

Neurotrauma research in Taiwan

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Summary

Because of the rapid industrial and economic growth, 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 traumatic brain injuries (TBI). In order to tackle this serious problem, stepwise approaches for TBI were implemented in Taiwan from 1991 to 2007.

Step 1 was to do a nationwide TBI registry in order to identify the risk factors and determinants. We found that the major cause of TBI in Taiwan was motorcycle-related injury, and very few motorcyclists wore a helmet. Step 2 was to launch the implementation of the helmet use law on June 1, 1997. A rapid decline of TBI hospitalizations and deaths was demonstrated soon thereafter. Step 3 was to enroll into international collaborations with the Global Spine and Head Injury Prevention Project (Global SHIP Project) groups for TBI. The comparative results thus obtained could be used to develop prevention strategies for developing countries. Step 4 was to implement clinical researches for TBI, which included a Propofol study, hyperbaric oxygen therapy (HBOT), brain parenchymal oxygen (PbtO₂) monitoring, etc. Step 5 was to develop guidelines for the management of severe TBI in Taiwan. Through a 2-year period of review, discussion, and integration, a 9-chapter guideline was published in June 2007. In summary, our experience and process for management of TBI in Taiwan can be used as a reference for other developing countries.

Keywords: Traumatic brain injuries; motorcycle injury; helmet use law; injury prevention.

Introduction

Among accidental injuries, traumatic brain injury (TBI) is regarded as the most important cause of death. About half of the injury deaths are related to TBI. Before 1997, Taiwan was one of the areas with the highest incidence

and mortality rate of TBI in the world. This situation mainly resulted from a large number of motorcyclists, of whom only very few wore a helmet [4, 24]. However, after the mandatory helmet use law was enforced, there was a drastic improvement in injury deaths [1, 15]. The researches and management of TBI in Taiwan started from epidemiological studies, intervention, and then gradually stepped into the field of clinical trial and development of TBI treatment guidelines. We hope that our 26-year experience with stepwise approaches for the prevention and treatment of TBI can be used as a reference for other developing countries.

Step 1: epidemiological study of traumatic brain injury

A total of more than 160,000 TBI patients were collected over the past 20 years (Fig. 1) [2–4, 6, 9, 11–13, 16–19, 21–24, 30]. From the period of 1987 to 1991, the incidence rate of TBI in the urban area – Taipei City was 220/10⁵, the mortality rate was 22/10⁵, 47% of TBI were caused by traffic injuries, and 56% of traffic injuries were motorcycle related, whereas in the rural area – Hualien County, the incidence rate of TBI was 380/10⁵, the mortality rate was 88/10⁵, 79% of TBI resulted from traffic injuries, and 66% of traffic injuries were motorcycle-related (Fig. 2) [20].

From 1991 to 1993, over 24,000 cases of head injury were collected from 4 counties of Eastern Taiwan and adjacent island: Ilan County, Hualien County, Taitung County, and Penghu Island (Table 1). The final results of incidence rates of TBI from Ilan County, Hualien

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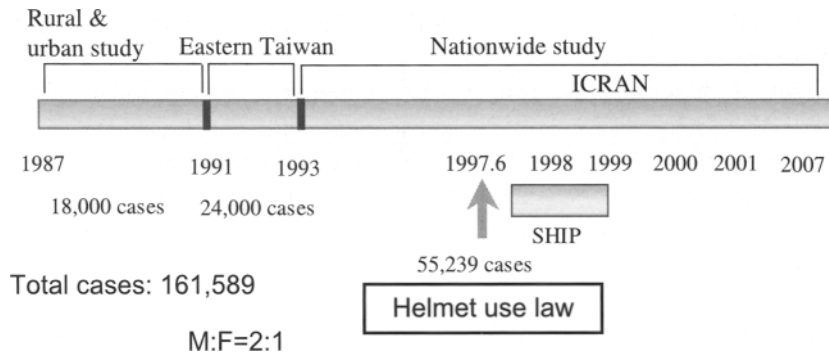


