnancy so that appropriate drug or dietary steps can be taken to control the blood glucose levels and to reduce the risk of complications. Several methods for monitoring blood glucose levels are used including self-monitoring, use of telemedicine, continuous glucose monitoring or clinic monitoring during regular antenatal visits. This review collected all the available high-quality research evidence in order to find out if one monitoring method is more effective than another in maternal glycaemic control (fasting blood glucose and glycosylated haemoglobin A1c (HbA1c)), controlling infant birthweight and reducing the risk of complications. The review determined that there is not enough evidence to say with any certainty which monitoring method is best. The nine included trials involved a total of 506 women (436 women with Type 1 diabetes and 70 women with Type 2 diabetes). The trials were from European countries and the USA. The trials looked at different techniques of monitoring and reported on different outcomes. Three comparisons were from single trials only. The number of women in each study was generally small. Five of the nine included studies were at moderate risk of bias and four studies were at low to moderate risk of bias. More research is needed to find out which monitoring method is best at reducing the risk of complications.

Techniques de surveillance glycémique pendant la grossesse chez les femmes atteintes de diabète préexistant

La grossesse affecte profondément la prise en charge du diabète et le diabète peut entraîner des complications pendant la grossesse. Les complications les plus courantes sont un accouchement prématuré, un gros bébé, un accouchement difficile et le recours à une césarienne. Les risques accrus chez les nourrissons incluent des saignements dans le cerveau (hémorragie intracrânienne), l'épaule du bébé se coince (dystocie de l'épaule), un faible taux de glycémie chez le nouveau-né (hypoglycémie), une jaunisse et une détresse respiratoire. Les bébés sont plus susceptibles d'être admis en unité de soins intensifs, et en grandissant, l'enfant a un risque accru de développer un diabète. Les femmes

atteintes de diabète qui n'est pas adéquatement contrôlé au moment de la conception et au cours du premier trimestre présentent un risque accru de fausse couche, d'accoucher d'un bébé atteint de malformations ou mort-né.

Il est important que le taux de glycémie soit adéquatement surveillé avec une attention particulière au cours de la grossesse, pour que des médicaments ou une alimentation appropriés soient prescrits afin de contrôler la glycémie et de réduire le risque de complications. Plusieurs méthodes pour surveiller les taux de glycémie sont utilisées, y compris l'auto surveillance, l'utilisation de la télémédecine, la surveillance en continu du glucose ou la surveillance clinique lors des visites prénatales régulières. Cette revue a rassemblé toutes les preuves disponibles issues de recherches de haute qualité afin de déterminer si une méthode de surveillance est plus efficace qu'une autre pour le contrôle de la glycémie de la mère (glycémie à jeun et hémoglobine glycosylée A1c (HbA1c)), contrôlant le poids de naissance du nouveau-né et réduisant le risque de complications.

La revue a indiqué qu'il n'existe pas suffisamment de preuves pour déterminer avec certitude la meilleure méthode de surveillance. Les neuf essais inclus portaient sur un total de 506 femmes (436 femmes atteintes de diabète de type 1 et 70 femmes atteintes de diabète de type 2). Les essais ont été effectués dans des pays européens et aux États-Unis. Les essais ont examiné différentes techniques de surveillance et rapportaient sur les différents critères de jugement. Trois comparaisons provenaient seulement d'essais uniques. Le nombre de femmes dans chaque étude était généralement de petite taille. Cinq des neuf études incluses présentaient un risque de biais modéré et quatre études étaient à risque de biais faible à modéré.

Des recherches supplémentaires sont nécessaires pour identifier la meilleure méthode de surveillance permettant de réduire le risque de complications.

Citation: Moy FM, Ray A, Buckley BS. Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes. *Cochrane Database of Systematic Reviews* 2014, Issue 4. Art. No.: CD009613. DOI: 10.1002/14651858.CD009613.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009613.pub2/pdf

3. Different strategies for diagnosing gestational diabetes to improve maternal and infant health

There is not enough evidence to judge which is the best way to identify women who have gestational diabetes. Insulin is a hormone produced in the pancreas that enables cells to absorb glucose in order to turn it into energy. During pregnancy maternal resistance to the action of insulin develops so that glucose can be more easily transported across the placenta to the growing fetus. Resistance to insulin becomes apparent in the second trimester and declines progressively to term. Insulin resistance returns to normal after pregnancy, usually within six weeks of the birth. For about seven in every 100 pregnant women, resistance to insulin is excessive and the woman's blood sugar becomes too high. This is known as gestational diabetes.

If gestational diabetes develops and the resistance to maternal insulin becomes too pronounced, fetal hyperinsulinaemia can cause accelerated growth with fetal adiposity, increased birthweight and perinatal complications. The woman and her baby can be harmed

by the high blood sugar levels if untreated, and there may be adverse effects after pregnancy. Evidence is increasing that the offspring are at increased risk of obesity and high blood pressure in later life.

Lowering blood sugar levels can reduce the harmful effects, but women will only receive treatment if they are correctly identified early enough in pregnancy. Several tests are used to find out if a woman has gestational diabetes. Most involve giving the woman a very sugary drink or food, and taking a series of blood sugar tests over one to three hours; this is known as the oral glucose tolerance test (OGTT). Limitations of the OGTT are that it requires women to fast from the night before, drink a glucose solution and wait for two or three hours before having the final blood test. Therefore, other tests have also been proposed that do not require this level of involvement by the pregnant women or healthcare staff. These include taking just one blood test after an overnight fast or taking just one test with no fasting. This review aimed to determine what was the best way of identifying women with gestational diabetes. We identified five small randomised trials (involving 578 women) of unclear quality, comparing different ways of giving a glucose load.

