



front line

A PUBLICATION OF THE MINNEAPOLIS NEUROSCIENCE INSTITUTE

Dear Colleagues,



It is with pleasure that I greet you as the new editor for the *Front Line* Newsletter. This newsletter has been part of our tradition for the past 17 years. Our goal is to share information on the newest developments in neuroscience at Abbott Northwestern Hospital with our physician colleagues.

I would like to introduce myself. I am a neurosurgeon who has been practicing at Abbott Northwestern for the past 23 years and am a partner with Neurosurgical Associates, LTD.

In this edition of the newsletter, we feature articles on the management of hyperglycemia in patients with stroke, the management of intracranial hypertension and image-guided radiation therapy for patients with brain tumors. I hope you find these articles interesting and informative.

If you wish to comment or have any recommendations for future topics, please contact me at the Minneapolis Neuroscience Institute at 612-863-3200.

Best regards,

Mahmoud Nagib, MD

Management of Intracranial Hypertension in the Neurological ICU

Management of intracranial hypertension presents a difficult set of challenges in the neurological intensive care unit. Patients have diagnoses that range from subdural and epidural hematomas to subarachnoid hemorrhages and intraparenchymal bleeding. Mechanisms of injury include the most violent trauma to spontaneous hemorrhage. Ages of patients vary from the young to the very old. Co-existing conditions in patients range from none to a multitude.

What these conditions have in common is that intracranial pressure is never static. This presents the greatest challenge to the intensive care team managing these patients.

As a refresher, “normal” intracranial pressure (ICP) is listed as 5-10 mm Hg, with abnormal values as greater than 20 mm Hg. This abnormal value is “generally treated, but this is an epidemiologically derived action.” (*J Neurosurg* 1977; 47: 503-516.) It is generally true that head trauma patients with ICP of greater than 20 generally do poorly.

Cerebral perfusion pressure (CPP) is the mean artery pressure minus the CVP or the ICP, whichever is greater. “Normal” CPP range is 70 to 95 mm Hg. Example mean artery pressures are 120/80 (mean 93), 140/90 (mean 106) and 160/100 (mean 120).

Implicit in all discussions regarding intracranial hypertension is that control of CPP and ICP reflects cerebral blood flow. Normal values for cerebral blood flow are 45-50 ml/100 grams of tissue/minute, with ischemic flow being 18 ml/100 grams of tissue/minute. Direct measurement of flow is difficult in the clinical setting and proxies such as Doppler studies or even level of consciousness are used as best estimates.

The brain attempts to autoregulate its blood flow. Lower and upper CPP limits are estimated to be 40 mm Hg and 140 mm Hg. Unfortunately, in situations of intracranial hypertension and ischemia, this autoregulation is either shifted or lost. Low cerebral flow/hypotension/hypoxia portend poor outcome and reflect a major increased risk in mortality. (*Chestnut, RM: Medical Complications of the Head Injured Patient. In Cooper PR (ed): Head Injury, 3rd ed, 1993, pp 459-501.*)

Also making management difficult is the lack of a natural time course for altered ICP and CPP. All

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Intracranial Hypertension,

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practitioners remember the notable “storms” of intracranial hypertension that these patients experience.

Is there a CPP that portends bad outcome? Or, is there a CPP that improves outcome?

The best answer to these two questions is a carefully phrased statement—“It appears that a CPP of 70-80 is an appropriate goal.”

The caveats to such a statement are important. This article addresses intracranial hypertension from many sources—trauma, mass, hemorrhage, edema, vasospasm—which makes it difficult to generalize. It is also true that practice standards are not robust. (See “The Guidelines for the Management of Severe Traumatic Brain Injury” by the Brain Trauma Foundation, 2003, and the Concise Definitive Review: Primer on Medical Management of Severe Brain Injury in CCM 33: 1392-1397, 2005. For a contrarian view, see the recommendations of the Lund group in Intensive Care Med 2006 Oct; 32(10): 1475-84 and a Netherlands

study in CCM 33(10): 2207-13, 2005.)

In light of the above, there is high utility in the neurological intensive care unit for using simple treatment options—a minimalist approach.

Treatment options include:

- **Ventriculostomy.** This has long been a treatment option, and it is noted that subarachnoid hemorrhage (SAH) and hydrocephalus are associated with worse outcomes. (*J Neurosurg* 1983; 58: 482-487.)
- **Maintenance of appropriate CPP.** Striving for a CPP of approximately 70 or even 80 does not cause an increased ICP. It also seems true that in some patients (as outlined in the guidelines from the Brain Trauma Foundation) a CPP goal of 60 is appropriate. Lastly, the literature does not support a “better” or “best” choice of vasopressors.
- **Normal capnia.** There is no proven improvement with hyperventilation and recommendations continue to suggest a pCO_2 of 35.