Fig. 1. Epidemiological study of TBI in Past 20 Years

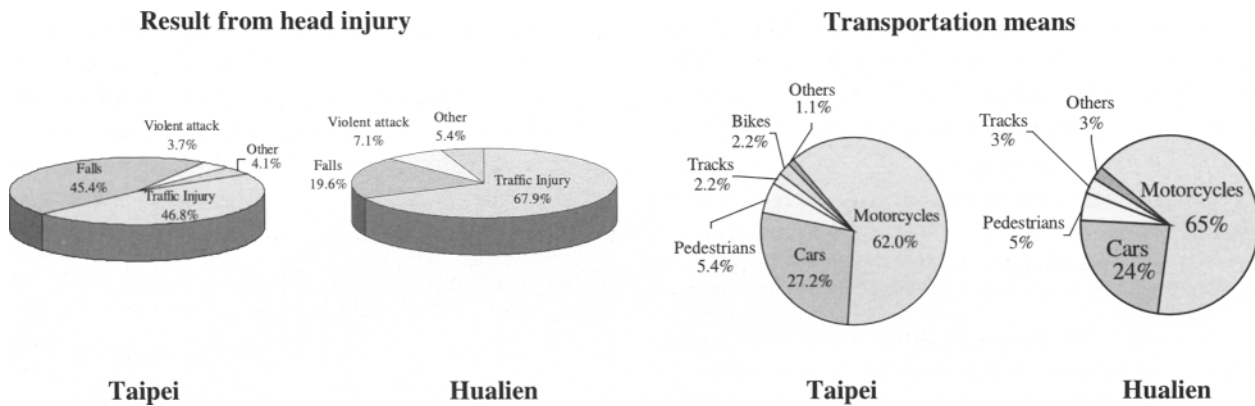


Fig. 2. Comparative study of TBI in Taipei City and Hualian county

Table 1. Epidemiological study of TBI in eastern Taiwan and adjacent island

Regions	Incidence rate	Mortality rate	Traffic injury related incidence (%)
Ilan county	311/100,000	53/100,000	60
Hualien county	437/100,000	72/100,000	61
Taitung county	341/100,000	83/100,000	54
Penghu county	260/100,000	84/100,000	74

County, Taitung County, and Penghu Island were $311/10^5$, $437/10^5$, $341/10^5$, $260/10^5$, and the mortality rates were $53/10^5$, $72/10^5$, $83/10^5$, $84/10^5$, respectively. Traffic injuries accounted for 60%, 61%, 54%, and 74% of TBI, respectively. The survey indicated that the incidence and mortality rates of TBI in Eastern Taiwan and island Counties were higher than in Taipei City.

From 1993 to 1997, a nationwide study from 56 hospitals was conducted, which showed that average incidence rate was $230/10^5$ from the database of about 50,000 patients, 69% of whom were related to traffic injury, and 70% of traffic injuries were caused by motorcycle injuries.

From our epidemiological studies, we conclude that: 1) the incidence of TBI was higher in the rural area than

in the urban area; 2) the major cause of TBI was traffic injury; 3) the most common cause of traffic injury was motorcycle related injury; 4) most of the motorcycle riders did not wear a helmet. So we asserted that the mandatory helmet use law would be the most important and effective policy to reduce and to prevent TBI in Taiwan [2, 4, 6, 12, 13, 16–21, 23, 24, 32].

Step 2: intervention

Nowadays motorcycles have become the most common and most important transportation vehicles in Taiwan. Since the implementation of the helmet use law in June 1997, helmet wearing has been required for all the motorcycle riders (including drivers and passengers). In order to clarify the effectiveness of the mandatory helmet use law, we collected 9860 motorcycle related TBI patients from 7 major hospitals in Taiwan between June 1st, 1994 and January 31st, 1998. Comparing the condition before and that after the mandatory helmet use law, we found that after the helmet use law there was a 17.4% decrease in the rate of motorcycle related TBI, a shorter hospitalization period, less severity of the injury, and better prognosis. Furthermore, the rate of disturbed

consciousness in these motorcycle related TBI was reduced by 15%, and the skull fracture and intracranial hemorrhage were reduced by 10–20%. All of these results were statistically significant ($P < 0.001$). It also showed that a motorcycle rider without a helmet carried a 7.08 times higher risk to have severe TBI than with a helmet [1, 14].