None evaluated the important question of when the best time is during pregnancy to test women for gestational diabetes or compared the 75 g or 100 g oral glucose tolerance test with other strategies. Large well-designed trials are needed to provide information about the best way of identifying women who have gestational diabetes.

Différentes façons de repérer les femmes atteintes de diabète gestationnel

On ne dispose pas de suffisamment d'éléments probants pour juger la meilleure façon de repérer les femmes atteintes d'un diabète gestationnel.

L'insuline est une hormone produite par le pancréas qui permet aux cellules d'absorber le glucose afin de le transformer en énergie. Pendant la grossesse, la résistance maternelle à l'action de l'insuline se développe de manière à ce que le glucose puisse être plus facilement transporté à travers le placenta vers le fœtus en croissance. La résistance à l'insuline devient apparente au deuxième trimestre et décline progressivement jusqu'au terme. La résistance à l'insuline revient à la normale après la grossesse, généralement dans les six semaines suivant l'accouchement. Chez environ sept femmes enceintes sur 100, la résistance à l'insuline est excessive et le niveau de sucre dans le sang devient trop élevé. Cela s'appelle le diabète gestationnel.

Si le diabète gestationnel se développe et que la résistance à l'insuline maternelle devient trop prononcée, une hyper-insulinémie fœtale peut provoquer une croissance accélérée de l'adiposité fœtale, une augmentation du poids de naissance et des complications périnatales. Si le taux de sucre sanguin élevé n'est pas traité, cela peut être préjudiciable à la femme et à son bébé et entrainer des effets néfastes après la grossesse. Il y a de plus en plus de preuves que la progéniture aura alors un risque accru d'obésité et d'hypertension artérielle dans sa vie ultérieure.

Abaisser le taux de sucre sanguin peut réduire les effets nocifs, mais les femmes ne pourront être traitées que si elles sont diagnostiquées suffisamment tôt dans la grossesse. Plusieurs tests sont utilisés pour savoir si une femme souffre de diabète gestationnel. La plupart impliquent de donner à la femme une boisson ou un aliment très sucré et d'effectuer une série de tests de glycémie sur une à trois heures ; c'est ce qui est appelé le test de tolérance au glucose oral (TTGO). Les limitations du TTGO

tiennent au fait qu'il demande à la femme de jeûner depuis la veille au soir, de boire une solution de glucose et d'attendre deux ou trois heures avant que ne soit effectuée la dernière prise de sang. C'est pourquoi d'autres tests ont également été proposés qui ne nécessitent pas un tel niveau de participation de la femme enceinte ou du personnel de santé. Il s'agit notamment de n'effectuer qu'une prise de sang à jeun le matin ou d'effectuer une seule prise de sang sans avoir à jeûner. Cette revue visait à déterminer la meilleure façon de repérer les femmes atteintes de diabète gestationnel. Nous avons identifié cinq petits essais randomisés (portant sur 578 femmes) de qualité incertaine, comparant différentes façons d'ingérer une charge de glucose. Aucune n'a abordé l'importante question de savoir quel est le meilleur moment pendant la grossesse pour diagnostiquer le diabète gestationnel ou pour comparer les doses de 75 g ou 100 g pour la tolérance au glucose oral avec d'autres stratégies. Des essais bien conçus et de grande dimension seront nécessaires pour fournir des informations sur la meilleure façon de repérer les femmes souffrant de diabète gestationnel.

Traduction réalisée par Cochrane France

Citation: Farrar D, Duley L, Lawlor DA. Different strategies for diagnosing gestational diabetes to improve maternal and infant health. *Cochrane Database of Systematic Reviews* 2011, Issue 10. Art. No.: CD007122. DOI: 10.1002/14651858.CD007122.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007122.pub2/pdf

4. Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria

Gestational diabetes mellitus (GDM) is usually said to be any degree of glucose intolerance or high blood glucose level (hyperglycaemia) that is first recognised during pregnancy. Yet no immediately obvious cut-off points can be labelled as abnormal. It is unclear when treatment should be provided to normalise the blood glucose, as the relationship between increased hyperglycaemia and adverse pregnancy outcomes appears to be continuous. Pre-eclampsia in the mother, birthweight greater than 4000 g (macrosomia), birth trauma with large-for-gestational age (LGA) babies, and a future risk of obesity and diabetes in the mothers and babies are all associated with hyperglycaemia during pregnancy. Intensive management involving lifestyle interventions and metabolic monitoring for women with GDM has been proven beneficial for women and their babies. This review found dietary advice or counselling and blood glucose level monitoring for women with borderline GDMhelped reduce the number of macrosomic and LGA babies. A single trial found that the interventions led to more inductions of labour. The interventions did not increase the risk of caesarean sections, operative vaginal births or women's weight gain in pregnancy. These findings were based on four small randomised controlled trials (involving 543 women). The trials were of moderate to high risk of bias and only data from 521 women and their babies is included in our analyses. Until additional evidence from large well designed randomised trials becomes available, current evidence is insufficient to make conclusive recommendations for the management of women with pregnancy high blood glucose concentrations not meeting GDM (or type 2 diabetes) diagnostic criteria.