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- **Normothermia.** There is no consensus on hypothermia in this patient population, but there are better outcomes with normothermia. Avoid 38 degrees or greater—“temperatures previously reported to worsen neurologic outcome after brain injury.” (*Mayo Clin Proc* 1998 July; 73(7): 629-35.)

- **Sedation and muscle paralysis are appropriate.** There is no apparent “better choice” of sedatives and muscle relaxants.

Treatment of the critically ill neurologic patient with intracranial hypertension remains a challenge for the entire treatment team. Maintenance of an appropriate cerebral perfusion pressure appears to be a reasonable clinical goal, and simplifying the approach seems to better the chance of meeting this goal. ■

New Tool for Image-Guided Radiation Therapy

Abbott Northwestern Acquires Varian Trilogy

Abbott Northwestern Hospital’s Radiation Therapy Department has installed and commissioned its Varian Trilogy unit for image-guided radiation therapy (IGRT). The Trilogy offers exciting refinements to the Radiation Oncology Program, a key component of the Virginia Piper Cancer Institute. Acquisition of the Trilogy unit is especially beneficial to advancing the Minneapolis Neuroscience Institute’s existing Stereotactic Radiosurgery (SRS) and Stereotactic Radiation Therapy (SRT) programs. Refinements include kilovoltage and CT imaging assistance in external beam radiation therapy, allowing for supreme accuracy in radiation treatment.

Modern radiation treatment requires certain key tools, technologies and specialized personnel. These include specialized treatment planning software, a source of high-energy radiation, devices to shape the radiation beams, quality assurance tools that check and fine-tune a position relative to the radiation beam before treatment begins, and highly trained physicians and physicists to assure appropriate care and delivery.

Sophisticated computer software and three-dimensional images of the tumor target and surrounding anatomy aid in establishing the

optimal way of treating a condition. The resulting treatment plan is unique to the individual, specifying the number of radiation beams, the energy of the beams and the angles necessary to precisely deliver the radiation dose prescribed by a patient’s physician while minimizing harm to surrounding healthy tissue.

Stereotactic Radiosurgery

SRS is the most precise method of external-beam radiation. It has been used for some time by neurosurgeons to treat vascular abnormalities and tumors in the brain, both benign and malignant. Recent advances in imaging, patient positioning and targeting have all made SRS appropriate for the treatment of cancers in other parts of the body as well.

Diagnostic images taken before treatment, including computed tomography (CT), positron emission tomography (PET) and magnetic resonance imaging (MRI) help determine where to aim the radiation, and can be fused together to define the most accurate volume requiring radiation management. The beams are shaped to match the contours of the tumor and are delivered from many different angles around the body, all converging precisely at the planned target location.

SRS’s precision destroys tumors with high doses of radiation, while sparing the surrounding healthy tissue. In this way, SRS provides a noninvasive alternative to surgery, sometimes allowing treatment of inoperable tumors.

Management of Hyperglycemia in Patients with Stroke

Hyperglycemia is a common feature of patients presenting with acute stroke. Some studies have suggested that as many as 40 percent of patients presenting with stroke have elevated glucose at presentation. This is due to the excess stroke risk (relative risk is 3.6 in women, 2.5 in men) of patients with diabetes. But stress hyperglycemia can also accompany stroke in patients without diabetes. Hyperglycemia is not just an incidental finding since many observational studies have documented a clear association of hyperglycemia with excess mortality, poorer functional recovery and stroke severity.

The strong association between hyperglycemia and poorer outcomes in stroke patients raises the obvious question of whether successful glycemic control in the hospital after stroke would lead to improved outcomes. Unfortunately, the question remains unanswered. The only trial addressing the issue, the GIST-UK trial, is scheduled for publication in early 2007. It is possible that even this trial may not provide a definitive answer since the insulin intervention is only 24 hours

in duration and since the trial excluded patients who were diabetic and previously treated with insulin.

For guidance about how to handle hyperglycemia in stroke patients, we can look to the evidence in other groups of patients. The strongest evidence in support of tight glycemic control in hospitalized patients comes from two studies, one done as a randomized control trial in surgical ICU patients, the other an ongoing quality improvement project with historical controls in cardiac surgery patients. Both provide substantial evidence in favor of tight control of glucose in the high-risk patients studied. Whether that information can be extrapolated to stroke patients or other hospitalized patients remains controversial.

