Do We Really Need a Better Way to Give Heparin in Acute Cerebral Ischemia?

Robert G. Hart, MD; J. Donald Easton, MD

In the early 1980s, we assiduously followed management guidelines advocating intravenous heparin for patients within 2 months of transient ischemic attack (TIA) and for most patients with acute ischemic stroke. Heparin flowed freely; there were always 2 to 3 patients receiving it on the neurology ward and a dozen partial thromboplastin times were urgently checked each day. Times have changed. High standards of evidence are expected to support management recommendations, grounded firmly in randomized clinical trials rather than traditional GOBSAT methods (Good Old Boys Sat At Table).1 Nine randomized trials have tested intravenous unfractionated heparin or related agents in acute stroke.2 Critical analysis of the accumulated evidence does “not support the routine use of any type of anticoagulant in acute ischemic stroke.”2 It is clear that intravenous heparin or related low-molecular-weight heparins do not benefit most patients with acute stroke caused by common cerebrovascular disorders. Of note, the mean interval from stroke onset to initiation of heparin averages about 20 hours in existing clinical trials.

Is the randomized trial reported in this issue of Stroke3 comparing two different methods to achieve therapeutic levels of anticoagulation with intravenous heparin much ado about nothing, 20 years too late? No. There is solid evidence favoring intravenous heparin use for acute cerebral venous thrombosis.4 In our view, shared by many other stroke experts,5 selected acute stroke patients with cerebral arterial dissection, with aseptic embolism from prosthetic cardiac valves, or with prothrombotic disorders likely benefit from intravenous heparin, although based on empiric evidence (as yet unfutured by randomized trials!). Heparin offers no overall benefit over aspirin for acute stroke patients with atrial fibrillation,6,7 but it probably is a mistake to generalize this observation to all cardioembolic sources, some of which have substantially higher rates of early recurrent embolism (eg, protruding left ventricular thrombi). Progression of ischemic stroke during the initial 48 to 72 hours is frequent, serious, and of multifactorial cause. Heparin is often used in this situation by clinicians compelled to “do something.”6 While there are no randomized trials of heparin specifically in progressing ischemic stroke, its lack of efficacy for prevention of progression argues against its value and routine use. All things considered, it is unlikely that additional clinical trials of intravenous heparin/heparinoids in unselected patients with acute ischemic stroke will demonstrate important overall benefits. Ironically, any future decline in heparin use in acute stroke will probably result not from additional “negative” trials testing heparin, but from “positive” trials of alternative therapies in clinical situations for which heparin is now used by default.

The situation is less clear for patients with TIAs, due to a paucity of randomized trials. In the largest trial of heparin in acute ischemic stroke, heparin reduced recurrent cerebral ischemia by about 25% (and by about 50% among those with atrial fibrillation), but this benefit was offset by accentuated brain hemorrhage.7,8 In TIA patients, who do not have substantial brain infarction predisposing to heparin-accentuated brain hemorrhage, the benefit versus risk equation may be different. The amount of brain infarction and the time to treatment after ischemia onset are likely to be critical factors. The value of intravenous heparin for high-risk subsets of acute TIA patients is unsettled and merits additional clinical trials.9 For now, antiplatelet agents are sensible initial antithrombotic therapy.

The study by Toth and Voll1 is a welcome contribution, demonstrating a safe, efficient, and user-friendly method to achieve therapeutic levels of anticoagulation with intravenous heparin. These results will be helpful immediately in an important minority of stroke patients (perhaps 5% of ischemic strokes) with specific uncommon causes for which intravenous heparin use remains reasonable, if of unproven benefit, and add a small, useful piece to the multifaceted puzzle of acute management of cerebral ischemia.

References


The opinions expressed in this editorial are not necessarily those of the editors or of the American Stroke Association.

From the Department of Medicine/Neurology (R.G.H.), University of Texas, San Antonio, and the Department of Neurology (D.E.), Brown University, Providence, RI.

Correspondence to Dr. Robert G. Hart, Department of Medicine (Neurology), University of Texas HSC, 7703 Floyd Curl Dr, San Antonio, TX 78229-3900. E-mail: HartR@uthscsa.edu

© 2002 American Heart Association, Inc.

(Stroke. 2002;33:659-660.)

Stroke is available at http://www.strokeaha.org


Key Words: cerebral ischemia  heparin  stroke, acute
Do We Really Need a Better Way to Give Heparin in Acute Cerebral Ischemia?
Robert G. Hart and J. Donald Easton

Stroke. 2002;33:659-660
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/33/3/659

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office.
Once the online version of the published article for which permission is being requested is located, click
Request Permissions in the middle column of the Web page under Services. Further information about this
process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/