Gestion des femmes enceintes qui sont à la limite du diabète gestationnel

Le diabète gestationnel (DG) est généralement défini comme un degré quelconque d'intolérance au glucose ou un niveau élevé de glucose sanguin (hyperglycémie) qui est observé pour la première fois durant une grossesse. Même si cela n'est pas immédiatement évident, il est possible de définir des valeurs seuil étiquetées comme anormales. Il n'est pas clair à partir de quand il convient d'entamer un traitement visant à normaliser la glycémie, car il semble exister une relation continue entre l'augmentation de l'hyperglycémie et les conséquences néfastes sur le pronostic de grossesse. La pré-éclampsie chez la mère, le poids de naissance supérieur à 4 000 g (macrosomie), le traumatisme de naissance du bébé gros pour son âge gestationnel (GAG) et le risque futur d'obésité et de diabète chez la mère et le bébé sont tous associés à l'hyperglycémie pendant la grossesse. La gestion intensive impliquant des interventions sur le mode de vie et la surveillance métabolique des femmes souffrant d'un DG s'est avérée bénéfique pour les femmes et leurs bébés.

Cette revue a permis de constater que le conseil diététique et la surveillance du taux de glycémie chez les femmes se trouvant à la limite du DG ont contribué à réduire le nombre de bébés macrosomes et GAG. Un seul essai a trouvé que les interventions conduisaient à plus d'inductions de travail. Les interventions n'avaient pas augmenté le risque de césarienne, d'accouchement vaginal opératoire ou de prise de poids durant la grossesse. Ces conclusions étaient basées sur quatre petits essais contrôlés randomisés (soit 543 femmes). Les risques de biais des essais étaient modérés à élevés et nous n'avons inclus dans nos analyses que les données de 521 femmes et de leurs bébés. Tant que l'on ne disposera pas de résultats supplémentaires provenant de vastes essais randomisés et bien conçus, les données seront insuffisantes pour formuler des recommandations concluantes concernant la gestion des femmes enceintes ayant un taux de glycémie élevé qui ne remplit pas les critères de diagnostic du DG (ou du diabète de type 2).

Citation: Han S, Crowther CA, Middleton P. Interventions for pregnant women with hyperglycaemia not meeting gestational diabetes and type 2 diabetes diagnostic criteria. *Cochrane Database of Systematic Reviews* 2012, Issue 1. Art. No.: CD009037. DOI: 10.1002/14651858.CD009037.pub2
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009037.pub2/pdf

5. Does taking a supplement of myo-inositol work as an effective treatment for women who develop diabetes during pregnancy?

What is the issue?

During pregnancy the mother develops resistance to insulin and the uptake of glucose from the blood is reduced to ensure the baby has a consistent supply of glucose. The mother has to produce extra insulin to keep her blood glucose levels under control or she is at risk of developing gestational diabetes mellitus (GDM). GDM is diabetes that occurs during pregnancy and resolves after the birth of the baby. It is an increasing problem around the world, causing both long- and short-term complications for the mother and her baby. Women with GDM are at greater risk of developing high blood pressure and having a caesarean section for the birth. Their babies can grow large for their gestational age, which increases the likelihood of having an injury at birth such as broken bones or a shoulder becoming stuck. In the long term both the mother and her child are at increased risk of developing type 2 diabetes.

Why is this important?

Dietary and lifestyle counselling is the first line of treatment for women with GDM. An oral hypoglycaemic drug or insulin therapy is recommended for the women who are still unable to maintain target blood glucose levels. Finding a treatment that controls the mother's blood sugar levels without harming the mother or her baby is important. Myo-inositol is a natural form of inositol that is found in fruits, vegetables, nuts and cereals. It is a simple carbohydrate nutrient the body requires for many cell functions. Myo-inositol is available as a dietary supplement, in water-soluble powder form or as capsules.

What evidence did we find?

We searched for evidence in April 2016 and identified two randomised controlled studies (involving 142 women and their babies). Both studies were conducted in Italy (and were judged to be at an unclear risk of bias). The women were diagnosed with GDM at 12 to 13 weeks' gestation in one study and at 26 weeks' gestation in the other. The findings from these trials suggested that myo-inositol can reduce fasting blood glucose levels. The need for supplementary insulin was not clearly different between the women receiving myo-inositol and the control groups. One of the studies showed reduced glucose levels at one hour after a meal (one study, 73 women) There was no evidence to suggest that the babies were at reduced risk of being born large-for-gestational age (one study, 73 infants). Myo-inositol appeared to reduce the risk of the baby having low blood sugar levels at birth and being born at a later gestational age, although the evidence was of low quality. Many of the infant and maternal outcomes identified as being of interest for this review were not reported in the included studies - these included: high blood pressure during the pregnancy, caesarean section, the development of type 2 diabetes (maternal), and the number of babies who died or were unwell, or the number of babies with neurosensory disability. No long-term outcomes were reported for the mother, infant as a child, infant as an adult or health service outcomes.

What does this mean?

Because of the limited number of studies reporting on myo-inositol for the treatment of women with GDM, lack of data on the outcomes of importance for this review and the low-quality evidence based on two small studies, we cannot be certain if myo-inositol is useful as a treatment intervention for women with GDM. The available evidence is insufficient to support the use of myo-inositol. Further high-quality trials with large sample sizes are required to investigate the role of myo-inositol as a treatment or a co-treatment for women with gestational diabetes.

