

**SEVERE TRAUMATIC BRAIN INJURY: OUTCOME
IN PATIENTS WITH DIFFUSE BRAIN INJURY
WITHOUT SURGICAL LESION MANAGED IN
HOSPITAL SULTANAH AMINAH, JOHOR BAHRU
– AN OBSERVATIONAL STUDY**

by

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ABSTRAK

Bahasa Malaysia

Topik :

ANALISA KESAN KECERDERAAN SERIUS OTAK BERKAITAN DENGAN KECERDERAAN OTAK SECARA DIFUSI TANPA TANDA KEPERLUAN PEMBEDAHAN DI KALANGAN PESAKIT YANG DIRAWAT DI HOSPITAL SULTANAH AMINAH, JOHOR BAHRU- SATU KAJIAN PEMERHATIAN.

Latar Belakang:

Kecerderaan serius otak telah menjadi salah satu faktor utama kematian di Malaysia. Penambahan bilangan pesakit yang mengalami kecederaan otak tidak dapat ditampung oleh kekurangan dari segi kemudahan rawatan rapi. Kekurangan tersebut telah menyebabkan rawatan kumpulan pesakit ini tidak tertakluk sepenuhnya ke atas cadangan rawatan yang disyorkan oleh Yayasan Kecerderaan Otak, terutamanya mereka yang tidak memerlukan sebarang rawatan intervensi neurosurgeri seperti pembedahan otak.

Objektif

Penyelidikan ini bertujuan membuat perbandingan kesan kecederaan serius otak yang dirawat menggunakan tiga kaedah rawatan yang berlainan, termasuk kumpulan yang mendapat pemerhatian tekanan dalam otak (ICP), kumpulan yang mendapat bantuan pernafasan dan kumpulan yang tidak mendapat kedua-dua kemudahan di atas. Penyelidikan ini juga bertujuan untuk mengetahui kepentingan kekerapan melakukan

imbasan otak di kalangan pesakit kecederaan otak yang serius yang mengalami kecederaan otak secara difusi. Di samping itu, ia juga untuk mengenal-pasti faktor-faktor yang berkaitan dengan tahap pemulihan pesakit yang mengalami kecederaan serius otak secara difusi tanpa tanda keperluan pembedahan dan untuk mengenal-pasti risiko kecederaan serius otak jenis ini.

Prosedur kajian

Kajian ini ialah kajian prospektif secara pemerhatian di kalangan pesakit yang mengalami kecederaan serius otak dalam bentuk kecederaan difusi otak yang tidak memerlukan rawatan pembedahan seperti yang dirumuskan dalam klasifikasi Marshall, dan dimasukkan ke Unit Rawatan Rapi Neurosurgeri (NICU), di Hospital Sultanah Aminah, Johor Bahru. Kajian ini dilakukan di antara 1hb Disember 2006 hingga bulan 31 hb Mei 2008 di mana seramai 72 orang pesakit terlibat dalam kajian ini. Pendaftaran pesakit dilakukan untuk kemasukan di antara 1hb Disember 2006 sehingga 30hb November 2007. Tempoh rawatan susulan adalah di antara tiga dan enam bulan pertama selepas dibenarkan keluar wad, dan berakhir pada 31hb Mei 2008. Semua pesakit yang mendapat kecederaan serius otak kedua-dua jantina dengan kemasukan skor kesedaran lapan dan ke bawah, mengalami kecederaan otak secara difusi tanpa tanda keperluan pembedahan dan dimasukkan secara kemasukan terus atau dari rujukan hospital lain dalam masa 24 jam selepas kemalangan dianalisa. Tanda keperluan pembedahan ditakrifkan sebagai kehadiran tanda dengan jumlah kandungan melebihi 25 cc sebagaimana yang ditakrifkan dalam klasifikasi CT oleh Marshall. Pesakit yang mengalami kecederaan organ lain dan mengalami ketidakstabilan tanda vital dan memerlukan pembedahan bukan otak dan

