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EDITORIAL

TMU: Brain Injury

1. Introduction

I consider it a significant opportunity and honor to begin the second year of *Journal of Experimental and Clinical Medicine* by devoting my editorial to the expertise of our Founding Editor-in-Chief, President W.T. Chiu. The review treats brain injury first, with a focus on what is being done at Taipei Medical University (TMU). Readers will quickly recognize a significant level of expertise at TMU and that the thrust of a subject occupies a prominent place in the Biomedical Community. Most of the articles reviewed are from the last 2 years, despite a few from 2004 and 2006, an attempt to include most of President Chiu's contributions. There is a pattern to the publications that has arranged them into my own orderly sequence.

To emphasize the significance of brain injury, a quick Wikipedia search reveals a rounded figure of 5,000,000 entries. Traumatic brain injury (TBI, also called intracranial injury) occurs when an external force traumatically injures the brain. TBI can be classified based on severity; mechanism (closed or penetrating head injury); or other features (e.g., occurring in a specific location or over a widespread area). Head injury usually refers to TBI, but is a broader category because it can involve damage to structures other than the brain, such as the scalp and the skull. TBI is a major cause of death and disability worldwide, especially in children and young adults. Its causes include falls, vehicle accidents, and violence. Prevention measures include the use of technology to protect those who are prone to accidents, such as seat belts and sports or motorcycle helmets, as well as efforts to reduce the number of accidents, such as safety education programs and enforcement of traffic laws. Brain trauma can be caused by a direct impact or by acceleration alone. In addition to the damage caused at the moment of injury, brain trauma causes secondary injury—a variety of events that take place in minutes and days after the injury. These processes, which include alterations in cerebral blood flow and the pressure within the skull, contribute substantially to the damage from the initial injury.

TBI can cause a host of physical, cognitive, emotional, and behavioral effects, and outcome can range from complete recovery to permanent disability or death. The 20^{th} century has seen critical developments in diagnosis and treatment, which have decreased death rates and improved the outcome. These include imaging techniques, such as computed tomography and magnetic resonance imaging. Depending on the injury, the treatment required may be minimal or may include interventions, such as medications and emergency surgery. Physical therapy, speech therapy, recreation therapy, and occupational therapy may be used for rehabilitation.

2. Basic Science

2.1. Apoptosis and circulation

Lin et al's[1] work on lessening disruption of tight junctions and apoptotic insults to mouse cerebrovascular endothelial cells (CECs) revealed that oxidized low-density lipoprotein (oxLDL) can induce apoptosis of mouse CECs. Resveratrol possesses chemopreventive potential. Analyses evaluated the effects of resveratrol on oxLDL-induced insults to mouse CECs and their possible mechanisms. Exposure of mouse CECs to 200μM oxLDL for 24 hours elevated oxidative stress and simultaneously induced cell apoptosis. However, resveratrol partially protected against oxLDL-induced CEC apoptosis. The oxLDL-induced alterations in levels of Bcl-2, Bax, and cytochrome c were completely normalized by resveratrol. Consequently, resveratrol partially decreased oxLDL-induced activation of caspases-9 and -3. In this study, Lin et al[1] also found that resveratrol would protect against oxLDL-induced damage of the blood–brain barrier by protecting against the disruption of tight junction structure and apoptotic insults to CEC.

Chang et al's[2] report summarized the animal models of heatstroke experimentation aimed at advancing current knowledge of therapeutic effects on cerebrovascular dysfunction, hypercoagulable state, and/or systemic inflammation characteristics related to heatstroke. This is significant because the rodent model allows the testing of new therapeutic strategies for heatstroke. Notably, brain cooling produced by the infusion of cold (4°C) normal saline through the jugular vein or whole-body cooling improved survival during heatstroke by reducing cerebrovascular dysfunction, multiple-organ failure, systemic inflammation, and hypercoagulable state.

