Determinants of Pneumonia During Endovascular Hypothermia: Editorial Commentary on Lyden *et al.*, 2013

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THERAPEUTIC HYPOTHERMIA is a neuroprotective therapy that has been tested in preclinical models of focal ischemia as well as in stroke patients (De Georgia *et al.*, 2004; Krieger *et al.*, 2001; Schwab *et al.*, 2001). To be most effective, a prolonged period of hypothermia may be necessary to maximize the beneficial effects of this treatment strategy. In stroke patients, hypothermia has been used in several clinical situations and has been proven effective in out-of-hospital cardiac arrest patients and in neonatal hypoxia-ischemia using surface cooling (Bernard *et al.*, 2002). In the Hypothermia After Cardiac Arrest Study (2002), endovascular therapeutic hypothermia was utilized in stroke patients who were awake and not paralyzed or intubated. This cooling approach in awake patients can be challenging to overcome the mechanisms that maintain normal body temperature, and sedatives such as meperidine are administered to help with the cooling procedure (Lyden *et al.*, 2012).

In an early study titled Intravenous Thrombolysis Plus Hypothermia for Acute Treatment of Ischemic Stroke (ICTuS-L Trial), patients that received intravenous thrombolytic therapy with the combination of hypothermia and an antishivering regimen demonstrated an increased incidence of pneumonia (Hemmen *et al.*, 2010). In a recent study, Lyden *et al.* (2013) sought to identify whether any specific factors could be identified that were responsible for the increased pneumonia risk. The authors reported that in a group of hypothermia patients that reported a 50% incidence of pneumonia, no specific variables were identified other than the baseline National Institutes of Health Stroke Scale that correlated with this clinical outcome. The authors concluded that future trials need to include rigorous definitions of pneumonia to minimize case assessment bias, and new methods to prevent pneumonia are required in patients treated with hypothermia.

This study is important to the stroke field in that it seeks to determine mechanisms by which the risk of pneumonia develops in individuals that undergo therapeutic hypothermia. The authors assessed gender, shivering, the area under the curve below 34°C, as well as total dose of meperidine. The fact that no particular baseline risk factor could be directly related

to pneumonia risk during endovascular therapeutic hypothermia failed to confirm that meperidine use may have promoted pneumonia in this and previous studies. Several limitations of the study as indicated by the authors include sample size and the lack of a clear definition of pneumonia by the study sites to define the incidence of pneumonia critically. Indeed several criteria including clinical assessment, radiographic or other unknown criteria were used to conclude that patients suffered from pneumonia. Thus, an important lesson from this study is that careful monitoring and prespecified diagnostic criteria for pneumonia will be important for future studies. Finally, continued emphasis should be placed on the possible relationship between meperidine use and pneumonia risk.

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