

# Cochrane for Clinicians

*Putting Evidence into Practice*

These brief overviews are summaries of reviews from the Cochrane Library.



The clinical content by Drs. Saguil and Pflipsen is available for evidence-based continuing medical education (EB CME) credit. See CME Quiz on page 1010.

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## Insulin for Glycemic Control in Acute Ischemic Stroke

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### Clinical Question

In patients with acute ischemic stroke, is glycemic control with insulin effective in decreasing death and disability?

### Evidence-Based Answer

Administering insulin to maintain glycemic control does not improve the rates of mortality or dependency, or the final neurologic outcome after an acute ischemic stroke. Additionally, in randomized controlled trials, patients in the intervention groups (those under tight glycemic control) had a 25-fold higher incidence of symptomatic hypoglycemia. (Strength of Recommendation: A, based on consistent, good-quality, patient-oriented evidence.)

### Practice Pointers

Hyperglycemia occurs in up to two-thirds of patients with acute ischemic stroke and predicts increased stroke mortality, independent of age and stroke severity. Compared with their normoglycemic counterparts, patients with hyperglycemic stroke are more than two times as likely to be dead at 90 days after stroke onset. Although some maintain that hyperglycemia is a physiologic response to the stress of an acute ischemic stroke, others posit that it augments stroke injury by enhancing cortical intracellular acidosis. Acidosis promotes glutamate release, which leads to cortical depression and necrosis of tissue in the ischemic penumbra, the potentially salvageable area surrounding the infarct.

The purpose of this Cochrane review was to determine whether controlling hyperglycemia during acute ischemic stroke influenced patient outcomes. The authors found seven eligible trials involving 1,296 participants with and without diabetes mellitus. Participants in the intervention groups were given insulin infusions with or without

mealtime subcutaneous insulin, with varying tight glucose targets (range = 70 to 110 mg per dL [3.89 to 6.11 mmol per L] to 90 to 144 mg per dL [5.00 to 7.99 mmol per L]). Patients in the control groups were given insulin infusion for a loose target of 70 to 200 mg per dL (3.89 to 11.10 mmol per L), subcutaneous insulin as needed for glucose levels in excess of 180 to 306 mg per dL (9.99 to 16.98 mmol per L), placebo, or no treatment.

The mean glycemic level was significantly lower in the intervention groups (mean difference =  $-8.3$  mg per dL; 95% confidence interval [CI],  $-12.1$  to  $-4.5$  mg per dL). However, there were no differences among the groups in dependence (defined as being severely dependent on others in activities of daily living) or deaths at 30 or 90 days, or final neurologic deficit (as measured by the National Institutes of Health Stroke Scale and the European Stroke Scale). Stratifying for studies with higher and lower numbers of patients with diabetes did not alter this result. There was an increased risk of symptomatic hypoglycemia in the treatment groups (odds ratio = 25.9; 95% CI, 9.2 to 72.7).

The 2007 American Heart Association (AHA) clinical practice guideline on the early management of ischemic stroke offers a consensus opinion that “The minimum threshold [to treat hyperglycemia]...likely was too high, and lower serum glucose concentrations (possibly  $> 140$  to  $185$  mg/dL) probably should trigger administration of insulin.”<sup>1</sup> However, the AHA guideline was published before the release of the negative results of the Glucose Insulin in Stroke Trial (the largest trial to date), and a growing body of literature has since demonstrated that tight glycemic control in critically ill patients does not provide benefit and may promote harm.<sup>2</sup> Although stroke-related hyperglycemia is associated with greater brain injury, poorer functional outcomes, and increased mortality, intensive therapy to lower blood glucose levels does not appear to improve functional outcomes or mortality rates.

Author disclosure: No relevant financial affiliations to disclose.

**Source:** Bellolio MF, Gilmore RM, Stead LG. Insulin for glycaemic control in acute ischaemic stroke. *Cochrane Database Syst Rev.* 2011;(9):CD005346.

The practice recommendations in this activity are available at <http://summaries.cochrane.org/CD005346>.

## REFERENCES

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2. Marik PE, Preiser JC. Toward understanding tight glycemic control in the ICU: a systematic review and metaanalysis. *Chest*. 2010;137(3):544-551.

## The Effects of Combination Contraceptives on Weight

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### Clinical Question

Does the use of combination contraceptives cause weight gain?

### Evidence-Based Answer

Compared with placebo or no intervention, the use of combination contraceptives was not associated with weight gain. Most studies comparing different types of combination contraceptives showed no statistically significant effects on weight. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

### Practice Pointers

Many women believe that the use of combination contraceptives (estrogen plus progesterone) is associated with weight gain.<sup>1</sup> Concerns surrounding weight gain can deter women from initiating use of these medications, or can lead to early discontinuation among current users.<sup>2</sup> Despite these commonly held beliefs and behavior

patterns, a causal relationship between the use of combination contraceptives and weight change has not been established.

The authors of this Cochrane review identified 49 randomized controlled trials that spanned at least three treatment cycles and compared a combination contraceptive with placebo, no intervention, or another combination contraceptive that differed in drug, dosage, treatment regimen, or study length. Only four of the 49 trials had a control group (placebo or no intervention). None of the four trials found a statistically significant difference in weight change between the combination contraceptive and control groups.

The remaining 45 studies compared two or more types of combination contraceptives (patch, pill, and vaginal ring), for a total of 79 different comparisons. Only seven of the 79 comparisons reported a statistically significant change in weight when comparing one type of combination contraceptive with another. Because no control group was used in these studies, these data have limited applicability. Also, several of the differences are likely to have occurred because of chance alone, given the number of comparisons.

When discussing contraceptive methods with patients, physicians should emphasize the evidence that the use of combination contraceptives does not cause weight gain.

Author disclosure: No relevant financial affiliations to disclose.

**Source:** Gallo MF, Lopez LM, Grimes DA, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight. *Cochrane Database Syst Rev.* 2011;(9):CD003987.

The practice recommendations in this activity are available at <http://summaries.cochrane.org/CD003987>.

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2. Wysocki S. A survey of American women regarding the use of oral contraceptives and weight gain (abstract). *Int J Gynecol Obstet*. 2000; 70(suppl 2):114. ■