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Response to Letter to the Editor regarding PCCM-D-016-00211 ("Effectiveness of Pharmacological Therapies for Intracranial Hypertension in Children with Severe Traumatic Brain Injury – Results from an Automated Data Collection System Time- Synched to Drug Administration")

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We thank Dr. Suzuki [1] for the thoughtful comments regarding our recent report in Pediatric Critical Care Medicine [2]. We obviously agree that intracranial hypertension portends unfavorable outcomes in children with traumatic brain injury [3] and a rapid response to mitigating its injurious effects should be part of standard practice for all institutions.

Moreover, we also agree that the measurement of intracranial pressure (ICP) – either by invasive or non-invasive means – is essential for optimal patient care. Lastly, we believe that the measurement of ICP with either an intraparenchymal device or an external ventricular drain represents the current “gold standard” and we feel our data contribute to the literature regarding to optimal treatment strategies for such emergencies.

We appreciate that these types of devices may not be available in all parts of the world and recognize that Dr. Suzuki has highlighted a potential device that might have some utility in such locations. Several methods have been described to estimate ICP including optic nerve sheath diameter (ONSD), impedance mismatch, tympanic membrane displacement, transcranial Doppler (tCD), near infrared spectroscopy and fontanometry [4]. To date, however, the published reports regarding the utility of these non-invasive techniques – particularly in children with severe TBI - have been limited. A recent report by O’Brien and colleagues demonstrated reasonable sensitivity and specificity of pulsatility index from the middle cerebral artery (measured by tCD) with intracranial hypertension - although the technique was not accurate enough to predict actual ICP values [5]. Similarly, Gwer and colleagues demonstrated some utility with the tympanic membrane displacement analyzer in

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comatose children from Kenya and children in idiopathic intracranial hypertension clinic in the UK [6]. In this report, both populations of children demonstrated higher values of tympanic membrane displacement in children found to have increased ICP by lumbar puncture.

Dr. Suzuki's letter focuses on the utility of OSND to predict - and ultimately treat - ICP in children with severe TBI. A systematic review and meta-analysis by Ohle and colleagues summarized 12 studies (478 subjects) and concluded that "ocular sonography shows good diagnostic test accuracy for detecting raised ICP compared to CT" [7]. However, closer scrutiny of this report is required for a full evaluation of the device. In this report, only 3 of the 12 studies included children and none of them compared the OSND values in clinical situations similar to those required for treating children with severe TBI (serial measurements, comparisons to indwelling ICP devices) as was implied by Dr. Suzuki's question. Encouragingly, Maissan and colleagues were able to demonstrate a relationship between ICP and OSND values in 18 children with severe TBI [8] after airway manipulation. However, Hall and colleagues demonstrated mean OSND was actually *lower* in children ultimately diagnosed with increased ICP in children who were being evaluated for ventriculoperitoneal shunt failure [9].

We appreciate and share Dr. Suzuki's desire to have an accurate, non-invasive measure of ICP for all regions of the world. We believe there may be some utility in the techniques that are currently being evaluated, yet none have currently demonstrated sufficient accuracy and reliability for children who are at risk for intermittent episodes of intracranial hypertension [10]. We believe that evaluation of these devices should continue and encourage investigators to publish studies of these devices so they can be thoroughly evaluated.

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