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Effects of early tranexamic acid administration on women with postpartum hemorrhage

The leading cause of maternal death is postpartum hemorrhage, which is defined as blood loss of more than 500 mL within 24 hours of giving birth. The majority of such deaths occur in low-income and middle-income countries. Because data support the administration of tranexamic acid to reduce mortality in trauma patients due to bleeding, investigators are interested in determining if the acid may help control postpartum hemorrhage. Tranexamic acid reduces bleeding by inhibiting the enzymatic breakdown of fibrinogen and fibrin by plasma. Early activation of fibrinolysis is common after childbirth and is similar to what is observed in trauma patients. World Health Organization guidelines from 2012 recommend that tranexamic acid be used to treat postpartum hemorrhage when uterotonics fail to control the bleeding or when the bleeding is due to trauma. The WOMAN (World Maternal Antifibrinolytic) trial collaborators conducted a study to assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with postpartum hemorrhage. They conducted a randomized, double-blind, placebo-controlled study involving women 16 years and older from 193 hospitals in 21 countries who had a clinical diagnosis of postpartum hemorrhage after a vaginal birth or cesarean section. The women were randomly assigned to receive either 1 g intravenous tranexamic acid or a matching placebo, in addition to the standard of care. If bleeding continued after 30 minutes or stopped and restarted within 24 hours of the first dose, a second dose of 1 g of tranexamic acid or placebo was administered. Between March 2010 and April 2016, 20,060 women were randomly enrolled in the trial. The study showed that death due to bleeding was significantly reduced in women given tranexamic acid as compared to controls (1.5 versus 1.9 percent, respectively), especially in women given tranexamic acid within three hours of giving birth (1.2 percent in the tranexamic acid group versus 1.7 percent in the placebo group). All other causes of death did not differ significantly by group. Adverse events, including thromboembolic events, also did not differ significantly between the tranexamic acid and placebo groups. The authors concluded that tranexamic acid reduces death due to bleeding in women with postpartum hemorrhage with no adverse effects. These results support the WHO guidelines but suggest that early treatment is more effective in reducing death from bleeding.

WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum hemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet.* 2017;389:2105–2116.

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Biomarkers of Alzheimer disease as identified in saliva using metabolomics

Alzheimer disease is a neurodegenerative disorder characterized by the accumulation of amyloid-β plaques and tau tangles. Mild cognitive impairment (MCI) is considered to be a transitional state between normal aging and Alzheimer disease (AD), with a conversion rate of approximately 10 percent per year. Therapies are limited and available only after diagnosis. The development of new biomarkers for AD will help clinicians identify patients at risk for the disease earlier and will be critical as newer therapeutic agents are developed. The authors conducted a

study in which metabolomics, the study of small molecules in cells, tissues, and fluids, was used to biochemically profile saliva from healthy control subjects and patients with MCI and AD. The profiling of multiple metabolite concentrations from saliva has recently been shown to help identify newer biomarkers for AD. The goal of the study was to determine if the salivary biomarkers can distinguish between MCI, AD, and healthy controls. The authors collected saliva samples from adult volunteers (12 controls, eight MCI, and nine AD). Logistic regression models were then used to detect MCI and AD. The results showed significant differences in the concentrations of a large number of salivary metabolites in those with AD and MCI versus in unaffected controls. Differences were also found when comparing the AD and the MCI groups. Study limitations included small sample size. Therefore, the results would need to be duplicated with larger studies. The use of other techniques, such as mass spectrometry or gas chromatography, or both, will further increase the number of salivary metabolomes identified as markers of AD. The authors concluded that preliminary evidence indicates that salivary metabolites may be useful for AD biomarker development. Because saliva can be easily obtained for analysis, they recommend larger studies to validate that salivary biomarkers are an ideal screening tool for people at risk of developing AD.

Yilmaz A, Geddes T, Han BS, et al. Diagnostic biomarkers of Alzheimer's disease as identified in saliva using 1H NMR-based metabolomics. *J Alzheimers Dis.* 2017;58:355–359.

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Correction

We reported an incorrect citation in the Clinical Pathology Selected Abstracts (May, page 77) for the abstract titled, "Case studies of professionalism in pathology as an educational tool." The correct citation is Domen RE, Johnson K, Conran RM, et al. Professionalism in pathology: A case-based approach as a potential educational tool. *Arch Pathol Lab Med.* 2017;141:215–219.