bantuan pernafasan, pesakit yang mengalami penyakit perubatan yang melibatkan kegagalan organ, endokrin dan darah, pesakit yang disuspek dalam penyalahgunaan dadah atau alkohol, kecacatan mental, riwayat hidup berkaitan dengan sawan, atau pesakit yang mengalami tanda-tanda ketiadaan fungsi batang otak dan gagal dalam usaha penstabilan tanda vital tidak dimasukkan dalam senarai pesakit yang dikaji. Keputusan kajian tersebut dianalisa dengan menggunakan aplikasi SPSS versi 12.0.1. Min dan tahap ralat dikira bagi nilai berterusan, frekuensi dan peratusan bagi nilai kategori. Ujian Pearson Chi-square digunakan untuk nilai kategori bandingan antara dua kumpulan (Keputusan baik atau buruk). Sekiranya nilai jangkakan frekuensi kurang dari lima bagi dua puluh peratus sel, maka Ujian Fisher Exact digunakan. Untuk nilai dikotomi di kalangan tiga kumpulan yang tidak berkaitan, ujian Chi-square digunakan. One-way ANOVA digunakan untuk nilai nombor bagi tiga kumpulan yang tidak berkaitan selepas pemeriksaan normal dan jangkakan dicapai. Jika tidak, ujian Kruskal-Wallis digunakan. Dalam ujian ini, sekiranya nilai p adalah nyata, maka ujian multi Mann-Whitney dilakukan dan diinterpretasikan. Nilai nyata ditentukan pada nilai p kurang dari 0.05. Faktor-faktor jangkakan kecederaan difusi otak di kalangan pesakit yang mengalami kecederaan otak yang serius ditentukan dengan menggunakan model Cox Proportional Hazards Regression.

Analisis statistik

Seramai tujuh puluh dua pesakit kecederaan serius otak yang mengalami kecederaan difusi otak yang telah dimasukkan ke Unit Rawatan Rapi Neurosurgeri, Hospital Sultanah Aminah, Johor Bahru di antara 1 hb Disember 2007 dan 30 hb November 2007 telah dikaji. Umur pesakit-pesakit tersebut di antara lapan dan 64.8 tahun, dengan umur median pada 34.1 tahun, umur mean pada 34.2 tahun dan tahap ralat sebanyak 14.7 tahun. Kebanyakan pesakit dikalangan lelaki dengan 61 orang (84.7%) dan perempuan seramai 11 orang. Daripada jumlah 72 pesakit, 41 (56.2%) pesakit dirawat dengan kaedah intubasi sahaja dalam memastikan penjagaan salur penafasan dan untuk pemberian oksigen melalui 'oxyvent' dan pemerhatian berterusan ketepuan oksigen. Sejumlah 16 pesakit dirawat dengan bantuan alat pernafasan termasuk mereka yang diberi rawatan "cerebral resuscitation". Seramai 15 pesakit (20.8%) diberi rawatan dengan pemerhatian tekanan dalam otak (ICP) dan tekanan perfusi otak (CPP). Sebelas pesakit mengalami kehilangan nyawa semasa di hospital (15.3%). Selebihnya, 49 (80.3%) datang semula dalam rawatan susulan tiga bulan pertama dengan tiga kematian dikesan, dan seramai 45 orang (77.5%) dalam rawatan susulan tiga bulan kemudiannya. Semasa tiga bulan pertama, hanya tujuh (15.2%) pesakit masih mengalami kecacatan serius, dengan empat kecacatan sederhana dan 29 (63%) pesakit dengan pemulihan yang memuaskan. Dalam rawatan susulan bulan ke-enam, hanya seorang pesakit mengalami kecacatan serius, dan selebihnya seramai 44 (97.8%) orang pesakit mengalami pemulihan baik dan sederhana baik. Keputusan yang buruk di kalangan kumpulan yang dirawat dengan kaedah ICP-CPP dengan median (IQR) skor GOS semasa discaj sebanyak 2.00(2) berbanding dengan kumpulan intubasi sebanyak 4.00(1) dan kumpulan ventilasi sebanyak 3.00(1).

