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REVIEW ARTICLE

Bundled care to optimize outcome after intracerebral hemorrhage: action for effective implementation

Menglu Ouyang[1,2] *and Craig S. Anderson*[1,2,3,4]*

[1]George Institute for Global Health, Faculty of Medicine, University of New South Wales, Sydney, Australia; [2]George Institute for Global Health, Beijing, China; [3]Department of Neurology, Royal Prince Alfred Hospital, Sydney Health Partners, Sydney, Australia; [4]Clinical Research Center, Faculty of Medicine Clinica Alemana Universidad del Desarrollo, Santiago, Chile

Abstract

Patients who experience acute intracerebral hemorrhage (ICH) are not managed with urgency or level of coordinated care as those with acute ischemic stroke. This is largely due to the lack of any proven treatment for ICH, which has led to therapeutic nihilism and a low threshold for the withdrawal of active care in these patients. The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3) is a landmark study which used a novel, quality improvement, implementation design across 122 hospitals in 10 countries, to show that the early intervention of bundled care with time- and target-based metrics, can substantially improve outcomes for patients who suffer ICH. We advocate the widespread adoption of an early bundle of care focused on urgent time-based metrics for the control of elevated blood pressure and other abnormal physiological parameters, and the emergency reversal of anticoagulation, for patients with ICH. Such coordinated interdisciplinary stroke care will optimise the chances of patients all over the world surviving free of major disability after suffering an ICH.

Keywords: *Intracerebral hemorrhage. Protocols. Health outcomes. Implementation. Stroke services.*

Atención agrupada para optimizar los resultados tras una hemorragia intracerebral: medidas para una aplicación eficaz

Resumen

Los pacientes que sufren una hemorragia intracerebral aguda (HIC) no se tratan con la urgencia ni el nivel de atención coordinada que los que sufren un ictus isquémico agudo. Esto se debe en gran medida a la falta de un tratamiento probado para la HIC, lo que ha llevado a un nihilismo terapéutico y a un umbral bajo para la retirada de los cuidados activos en estos pacientes. El tercer Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3) es un estudio de referencia que utilizó un novedoso diseño de implementación para la mejora de la calidad en 122 hospitales de 10 países, con el fin de demostrar que la intervención temprana de la atención agrupada con métricas basadas en el tiempo y los objetivos puede mejorar sustancialmente los resultados de los pacientes que sufren HIC. Abogamos por la adopción generalizada de un paquete de atención temprana centrado en parámetros urgentes basados en el tiempo para el control de la presión arterial elevada y otros parámetros fisiológicos anormales, y la reversión urgente de la anticoagulación, para pacientes con HIC. Esta atención interdisciplinaria coordinada optimizará las posibilidades de que los pacientes de todo el mundo sobrevivan sin discapacidades graves tras sufrir una HIC.

Palabras claves: *Hemorragia intracerebral. Protocolos. Resultados sanitarios. Implementación. Servicios de ictus.*

***Correspondence:**
Craig S. Anderson
E-mail: canderson@georgeinstitute.org.au

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Introduction

Acute intracerebral hemorrhage (ICH) is the most serious and least treatable form of stroke, which accounts for approximately 20% of nearly 20 million new cases of stroke that occur in the world each year[1]. Compared to modern reperfusion therapy with thrombolytics and endovascular clot retrieval which has transformed systems of care for patients with acute ischemic stroke, there has not been any clearly proven medical or surgical treatment for ICH. This has led to disorganized and widely variable patterns of care for patients with ICH, a sense of nihilism among clinicians, and frustration in the research community. Fortunately, this situation has now changed with the positive results announced for several completed randomized and controlled trials (RCTs) in ICH in early 2023, led by the third intensive care bundle with blood pressure (BP) reduction in acute cerebral hemorrhage trial (INTERACT3)[2].

INTERACT3 was undertaken to resolve the controversy over the effects of early intensive BP lowering treatment in acute ICH. Although elevated BP is common after the onset of ICH and strongly associated with poor outcomes, RCTs that have evaluated early intensive BP control have produced inconsistent results that have been limited to patients with mild-moderate ICH who do not require neurosurgical intervention[3]. This level of evidence has restricted the uptake of a relatively simple and low-cost management strategy in clinical practice, and where guidelines have generally produced an intermediate strength to the recommendations given toward treatment[4].

