



Drug Monitor

ONLINE EDITION

Comparing SC and IV Insulin Administration for Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) usually is treated by administering an intravenous (IV) infusion of low dose, regular insulin—which often involves the use of costly infusion pumps and patient admission into the intensive care unit (ICU). Subcutaneous (SC) administration of rapid-acting insulin analogs, however, does not require ICU admission. With this in mind, researchers from the University of Pennsylvania, Philadelphia set out to determine whether the latter treatment is a useful and cost-effective alternative to the former for uncomplicated DKA.

After conducting a literature search using MEDLINE, EMBASE, and The Cochrane Library, the researchers located four English-language articles that compared the treatments. These studies analyzed data on a combined 155 patients who were treated with either IV insulin in an ICU setting or SC rapid-acting insulin analogs (lispro in three of the four studies) on a medical floor or step-down unit.

All four studies indicated that the biochemical profiles, mean venous pH, and mean anion gap were similar between the IV-treated and SC-treated groups. Three of the four studies found that the time to resolution of ketoacidosis was similar among the treatment groups; although one study found a mean 18 hours to resolution in the SC-treated group versus a mean 12 hours to resolution in the IV-treated group, its authors theorized that the four-hour intervals between SC injections employed in the study were too long. In addition, three studies recorded the number of hypogly-

cemic episodes and found that they did not differ significantly between the treatment groups, and two studies analyzed the lengths of hospitalization and found that they did not differ significantly between the groups. The amount of insulin required to treat patients' DKA was similar between the treatment groups in all four studies.

The researchers conclude that SC administration of rapid-acting insulin analogs every hour (0.3 U/kg bolus followed by 0.1 U/kg) or two hours (0.3 U/kg bolus followed by 0.2 U/kg) “may be a reasonable alternative” to IV regular insulin infusion for treating uncomplicated DKA. They say that SC administration also might lead to cost savings; the one study that analyzed costs found that the SC administration route was associated with a 39% savings. The researchers note, however, that their results may be limited because they only identified a few studies, the analyzed studies focused mainly on only one analog, and most studies were industry-supported.

Source: *Ann Emerg Med.* 2009;53(2):259–263. doi:10/1016/j.annemergmed.2008.07.023.

Sex Differences in Metabolic Syndrome and Response to Thrombolysis

Fibrinolysis is impaired endogenously in metabolic syndrome, leading to elevated risk of ischemic stroke—and a worsened patient response to thrombolytic therapy (such as tissue-type plasminogen activator [tPA]) aimed at prompting clot lysis and treating acute ischemic stroke. Recent research has shown that metabolic syndrome increases the risk of stroke in women more than in men. But are women also less affected by thrombolytic

therapy? Researchers from Universitat Autònoma de Barcelona, Barcelona; University of Santiago de Compostela, Santiago de Compostela; and University of Valladolid, Valladolid, all in Spain, and Pontificia Universidad Católica de Chile, Santiago, Chile conducted a prospective study involving 75 men and 50 women who experienced acute ischemic stroke to find out.

All patients had been admitted consecutively to a stroke unit for strokes affecting the middle cerebral artery region and were treated with tPA 0.9 mg/kg IV within the first three hours of stroke onset. The mean (SD) age of the patients was 67.6 (11) years and 48 (96%) of the women were postmenopausal. Metabolic syndrome was diagnosed in 76 (61%) of the 125 patients. The significant baseline differences between the sexes included younger age, more frequent smoking, lower body mass index, and lower high-density lipoprotein cholesterol values in the men. In addition, the women experienced more cardioembolic strokes than the men.

The researchers observed resistance to clot lysis at 24 hours in 53 (42%) of the patients. Metabolic syndrome was associated with a significantly higher resistance to thrombolysis in women (odds ratio [OR] = 17.5; 95% CI, 1.9 to 163.1) than in men (OR = 5.1; 95% CI, 1.6 to 15.6; $P = .0004$). The researchers also found that, for women, obesity contributed the strongest impact to thrombolytic therapy resistance, while, for men, elevated fasting blood glucose played the greatest role in thrombolytic resistance.

The researchers say that while the reasons for these sex differences can only be guessed at, a derangement of the endogenous fibrinolytic system

related to insulin resistance may be more pronounced in postmenopausal women. Citing pediatric studies that have shown girls to be more insulin resistant than boys, they suggest that this difference may reappear later in life when women's estrogen levels lower due to menopause. They also cite findings that insulin resistance leads to a greater impairment of the fibrinolytic system in women compared with men.

The researchers note several study limitations, including the small sample size; the use of body mass index rather than waist circumference as a measure of patients' total body fat; the definition of metabolic syndrome used (poststroke measurements of blood glucose, cholesterol, and triglyceride levels); the use of bivariate analyses despite a small number of end points; and a lack of assessment of environmental and socioeconomic

factors. In addition, some patients were receiving neuroprotective drugs as part of their enrollment in ongoing acute stroke clinical trials at the time this study was conducted. Eight patients were taking disufenton sodium or placebo and 15 were taking citicoline. ●

Source: *Stroke*. 2009;40(2):344-349. doi:10.1161/STROKEAHA.108.531079.