Due to above positive results, we carried out another nationwide survey from June 1, 1996 to May 31, 1998. We collected data on 8795 cases of motorcycle-related head injuries from 56 major Taiwanese hospitals, and compared the situation 1 year before and immediately after implementation of the helmet use law. After implementation of the law, the number of motorcycle-related head injuries decreased by 33%, from 5260 to 3535. A decrease in the length of hospital stay, severity of injury, and better outcome were also seen. The likelihood ratio χ^2 test showed that severity decreased after implementation of the law ($P < 0.001$). Furthermore, full helmets were found to be safer than half-shell helmets [15].

According to the reports from the Bureau of National Health Insurance, traffic injuries-related in-patient medical expenditures were reduced by one hundred and ten million US dollars in average per month after implementation of the mandatory helmet use law. The data from the Transportation Bureau showed that the numbers of motorcycle-related deaths were reduced by 423 persons per month as compared with the same duration before the legislation. The data from the Department of Health, Executive Yuan, ROC also showed the same tendency. From all of these data, we proved that helmet wearing is very effective not only in dramatic reduction of the mortality rate and severity of head injury, but also in greatly decreased medical expenditure.

Conclusions from our helmet use law intervention included; 1) a decrease in the number of TBI, 2) a decreased in the rate of intracranial hemorrhage, 3) a decreased in the number of cranial operations, 4) a reduced number of mortality, and 5) achievement of better prognosis. However, the helmet use rate has gradually decreased recently. Therefore, we have to re-enforce the helmet use law, to modify the speed limit, and to reeducate the motorcyclists for safety driving behavior [5, 9, 15, 22].

Step 3: international collaborative program

TBI is a tough and complicated issue for developing countries. However, most of the developing coun-

tries can only afford a limited budget for prevention and treatment. As a result, these developing countries suffer from a lack of human resources and medical facilities. The most important and urgent thing for the developing countries is to cooperate with other developed countries to compensate for inadequate resources and to develop their own strategies and databases.

Kraus *et al.* reported in 1990 that the annual incidence rate of head injury was 132–430/10⁵, and the annual mortality rate was 9–32/10⁵. Most of these data were collected from western countries. The developing countries, such as, Taiwan, Pakistan, India, Burkina Faso, Colombia, and Algeria, lack epidemiological data on TBI. After the year of 1990, developing countries gradually understood the fact that they faced the serious problem of TBI even more frequently than the western countries. From 1992 to 1995, comparative studies between developing countries (Taiwan, Algeria, Colombia, India, and Pakistan) and developed countries (Norway, Italy, USA, and Britain) were coordinated by the Global Spine and Head Injury Prevention Project (Global SHIP Project) [3, 10, 26, 27]. In 1997, a report on the incidence rates and mortality rates of TBI in 5 developing countries and 4 developed countries appeared, as shown in Table 2. The comparative results can be used to develop and support their own injury prevention strategies for the developing countries [11, 25, 28, 30, 33].

Table 2. Comparison of mortality rates and incidence rates related to TBI between developing countries and developed countries [28]

	Incidence (/100,000)	Mortality (/100,000)	Year	Case fatality rate (%)
Developing countries				
Algeria, Blida	80	5	1989	–
Colombia, Cali	676	120	1990	–
India, Bangalore	150	–	1990	9.6
Pakistan, Multan	81	11	1990	–
Taiwan				
Taipei	182	19	1988–1992	10.6
Hualien	304	87	1988–1992	28.7
Developed countries				
Norway				
Trodslag	200	5.5	1984	2.8
Italy				
San Marino	468	–	1981–1982	–
USA				
San Diego	180	30	1984	6
Britain				
England	270	9	1981	–
Scotland	313	9	1981	–

Step 4: clinical research in moderate and severe TBI

In the past 5 years, several clinical trials were conducted in Taiwan and most of them were multi-center trials. All these trials focused on the acute stage, subacute stage, and long term monitoring of the TBI patients to reduce the severity and mortality rates and to improve their quality of life [8, 29].