2.2. Brain tissue oxygen monitoring in TBI

A current treatment principle for TBI concerns the prevention of secondary brain injury. Thus, this may become the major prognostic factor when considering a patient's outcome. The main causes of secondary brain injury include blocking of the delivery of brain oxygen and the blood supply; damage caused to the cerebral autoregulation, causing increased intracranial pressure; decreasing of cerebral perfusion pressure, and hypoxia. In a recent publication, for the future, researchers are advised to focus on exploring optimal fraction of inspired oxygen and its ratio to positive end-expiratory pressure and the range of partial pressure of oxygen in arterial blood. This would maintain the tissue oxygen partial pressure at proper levels. Furthermore, researchers are also advised to examine in clinical trials tissue oxygen partial pressure to aid in applying medication and managing brain metabolic wastes.[3]

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3. Clinical Analyses

Chiu et al's[4] analysis was retrospectively aimed at evaluating the efficacy of propofol, a new choice of pharmacotherapy in head injury patients. A higher survival rate was found in the propofol group (81.8% *vs.* 46.7%, $p < 0.001$). This work is significant because it demonstrated that propofol improved the outcome in the recovery phase of head-injured patients.[4]

In another approach, Tsai et al[5] determined the causes of pediatric TBIs in children aged 14 years or younger and identified various types of craniocerebral damages that result from different mechanisms of injury. Tsai et al's[5] patients' data were collected from 56 major hospitals among the 0- to 14-year age group. Results suggest that it is important to significantly decrease all risk factors in the environments of homes and public areas. Wearing helmets and development of public transportation are essential for the prevention of head injuries.[5]

4. Brain Injury Legislation and Litigation

According to Liao et al,[6] there are different views on trauma mechanisms, pathogenesis, and managements in different areas. Individualized guidelines for different countries would be necessary, and Taiwan is no exception. Liao et al[6] have completed the preparation of the first evidence-based, clinical practice guidelines for severe TBIs. The guidelines may provide concepts and recommendations to promote the quality of care for severe TBIs in Taiwan.[6]

To evaluate the impact of three major determinants (time, geography, and legislation) on epidemiology on TBI, Chiu et al conducted a prospective study in 2001 and used the 1991 data to examine the differences in TBI distribution in urban and rural Taiwan a decade after laws had been passed.[7] Results revealed that causes and age distribution had shifted significantly over the 10-year period. In 2001, the age group with the highest incidence was 20–29 years, whereas in 1991, it was the older-than-70-years age group. Although traffic-related TBI had decreased, falls and assaults had increased in 2001. Comparative studies of TBI in urban and rural areas reveal that time, legislation, and geography are crucial determinants of TBI epidemiology. Although time and legal interventions seem to exert a significant impact, geography also affects TBI outcomes.[7]

Yang and Chiu[8] assessed the risk of litigation in district courts as related to care for head injury patients, that is, from the perspective of epidemiology. They analyzed the incidences of litigations arising from head injury inpatients under neurosurgical care, all neurosurgical inpatients, and birth inpatients in Taiwan, and computed their relative risks. The study period was from 1998 to 2002. Findings indicated that, for inpatient populations, whether head injury patients or not, neurosurgeons in Taiwan were facing a relatively lower rate of litigation in comparison with those treating birth patients. Nonetheless, head injury patients still pose a major challenge, and misdiagnosis remains the major complaint of plaintiffs in subsequent legal analyses.[8]

Patients suffering head injury in remote islands of Taiwan, where there is a shortage of personnel and facilities, depend on Emergency Air Medical Services (EAMS) for prompt and definitive treatment. Tsai et al[9] concluded that the higher incidence of head injury (26.5%) in EAMS than in ground transportation (19.8%) suggests that preflight assessment and in-flight management of patients conducted by an experienced escort team following guidelines for head injury in EAMS remain an important concern.

5. World Health Organization Quality of Life

Research of Lin et al[10] tracked the health-related quality of life (HRQL) after discharge and after 5 and 12 months after a TBI to examine those factors associated with changes in each HRQL domain. World Health Organization Quality of Life (WHOQOL) scores on all WHOQOL-BREF domains except social relationships greatly improved over the first 6 months and showed continued improvement at 12 months after injury. The domain scores of the WHOQOL-BREF at discharge were associated significantly with the preinjury HRQL level, marital status, alcohol consumption at the time of injury, Glasgow Outcome Scale level, cognition, activities of daily living, social support, and depressive status. However, after adjusting for these baseline differences, only the Glasgow Outcome Scale level and depressive status significantly influenced the longitudinal changes in the psychological and social domains over the 12-month period. Changes in the physical and environmental domains were not significantly associated with this study.

6. The Future

Taiwan and other developing countries have faced an enormous increase in the number of motorcycles, which has subsequently caused a rapid increase of the motorcycle-related TBIs. Thus, for the future, there are two approaches at TMU: (1) preclinical and clinical analyses of wireless brain monitoring system for neurological disorders and (2) research devoted to neurodegenerative diseases.

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