Citation: Brown J, Crawford TJ, Alsweiler J, Crowther CA. Dietary supplementation with myo-inositol in women during pregnancy for treating gestational diabetes. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD012048. DOI: 10.1002/14651858.CD012048.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012048.pub2/epdf

6. Short-acting insulin analogues versus regular human insulin for type 1 diabetes mellitus

Review question

Are short-acting insulin analogues more useful than regular human insulin for adults with type 1 diabetes?

Background

Diabetes is a condition that causes a person's blood sugar (glucose) level to become too high. Insulin is a hormone that is released by the pancreas (a small organ behind the stomach); it controls the blood levels of glucose. In type 1 diabetes, the pancreas does not produce any insulin so the person has to inject insulin to control their glucose levels and keep well. Short-acting insulin analogues (such as insulin lispro, insulin aspart and insulin glulisine) act more quickly than regular human insulin. They can be injected immediately before meals and lead to lower blood sugar levels after food intake.

Study characteristics

We found nine randomised controlled trials (clinical studies where people are randomly put into one of two or more treatment groups) comparing the insulin analogues, insulin lispro and insulin aspart, to regular human insulin delivered to 2693 participants. The people in the included studies were monitored (called follow-up) for between 24 and 52 weeks.

This evidence is up-to-date as of 15 April 2015.

Key results

According to our analysis, short-acting insulin analogues were slightly better than regular human insulin regarding long-term glycaemic control (where blood glucose is at controlled levels) and showed similar episodes of low blood sugar (called hypoglycaemia), especially with regard to severe (night-time) hypoglycaemia. We found no information on late diabetes complications such as problems with the eyes, kidneys or feet. The studies did not report costs and they were too short to investigate death from any cause reliably. We also found no clear evidence for a marked effect of insulin analogues on the health-related quality of life (which is physical, mental, emotional and social health).

Quality of the evidence

The quality of the included studies was low or very low, mainly because none of the studies was carried out in a blinded way (where healthcare professionals and participants do not know which treatment they received) so that risk of bias, especially for outcomes such as hypoglycaemic episodes, was present in all of the studies. Furthermore, several studies showed inconsistencies in the reporting of methods and results.

Citation: Fullerton B, Siebenhofer A, Jeitler K, Horvath K, Semlitsch T, Berghold A, Plank J, Pieber TR, Gerlach FM. Short-acting insulin analogues versus regular human insulin for adults with type 1 diabetes mellitus. *Cochrane Database of Systematic Reviews* 2016, Issue 6. Art. No.: CD012161. DOI: 10.1002/14651858.CD012161.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012161/epdf

7. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes

What is the issue?

Diabetes is a condition in which glucose (sugar) in the blood is too high because the body does not respond to insulin or not enough insulin is made. Insulin is a hormone made by the pancreas, which allows glucose to enter the cells where it is used as fuel by the body.

Controlling blood sugar levels is important because levels that are too high or too low can affect the brain and other organs of the body. Poor blood sugar control in pregnant women with diabetes can lead to large babies who may then have a difficult birth. It also increases the chance of abnormalities in the baby, miscarriage, or stillbirth.

Traditionally, insulin is given as multiple daily injections (MDI), however a small pump can continuously give insulin through a fine tube under the skin (CSII).

Why is this important?

An insulin pump may help pregnant women keep their blood glucose more stable than multiple injections. It might stop the woman's blood sugar level going too high or too low, which would be better for the mother and her baby and it may be more acceptable to women. This review compared the positive and negative effects of CSII and MDI to work out which is best for mothers and infants.

What evidence did we find?

Five randomised trials involving 153 women (154 pregnancies) were included.

These trials did not report many of the outcomes we had hoped to look at. The evidence was judged to be very low quality for important outcomes (caesarean section, large-for-gestational age, perinatal mortality, and neonatal hypoglycaemia). This was because the trials were small, may not have been fair tests, and did not show a clear difference between MDI and CSII.

There were no clear differences in any of the reported outcomes between women who had insulin via a pump rather than as multiple injections. For mothers, this included caesarean section, weight gain during pregnancy, and blood sugar levels. For babies, this included the baby's weight, if they were born premature, and problems such as difficulty breathing, a low Apgar score at birth, low blood sugar, jaundice, or physical abnormalities.

In one small trial, there was no difference in the number of days mothers spent in hospital. This was the only measure of cost or use of health service resources reported.

What does this mean?

The trials did not provide enough information to know whether an insulin pump or multiple injections are better for a pregnant woman with diabetes or her baby. More research is needed, with bigger groups of women, good reporting of how the trials were undertaken, more outcomes assessed and reported, and using the latest pump technology and insulins.

Citation: Farrar D, Tuffnell DJ, West J, West HM. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes. Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD005542. DOI: 10.1002/14651858.CD005542.pub3
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005542.pub3/epdf

8. What is the best blood glucose target for pregnant women who have type 1 or type 2 diabetes before becoming pregnant?

What is the issue?

Pregnant women with diabetes need to keep their blood glucose levels stable, using diet, exercise, insulin or other drugs, clinic visits and monitoring. This review looked at the best blood glucose target for pregnant women with diabetes.

Why is this important?

Women who have either type 1 or type 2 diabetes before they become pregnant have an increased risk of pregnancy loss, large babies, and babies dying. When a pregnant woman has high blood glucose and insulin resistance this can affect the development of the baby's heart and other organs. Babies born to diabetic mothers may also have a higher risk of developing obesity and type 2 diabetes.

