IMMDA ADVISORY STATEMENT

Hypertonic (3%) Saline for Emergent Treatment of EAH Encephalopathy

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Advisory Statement:

We recommend the emergent use of hypertonic saline for the treatment of life threatening EAH Encephalopathy at a location determined by the medical director.

Background:

Hypertonic (3%) saline has been clearly shown to be the emergent treatment of choice for life threatening EAH encephalopathy. Marathon runners with delirium, seizures or coma have responded well to an intravenous 100 ml bolus to reverse cerebral edema as soon as possible at a medical facility with blood [Na+] testing capability as determined by the race medical director. Emergent symptoms have responded well to hypertonic (3%) saline drips in emergency rooms since 1999 [3,4].

Introduction:

Revised Fluid Recommendations for Runners and Walkers was approved by the International Marathon Medical Directors Association [IMMDA], Barcelona, Spain, 6 May 2006, to decrease risk for this condition especially in the most susceptible runners.[1] *Hypertonic (3%) Saline for Emergent Treatment of EAH Encephalopathy* is a complementary position statement to minimize morbidity and mortality from this condition when prevention fails. Having this solution on hand is at treting facilities is critical to treat these patients rapidly.

Exercise-associated hyponatremia (EAH) is an imbalance in body fluid homeostasis leading to a blood sodium concentration [Na^+] less than 135 mmol/L during or within 24 hours after endurance exercise. Initially described in ultra-distance runners in 1985,[2] exercise-associated hyponatremia (EAH) was reported in marathon runners in 1999 followed by cases of fatal pulmonary and cerebral edema in 2000.[3,4,5]

EAH was subsequently identified in 13% of Boston marathon runners in 2002 with over consumption of fluids as an independent risk factor especially in slower runners.[6] Subsequent studies in collapsed Boston marathon runners including a fatal case in that same year showed a decrease in free water excretion as a collateral cause for EAH.[7] Exertional rhabdomyolysis with release of muscle-derived interleukin(IL)-6 may account in part for this inappropriate antidiuresis based upon non-osmotic secretion of arginine vasopressin (AVP).[8] EAH fulfilled all of the diagnostic criteria for the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) first described in 1957.[9] By this paradigm, EAH occurs not solely from over consumption of fluids but when the intake of hypotonic fluids exceeds total losses, including a decreased ability of the kidneys to excrete free water.[10,11] This paradigm accounts for otherwise unexpected clinical features of EAH including cases after only moderate fluid intake, with a delayed onset after races and associated with use of non-steroidal anti-inflammatory drugs known to enhance the action of AVP.

Given the similar clinical presentations of opposite disorders of body fluid homeostasis, blood [Na^+] testing is required to differentiate cases with hypernatremia and hyponatremia for triage to divergent treatment protocols.[12] Normal saline as indicated for the former was associated with onset of seizures in EAH and the several reported fatalities.[3,4,5,13] In contrast, these studies demonstrated a timely and safe recovery using hypertonic (3%) saline without any associated morbitity or mortality.[14] Some have recommended emergent treatment with hypertonic saline using a 100 ml bolus to augment reversal of

cerebral edema as subsequently endorsed for sports medicine practice [11,15,16] Others clearly recommend a hypertonic saline drip [3,4]

The explanation for the clinical advantage of treatment with hypertonic saline relates to its ability to rapidly increase blood [Na+] or tonicity by 2-3 mmol/L, which reverses the osmotic gradient for the flow of water in brain cells. The endpoint is improvement in neurological status, which can be achieved using the concentrations of hypertonic saline available in different venues. Successful outcomes have been reported using 2% saline after the 2005 London marathon and 5% saline after an iron distance triathalon in Cape Town, SA.[17,18] Sequential determinations of blood [Na+] are needed to monitor compliance with safe rates of correction as a standard of care for this condition in general medical practice. [19]

The majority of marathons utilize rapid transport of collapsed runners to hospital based emergency services, where the race medical director has an established protocol in place for hypertonic saline in critical cases.[20,21] An alternative strategy is to utilize on site blood [Na+] testing in the medical tent (Houston, Chicago) followed by transfer of cases to the hospital for treatment. Some races currently undertaken both [Na+] testing and initiation of hypertonic saline treatment in the field (Boston, Marine Corps and London marathons) analogous to such pre-hospital treatment for cerebral edema in cases of acute brain injury.[22,23,24] The goal of this IMMDA Advisory statement is to recognize the importance of emergent use of hypertonic saline at races worldwide at a location determined by the medical director and to ensure the availability for its use in a rapid safe fashion.

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