After 1970, many researches showed that application of intensive care on severe TBI patients significantly decreased the severity and mortality rates. During the intensive care period, the most important strategies for the treatment of TBI were to reduce brain edema and prevent secondary insults to the ischemia brain. Based on the above concepts, we processed several trials as follows:

Our first trial showed that sedation with Propofol for severe and moderate TBI patients during the first 3–5 days of ICU stay effectively reduced intracranial pressure (ICP) and mortality rate, and maintained cerebral perfusion pressure (CPP) and the Glasgow Coma Scale (GCS) level. This trial also showed that ICP under 25 mmHg reduced the mortality rate to one fourth in comparison with those with ICP > 25 mmHg. The only major complication to avoid was the Propofol infusion syndrome. This complication is rare in clinical practice, but extremely dangerous once it has occurred [31].

However, another trial of hypertonic saline infusion, which was reported effective by some another in brain edema control, did not show much benefit for our TBI patients. The risk of complications induced by hypertonic saline, such as acute renal failure, was too high to be compensated by the benefits of the edema control.

In our recent ongoing trial, we have measured the brain tissue oxygenation level (PbtO₂) directly in 16 patients, and incorporated the data with ICP and CPP values. Our initial result showed that maintenance of adequate PbtO₂ by adjusting FiO₂ improved outcome in severe TBI patients.

For TBI patients in the subacute stage, we made a prospective trial for hyperbaric oxygen therapy (HBOT). We tried to apply HBOT concurrently with rehabilitation to TBI patients after stabilization of their condition, and HBOT improved the GCS level considerably in these subacute stage TBI patients. However, HBOT offered some benefits only for patients with GOS 4, but not for those with GOS 2 or 3. With concurrent therapy of rehabilitation, HBOT can provide some benefits for the subacute stage TBI patients (In submission).

In addition, we also used GOS, GOSE, and the Health-Related Quality of Life (HRQL) to follow up patients continuously. This will allow us to detect whether there were differences in prognosis and quality of life after the application of ICP monitoring and CPP treatment protocol. With the above experience, we further conducted another international collaborative study of Quality of Life after Brain Injury (QOLIBRI), which was coordinated by Prof. Jean-Luc TRUELLE. There were 23 institutes from 12 countries and regions joined in the project. With this trial we evaluated patients not only with GOS or GOSE, but also with overall health condition, feeling, emotion, action, human relationship, etc. These results could provide the long-term effectiveness for the application of ICP, CPP, PbtO₂, HBOT, etc.

Step 5: guidelines for management of severe TBI in Taiwan

The incidence of TBI in Taiwan has decreased gradually after implementing of the helmet use law. But the mortality rate of severe TBI still remains as high as 35%. The management principles of TBI have greatly changed in the past 20 years. In recent years, due to developments of new monitoring techniques, the management of severe TBI has been changed from mere lowering of ICP to prevention of brain ischemia, maintenance of CPP, and lowering of brain metabolism. The publications on TBI treatment principles have been updated rapidly, and therefore it is difficult to review all the articles with limited personnel.

Before and during meetings on severe TBI, we chose nine topics: ER Treatment, ICP monitoring, CPP fluid therapy, use of sedatives, nutrition, intracranial hypertension, seizure prophylaxis, second tier therapy and assigned each topic to one contributor. The contributors searched relevant information from 1966 to 2006 on Medicine database for English and Chinese articles. With their help, a guideline for management of severe TBI in Taiwan was eventually published in June 2007.

With this guideline, we can reeducate neurosurgeons and standardize the treatment procedures for moderate to severe TBI patients [7].

Summary

With our 26-year experience of severe TBI, stepwise approaches for prevention and treatment of TBI were implemented from 1991 to 2007. The project started from epidemiological studies of TBI, and then stepped into the multi-center trials and establishment of guide-

lines through intervention and international collaboration programs. The results from those approaches were significant with a drastic decline of TBI deaths. However, further studies including stem cell therapy, neurobehavioral studies, etc. are recommended.

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