Monitoring a diabetic pregnant woman's blood glucose level and staying within a target range may help to reduce these risks. We wanted to find out what the best blood glucose target is for pregnant women who had type 1 or type 2 diabetes before becoming pregnant.

What evidence did we find?

We found three small trials (in total 223 pregnant women with type 1 diabetes) looking at different blood glucose targets: very tight, tight, moderate, and loose. The quality of the studies and therefore the strength of the evidence was very low or low, so future research may change the results.

There were very few differences between very tight and tight-moderate blood glucose targets in two trials, although there were more cases of low blood glucose (hypoglycaemia) and longer hospital stays for women who had very tight blood glucose control.

A single trial compared tight, moderate, and loose blood glucose targets. In the loose target group, more women had pre-eclampsia, and there were more caesareans and large babies. There were few differences between the tight and moderate groups, although more women in the tight control group had low blood glucose in the first half of pregnancy.

What does this mean?

The evidence does not show much difference between moderate, tight and very tight blood glucose targets, although a loose blood glucose target may be worse for mothers and babies. However, the studies were small and the evidence is weak, so we do not yet know the best blood glucose target for women who have diabetes before becoming pregnant.

Citation: Middleton P, Crowther CA, Simmonds L. Different intensities of glycaemic control for pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD008540. DOI: 10.1002/14651858.CD008540.pub4.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008540.pub4/epdf

9. Oral dextrose gel for treatment of newborn infants with low blood glucose levels

Review question: For hypoglycaemic newborn infants, is oral dextrose gel more effective than placebo, no treatment or other active treatments in correcting hypoglycaemia and reducing long-term neurodevelopmental impairment?

Background: Low blood glucose levels in newborn infants are common and occur frequently in certain at-risk groups (infants of diabetic mothers, preterm infants, small and large infants). Infants with low blood glucose levels are at higher risk for developmental problems later in childhood. Therefore, active treatments are generally used to treat these infants, and such treatments frequently require use of formula milk or admission to the neonatal unit, resulting in temporary separation from the mother.

Study characteristics: Two trials to date have assessed use of dextrose gel to reverse low blood glucose levels while the baby remains in the mother's care; these studies included a total of 312 infants. Investigators rubbed dextrose gel into the inside of the infant's cheek; they provided a normal feed for 157 of these infants and placebo gel plus a normal feed, or a normal feed alone, for 155 infants.

Key results: Results suggest that dextrose gel is effective in keeping mothers and infants together and improving the rate of full breast feeding after discharge from hospital. Researchers reported no adverse effects when dextrose gel was given to infants and no effects on development at two years of age.

The review is limited by lack of data for the important outcomes of effectiveness of treatment for individual episodes of low blood glucose levels and effects on brain injury. Further research is required to address these important questions.

Dextrose gel applied to the inside of the cheek is a simple and safe treatment for initial care of infants with low blood glucose levels.

Quality of evidence: Overall the quality of the evidence was moderate to very low. Reasons for downgrading the quality of evidence included imprecision (variation in data), publication bias (evidence based on data from a single trial; one publication in abstract format only), insufficient detail to allow a judgement about risk of bias and/or high levels of disagreement for a particular outcome.

> **Citation**: Weston PJ, Harris DL, Battin M, Brown J, Hegarty JE, Harding JE. Oral dextrose gel for the treatment of hypoglycaemia in newborn infants. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD011027. DOI: 10.1002/14651858.CD011027.pub2.
> http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011027.pub2/epdf

10. Insulin and oral agents for managing cystic-fibrosis related diabetes

Review question

We reviewed the evidence regarding the use of insulin and oral agents for managing cystic fibrosis-related diabetes.

Background

Cystic fibrosis is the most common life-limiting genetic disease in white populations; it damages the lungs and pancreas. The pancreas makes insulin, which is a hormone needed by the body to take sugar into the cells (like those in the liver, muscle and fat) and convert it into energy. People with cystic fibrosis need high-calorie diets to maintain enough muscles to make up for breathing difficulties resulting from lung damage. It is therefore important for people, who have diabetes as an additional complication to their cystic fibrosis, to turn sugar into energy efficiently, so that they can manage their breathing difficulties and maintain an ideal body weight. The inflammatory processes in cystic fibrosis can firstly reduce insulin production and then lessen its effect by causing insulin resistance. An increased in life expectancy for people with cystic fibrosis means the likelihood of developing cystic fibrosis related diabetes is now at 50%. We therefore wanted to assess different treatments to minimize a decline in health. These treatments include artificial sources of insulin (like long-acting glargine or short-acting protamine insulin) and medications that enhance a person's own insulin release or which affect insulin resistance (specifically as this relates to inflammation seen in this disease process).

Search date

The evidence is current to: 18 February 2016.

Study characteristics

We included four randomized trials with a total of 200 participants. The trials' duration ranged from single doses to 24 months of treatment. Three trials compared insulin (given via a syringe) to repaglinide tablets and recruited 180 people between them. Trial participants had an average age of 25 years and mild to severe diabetes. One of these trials (73 people) compared the two treatment groups directly over a two-year period; the remaining two trials each had a third treatment arm - one (seven people) compared single doses of insulin to repaglinide and to no treatment and the other (100 people) compared insulin to repaglinide and to a placebo (a dummy tablet with no active medication) for 12 months. The fourth trial recruited 20 participants with an average age of 34 years and compared the long-acting insulin glargine to short-term neutral protamine Hagedorn insulin over a 12-week period.