Despite the lack of treatment studies in stroke, it is hard to ignore the observational data on the hazard of hyperglycemia. Expert groups have recommended improved glycemic control in all hospitalized patients. The American College of Endocrinology 2004 position statement recommended extremely tight control in all hospitalized

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patients, aiming for glucose of 110 in ICU patients and premeal glucoses of 110 in all patients in the hospital. That recommendation has been criticized, and an American Diabetes Association position statement in 2005 recommended glucoses "as close to 110 as possible" in the ICU and "as close to 90-130 as possible" on general wards. Two recent stroke guidelines stated that the evidence was not sufficient to make recommendations about the level of glycemic control.

There is consensus that severe hyperglycemia should not be left without effective treatment.

What constitutes effective treatment?

Insulin infusion is the most rapid and reliable way to achieve glycemic control and is appropriate for patients with severe hyperglycemia or significant deficits. There are several effective protocols available. It is not clear whether any of them are superior to the others but an institution should train with one. There is no need to start from scratch.

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With SRS, the full radiation dose is delivered in one session. Most patients can be treated as outpatients and can return home immediately after the procedure.

SRS is most often used to treat tumors or abnormalities in the brain and spine. With new technologies for more precise targeting and compensation for any tumor motion that occurs as a patient breathes during treatment, SRS is starting to be used more widely for treatments in other regions of the body. The Virginia Piper Cancer Institute will be implementing "respiratory gating," a method of taking into account respiratory activity during treatment, to support expansion of safe and precise SRS treatment in all body sites.

Stereotactic Radiation Therapy

During SRT the total radiation dose is delivered over a course of several treatment sessions, rather than all at once. SRT is also known as fractionated radiosurgery because a fraction of the total radiation dose is delivered at each session.

SRT is used to treat tumors or abnormalities in the brain, head, neck and spine. It may also be used to treat tumors or abnormalities in other parts of the body like the lungs, liver, kidneys or pancreas.

In addition to its unparalleled accuracy, the Trilogy unit is noteworthy for its ability to rapidly generate a high X-ray output which allows for faster treatment times and, ultimately, improved patient comfort. ■



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There is no clear guidance about a glucose threshold at which insulin infusion is necessary. Subcutaneous regimens can also achieve control. There is consensus that “sliding scale insulin” given as the sole method of glucose control is inappropriate in all Type I diabetics and ineffective as a strategy in most Type II diabetics. Effective subcutaneous regimens incorporate long-acting insulins, such as glargine or NPH as basal insulin, prandial (scheduled pre-meal) insulin and corrective dose insulin. The prandial and corrective dosing can be given as regular insulin or a rapidly acting analogue (lispro or aspart), though many experts find the peak and duration of lispro and aspart more appropriate for these uses. It is appropriate in some patients to start with corrective dose alone (which is the same as sliding scale) in order to control mild hyperglycemia or to get a sense of the degree of insulin sensitivity. This temporary strategy would not be acceptable

in Type I diabetics who must be provided some basal insulin at all times.

Oral antidiabetic agents are not the mainstay of inpatient treatment of diabetes. Sulfonylureas in particular are prone to cause hypoglycemia in patients whose oral intake is uncertain and who have worsened renal function. Metformin is less likely to cause hypoglycemia, but the issues of patients receiving intravenous contrast, renal insufficiency and other medical illnesses prevent metformin from being a helpful agent in most hospitalized patients. However, oral agents can be continued in stroke patients who are eating, in whom prior control has been good and who have no contraindications.

There is a definitive reference on the topic of inpatient management of diabetes. It is a “technical review” by Steven Clement, MD, and many other national experts, published in the February 2004 issue of *Diabetes Care* and available on line at <http://care.diabetesjournals.org>.

Summary

Hyperglycemia is a frequent finding in acute stroke patients. It is strongly associated with poorer outcomes in stroke patients. There are not yet treatment studies in stroke to give guidance about glycemic management in stroke patients, though influential studies in surgical ICU and cardiac surgery patients have demonstrated improved outcomes. Diabetes experts favor at least moderately tight glycemic control in all hospitalized patients. Two stroke guidelines did not make specific recommendations about a threshold at which to institute aggressive glycemic management. Insulin infusion is the most rapid and reliable method with which to achieve glycemic control in unstable patients. Subcutaneous regimens incorporating basal and prandial insulin can also be effective. Relying on “sliding scale” alone is not likely to lead to good diabetic control in stroke patients. ■