What we now know?

INTERACT3 was a landmark study in producing a positive result through conduct on an international scale and overcoming the adversity of the COVID-19 pandemic. It used a novel, quality improvement, and stepped-wedge cluster randomized "implementation" design across 121 hospitals in 10 countries, including Mexico, between December 2017 and December 2021, to show that the early intervention of bundled care with time- and target-based metrics can substantially improve outcomes for patients who suffer ICH. The care bundle protocol included the early lowering of systolic BP (target < 140 mmHg), strict glucose control (target 6.1-7.8 mmol/L in those without diabetes and 7.8-10.0 mmol/L in those with diabetes), antipyrexia treatment (target body temperature ≤ 37.5°C), and rapid reversal of warfarin-related anticoagulation (target international normalized ratio < 1.5) within 1 h of treatment, in patients where these variables were abnormal. The likelihood of a poor functional outcome, measured on the distribution of full range of scores on the modified Rankin Scale (mRS), was less in the care bundle group (common odds ratio 0.86, 95% confidence interval 0.76-0.97; p = 0.02). The favorable shift in scores on the mRS in the care bundle group was generally consistent across a range of sensitivity analyses. Patients in the care bundle group had significantly improved survival, better health-related quality of life, shorter time in hospital, and fewer serious adverse events, than those in the usual care group. Treatment with the care bundle in every 35 patients was estimated to prevent one patient from death or major disability.

What are the implications on INTERACT3?

The INTERACT3 results provide strong support for the rapid control of BP and other physiological variables to be incorporated into clinical practice as a part of active management plan for this serious disease. Given requirements to standardize best practice and use quality performance indicators to reduce unwarranted clinical variation in healthcare, the care bundle protocol is a welcome addition to the list of evidence-based management strategies to compliment reperfusion and other protocols that are now in place for patients with acute ischemic stroke. The combination allows an implementation strategy to enhance stroke services in both low- and middle-income countries (LMIC) as well as in many parts of high-income countries. The global stroke community and accreditation organizations should be engaged to standardize recommendations over the incorporation of the care bundle protocol in guidelines and as advocates for relevant education activities and updates of policies.

As a hybrid effectiveness-implementation trial, INTERACT3 simultaneously tested the effect of a simple and widely applicable intervention while measuring the implementation processes and addressing contextual factors that may have impacted on the uptake of the intervention in routine clinical practice. Some implementation difficulties were noted through a process evaluation embedded in INTERACT3. Of note were concerns that health professionals had that the protocol-defined targets for systolic BP and glycemic control might harm patients, and there being contextual factors in relation to staffing processes and medication supply in low-resource areas[5]. Thus, before implementation can proceed, efforts need to be made to reduce such safety concerns in clinicians and nurses over the care bundle and in finding solutions to ensure equipment (i.e., infusion pumps and electronic BP monitors) and intravenous antihypertensive agents are readily available.

What next?

Several INTERACT3 investigators are collaborating with the World Stroke Organization (WSO) to incorporate the care bundle as a recommendation in the organization's Living Clinical Guidelines to improve clinical practice for ICH management. Efforts are also being made to seek donations and sponsorship to support the availability of resources (e.g., electronic BP monitors, infusion pumps for insulin, and intravenous antihypertensive medications) in LMIC. Ongoing communication, engagement, and partnerships with a variety of stakeholders, and the broader stroke community network, will facilitate the translation of the care bundle into clinical practice.

A broad multifaceted implementation program will help to promote the uptake of the care bundle globally and identify implementation strategies that are appropriate at regional/national levels. Training and education could be incorporated under such a program to improve knowledge and assist behavioral change for local adaption of the care bundle. In the minimal setting of Sub-Saharan Africa (SSA), for example, stroke services are often configured within general medical services, and there are few established stroke units/essential services. Through WSO, an implementation program incorporating the INTERACT3 care bundle together with thrombolysis management and other evidence-based care strategies, training, policies, and investment could help advance the quality of care and minimize the burden of stroke in SSA. Such a program could be a welcome additional to enhancing stroke services in Mexico where current systems are not optimal for the recovery and survival of patients who suffer from ICH.

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Conflicts of interest

CSA and MO are investigators on the INTERACT3 study. CSA reports receiving funding from Penumbra outside of this work which was paid to his institute. MO declares no conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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