Key results

We were not able to show that any of the treatments were better than the others. Only a few cases of hypoglycemia (low blood sugar) were seen in three out of the four trials (none in the longest trial), but these events resolved without further treatment. Longer-term studies are still needed to see how controlling cystic fibrosis-related diabetes affects lung function. There also needs to be research into the use of agents used together with insulin to enhance its action, especially those agents with additional anti-inflammatory potential.

Quality of the evidence

The participants would have been mostly able to tell which treatment they were receiving (e.g. insulin via a syringe or repaglinide as a tablet), so we thought there was a high risk from blinding in all trials (except when comparing repaglinide tablets to placebo (dummy) tablets). In two trials we are satisfied that participants were put into the different treatment groups completely at random; however, the other two trial reports were not clear on how it was decided which group the participants were put into. In only one trial was it clear that no one knew in advance which group a participant would be put into, in the other three trials there were no details given. There could be some bias if it was known in advance which group the next participant would be in, e.g. healthier participants might be put into one group to show better results for that treatment. There were also many results which were not fully reported in the publications. Finally, there may be bias in the results as the amounts of insulin and repaglinide given were not comparable.

Citation: Onady GM, Stolfi A. Insulin and oral agents for managing cystic fibrosis-related diabetes. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD004730. DOI: 10.1002/14651858.CD004730.pub4.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004730.pub4/epdf

11. What is the most effective blood sugar range to guide treatment for women who develop gestational diabetes mellitus (GMD) in their pregnancy?

What is the issue?

Up to a quarter of pregnant women develop gestational diabetes mellitus (GDM) depending on their ethnicity and the diagnostic criteria used. GDM is evident as high blood sugar levels (hyperglycaemia) during pregnancy and is associated with an increased risk of developing high blood pressure (hypertension) and protein in the urine during pregnancy (pre-eclampsia). These women are more likely to have a caesarean birth, develop type 2 diabetes, postnatal depression, and cardiovascular disease later on in life. The high blood sugar levels that are associated with GDM often return to normal as soon as the baby is born, but women with GDM are at risk of again developing GDM in future pregnancies. Babies whose mothers have been diagnosed with GDM are at an increased risk of having a birthweight greater than 4000 g, increased risk of birth trauma because of their size and developing breathing difficulties after birth. The babies are also at risk of future obesity and type 2 diabetes.

Why is this important?

Women with GDM are treated with the aims of controlling high maternal blood sugar levels and reducing the risks of GDM for the mother and the baby. Blood sugar control is monitored by measuring blood sugar concentrations to ensure they are maintained within a pre-defined level or range. The blood sugar results are usually obtained by the mother using a finger prick to collect a drop of her blood on a test strip, which is inserted into a small machine (a

glucometer) that reads the sugar level of the blood on the test strip. The glucometer reading alerts the pregnant woman to her current blood sugar level and is used to guide her treatment. For example, how many units of insulin she requires before eating. However, it is currently unclear how to advise pregnant women with newly diagnosed GDM what is the most effective blood sugar range to aim for and guide treatment.

What evidence did we find?

We searched for evidence on 31 January 2016 and found one small randomised controlled trial (abstract only) that was of poor quality and involved 180 women from Canada.The trial compared two blood sugar ranges, one strict the other more liberal, and reported a very few health outcomes for the pregnant woman and her baby.

The trial did not provide any data for this review's main outcomes. For the woman, these related to the development of high blood pressure and protein in the urine during pregnancy, developing type 2 diabetes. For the baby, these outcomes related to death of the baby, increased birthweight, increased risk of birth trauma because of their size, and disability.

More women were on insulin in the strictly controlled group (but this result is based on very low quality evidence). No clear differences were reported for caesarian section rates. No other secondary outcome data for women with GDM relevant to this review were reported. No differences were reported for the number of babies that had a birthweight greater than 4000 g or were small-for-gestational age. No other secondary outcomes for the babies relevant to this review were reported.The study did not report on adverse events.

What does this mean?

This review found that there is not yet enough evidence from randomised controlled trials to determine the best blood sugar range for improving health for pregnant women with GDM and their babies. Four studies are ongoing but not yet complete. More high-quality studies are needed that compare different targets for blood sugar levels and assess both short-term and long-term health outcomes for women and their babies to guide treatment. Studies should include women's experiences and assess health services costs.

Citation: Martis R, Brown J, Alsweiler J, Crawford TJ, Crowther CA. Different intensities of glycaemic control for women with gestational diabetes mellitus. Cochrane Database of Systematic Reviews 2016, Issue 4. Art. No.: CD011624. DOI: 10.1002/14651858.CD011624.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011624.pub2/epdf

12. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes

What is the issue?

Diabetes is a condition in which glucose (sugar) in the blood is too high because the body does not respond to insulin or not enough insulin is made. Insulin is a hormone made by the pancreas, which allows glucose to enter the cells where it is used as fuel by the body.

Controlling blood sugar levels is important because levels that are too high or too low can affect the brain and other organs of the body. Poor blood sugar control in pregnant women with diabetes can lead to large babies who may then have a difficult birth. It also increases the chance of abnormalities in the baby, miscarriage, or stillbirth.

Traditionally, insulin is given as multiple daily injections (MDI), however a small pump can continuously give insulin through a fine tube under the skin (CSII).

Why is this important?

An insulin pump may help pregnant women keep their blood glucose more stable than multiple injections. It might stop the woman's blood sugar level going too high or too low, which would be better for the mother and her baby and it may be more acceptable to women. This review compared the positive and negative effects of CSII and MDI to work out which is best for mothers and infants.

What evidence did we find?

Five randomised trials involving 153 women (154 pregnancies) were included.

These trials did not report many of the outcomes we had hoped to look at. The evidence was judged to be very low quality for important outcomes (caesarean section, large-for-gestational age, perinatal mortality, and neonatal hypoglycaemia). This was because the trials were small, may not have been fair tests, and did not show a clear difference between MDI and CSII.

There were no clear differences in any of the reported outcomes between women who had insulin via a pump rather than as multiple injections. For mothers, this included caesarean section, weight gain during pregnancy, and blood sugar levels. For babies, this included the baby's weight, if they were born premature, and problems such as difficulty breathing, a low Apgar score at birth, low blood sugar, jaundice, or physical abnormalities.

In one small trial, there was no difference in the number of days mothers spent in hospital. This was the only measure of cost or use of health service resources reported.

What does this mean?

The trials did not provide enough information to know whether an insulin pump or multiple injections are better for a pregnant woman with diabetes or her baby. More research is needed, with bigger groups of women, good reporting of how the trials were undertaken, more outcomes assessed and reported, and using the latest pump technology and insulins.

Citation: Farrar D, Tuffnell DJ, West J, West HM. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes. *Cochrane Database of Systematic Reviews* 2016, Issue 6. Art. No.: CD005542. DOI: 10.1002/14651858.CD005542.pub3. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005542.pub3/epdf

13. Oral anti-diabetic agents for women with diabetes or previous diabetes planning a pregnancy, or pregnant women with pre-existing diabetes

What is the issue?

Pre-existing diabetes and gestational diabetes can increase the risks of a number of poor outcomes for both mothers and their babies. For the mother, these include pregnancy-induced high blood pressure (pre-eclampsia) with additional fluid retention and protein in the urine; and giving birth by caesarean. For the infant, these can include preterm birth; as well as an increased risk of the presence of physical defects at birth such as heart defects, brain, spine, and spinal cord defects, Down syndrome; and spontaneous abortion. Other complications at birth include babies that are large for their gestational age, and obstructed labour (shoulder

dystocia) caused by one of the shoulders becoming stuck in the birth canal once the baby's head has been born.

Why is this important?

Being pregnant can trigger diabetes (gestational diabetes) in women with impaired glucose tolerance. Women who have had gestational diabetes are at risk of developing diabetes later in life. This means that management is important for women with impaired glucose tolerance or previous gestational diabetes, as well as for women with established diabetes. Women with established diabetes need good blood sugar control before they become pregnant. Insulin gives good blood sugar control and does not affect the development of the baby, but women may find oral anti-diabetic agents more convenient and acceptable than insulin injections. However little is known about the effects of these oral agents.

This review sought to investigate the effects of oral anti-diabetic agents in women with established diabetes, impaired glucose tolerance or previous gestational diabetes who were planning a pregnancy, or pregnant women with pre-existing diabetes, on maternal and infant health. This review is an update of a review that was first published in 2010.

What evidence did we find?

We searched for evidence from randomised controlled trials (RCTs) on 31 October 2016 and included six RCTs (707 women). Three RCTs included women with current gestational diabetes and did not report data separately for the population of women relevant to this review. Therefore we have only included outcome data from three RCTs, involving 241 pregnant women and their infants. The quality of the evidence was assessed as being low or very low and the overall risk of bias of the RCTs was varied. The three RCTs all compared an oral anti-diabetic agent (metformin) with insulin in pregnant women with pre-existing (type 2) diabetes.

There was no clear difference in the development of pre-eclampsia (high blood pressure and protein in the urine) for women who received metformin compared with insulin (2 RCTs; 227 women; very low-quality evidence), though women receiving metformin were less likely to have pregnancy-induced high blood pressure in one RCT (206 women; low-quality evidence). Women who received metformin were less likely to have a caesarean section birth (3 RCTs; 241 women; low-quality evidence), though no difference was observed in induction of labour (2 RCTs; 35 women; very low-quality evidence). There was no clear difference between groups of infants born to mothers who received metformin or insulin for being large-for-gestational age (1 RCT; 206 infants; very low-quality evidence), though infants born to mothers who received metformin were less likely to have low blood sugar (hypoglycaemia) (3 RCTs; 241 infants; very low-quality evidence). There were no infant deaths (before birth or shortly afterwards) (2 RCTs; very low-quality evidence). The RCTs did not report on many important short- and long-term outcomes, including perineal trauma and a combined outcome of infant death or morbidity, postnatal depression and weight retention for mothers, and adiposity or disability in childhood or adulthood for infants.

What does this mean?

There is not enough evidence to guide us on the effects of oral anti-diabetic agents in women with established diabetes, impaired glucose tolerance or previous gestational diabetes who are planning a pregnancy, or pregnant women with pre-existing diabetes. Further large, well-designed, RCTs are required and could assess and report on the outcomes suggested in this review, including both short- and long-term outcomes for mothers and their infants.

Citation: Tieu J, Coat S, Hague W, Middleton P, Shepherd E. Oral anti-diabetic agents for women with established diabetes/impaired glucose tolerance or previous gestational diabetes planning pregnancy, or pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD007724. DOI: 10.1002/14651858.CD007724.pub3.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007724.pub3/pdf

14. Methods for monitoring blood glucose in pregnant women with diabetes to improve outcomes

What is the issue?

If a mother already has diabetes when she becomes pregnant, she and her baby are at a higher risk of various problems in pregnancy, labour, birth and later. During pregnancy, the mother will have her blood glucose levels (sometimes referred to as blood sugar levels) monitored so appropriate steps can be taken to control her blood glucose. This Cochrane review looked for the best test for measuring blood glucose during pregnancy in order to control blood glucose levels and so reduce problems for babies and mothers. We collected and analysed all relevant studies to answer this question (search date: November 2016).

Why is this important?

Diabetes can cause problems for pregnant women and their babies, including early births, large babies, difficult births and the need for caesarean section. The problems also include a risk to the baby of bleeding in the brain (intracranial haemorrhage), and during labour, there is an increased risk of the baby's shoulder becoming stuck (shoulder dystocia). After the birth, there is an increased risk of low blood sugar (hypoglycaemia), jaundice and breathing problems. The babies are more likely to be admitted to an intensive care unit. Later, there is an increased risk of the baby developing diabetes as a child.

Women with existing diabetes that is not well-controlled at the time of conception and in the first three months of pregnancy are at increased risk of miscarriage, of having a baby with developmental problems or stillbirth. Several methods for monitoring blood glucose levels are used including regular testing at antenatal clinics, self-monitoring, or the use of special equipment that can continuously monitor glucose levels during pregnancy. A more accurate measure of blood sugar may lead to more effective control of blood glucose and a reduction in the potential problems for babies and mothers.

What evidence did we find?

We found 10 trials involving 538 women and babies. We found studies that compared various methods of glucose monitoring: self-monitoring versus standard care, self-monitoring versus hospitalisation, monitoring before meals versus monitoring after meals, glucose monitoring, automated monitoring versus conventional system, continuous glucose monitoring (CGM)

versus intermittent monitoring and constant CGM versus intermittent CGM. The trials were from European countries and the USA. They looked at different techniques of monitoring and reported on different outcomes. The number of women in each study was generally small. The evidence was mostly of very low-quality, so we cannot be certain of the results.

The results did not show that any one monitoring technique was better than others. There was no clear difference between the monitoring techniques when mothers' control of blood glucose or high blood pressure disorders were looked at. Similarly, we found no difference in rates of caesarean section, the number of large babies, the number of babies who died or had serious health problems, or the number of babies being born too early (preterm). We do not know if this is because there is no difference between the techniques, or if there is a difference that these studies did not manage to show.

What does this mean?

The review showed that there is not enough evidence to say with any certainty which monitoring method for blood glucose is best. More research is needed to find out which monitoring method, if any, is best at reducing the risk of complications.

Citation: Moy FM, Ray A, Buckley BS, West HM. Techniques of monitoring blood glucose during pregnancy for women with pre-exist-ing diabetes. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD009613. DOI: 10.1002/14651858.CD009613.pub3.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009613.pub3/epdf

15. Psychological interventions for diabetes-related distress in adults with type 2 diabetes mellitus

Review question

To investigate the effects of psychological interventions on diabetes-related distress in adults aged 18 years and older with type 2 diabetes mellitus.

Background

Diabetes-related distress has to do with the emotional experiences of people with diabetes mellitus, namely their concerns about disease management, support, emotional burden and access to health care. About half of people with type 2 diabetes mellitus experience this distress, which is associated with poor diabetes self-care and disease control. Many psychological interventions have tried to reduce diabetes-related distress, but it is uncertain which interventions are effective.

Study characteristics

We found 30 randomised controlled trials (clinical trials where people are randomly put into one of two or more treatment groups) with 9177 participants. The duration of the interventions ranged from 1 week to 12 months and follow-up after treatment from 0 to 12 months. Most studies took place in community settings, almost all in high-income countries and two each in Asia and Latin America. The studies included a wide spectrum of interventions and were both individual- and group-based.

Key results

Psychological interventions have a small and positive effect on confidence for self-care and glycosylated haemoglobin A1c (HbA1c - a long-term measure of glucose control) in adults with type 2 diabetes. Compared to usual care, psychological interventions showed no firm effect on diabetes-related distress, health-related quality of life, death from any cause, adverse events or blood pressure levels. No study reported on diabetes-related complications (like stroke, heart attacks or kidney impairment) or socioeconomic effects (such as absence from work or costs for medication).

This evidence is up to date as of 21 September 2016.

Quality of the evidence

Overall, the quality of the evidence was low because of small studies, missing data, and limitations in the design and implementation of the included studies. Four studies are awaiting further assessment, and 18 studies are ongoing with results hopefully be published in the near future.

Citation: Chew BH, Vos RC, Metzendorf MI, Scholten RJPM, Rutten GEHM. Psychological interventions for diabetes-related distress in adults with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD011469. DOI: 10.1002/14651858.CD011469.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011469.pub2/pdf

Contacts:

Phone number. +237 242 08 19 19
Email: camer.cdbpsh@gmail.com
Website: www.cdbph.org
Observatoire du Médicament (OdM) au Cameroun : http://newsinhealth.org/
Cameroun, Yaoundé Avenue Henry Dunant – Messa