Keputusan ini terbukti secara statistik dengan keputusan buruk di kalangan kumpulan ICP-CPP berbanding kumpulan intubasi ($p=0.001$). Perbezaan ini juga dilihat selepas tiga bulan kecederaan dengan perbezaan nyata di antara kumpulan intubasi dan ventilasi ($p=0.012$) dengan median skor GOS yang lebih rendah bagi kumpulan ventilasi. Pada enam bulan selepas kecederaan, kumpulan intubasi mempunyai median skor GOS yang lebih baik berbanding kumpulan ICP-CPP dan kumpulan ventilasi, dengan nilai nyata statistik p sebanyak <0.001 dan $p=0.004$ bagi setiap satu perbandingan. Rutin dalam melakukan ulangan imbasan otak di kalangan 42 (80.8%) orang pesakit menunjukkan bahawa imbasan tersebut tidak menunjukkan apa-apa perubahan. Tiada pesakit yang menunjukkan perubahan dalam imbasan otak tanpa perubahan klinikal diberi rawatan lain. Analisa berkaitan dengan faktor-faktor yang nyata secara statistik yang mempengaruhi keputusan semasa enam bulan selepas kecederaan termasuk skor tindakan motor semasa kemasukan ($p=0.012$), GCS semasa kemasukan ($p=0.007$), 'rapid eye movement' ($p=0.001$), dan jenis kecederaan difusi otak ($p=0.009$). Risiko kematian di kalangan kumpulan ICP-CPP adalah nyata secara statistik dibandingkan dengan kumpulan intubasi ($p=0.008$)

Rumusan

Dalam kecederaan otak secara difusi tanpa tanda keperluan pembedahan, keseriusannya tidak seteruk yang dialami dalam kecederaan otak secara difusi bersama pendarahan dalam otak yang memerlukan pembedahan. Rumusan ini berpandukan kepada kadar kematian di hospital yang lebih rendah (15.3%) berbanding dengan kumpulan pesakit yang melibatkan mereka yang mengalami tanda keperluan pembedahan dengan peratusan

kematian di antara 20.7% dan 37.8%. Keputusan ini mungkin disebabkan oleh bilangan ramai pesakit dalam kumpulan kecederaan difusi jenis I dan II yang tidak berkait dengan tekanan tinggi dalam otak berbanding dengan jenis III dan IV. Dalam cadangan pengurusan kecederaan otak, kaedah rawatan spesifik diperlukan untuk pesakit kecederaan otak secara difusi tanpa tanda keperluan pembedahan. Kesan buruk dalam perawatan pesakit secara yang dicadangkan memberi peringatan kepada kita sekiranya kita telah melakukan lebih dari yang diperlukan. Walau bagaimanapun, kesan buruk dalam kumpulan pesakit ini mungkin disebabkan kecederaan primer itu sendiri, kerana kebanyakan mereka mengalami tahap ketidak-sedaran yang mendalam semasa kemasukan dengan imbasan CT yang lebih serius. Berdasarkan dengan kajian ini, saya ingin mencadangkan rawatan yang lebih sederhana yang difikirkan lebih sesuai di kalangan kumpulan pesakit yang mengalami kecederaan difusi jenis I dan II dalam imbasan CT, yang mempunyai GCS kemasukan antara enam dan lapan, respons motor yang normal dan mempunyai respons 'rapid eye movement' yang nyata semasa kemasukan. Sekiranya tidak, mereka perlu dirawat dengan segala kemudahan yang terbaik seperti yang dicadangkan oleh 'Brain Trauma Foundation'.

ABSTRACT

Title:

SEVERE TRAUMATIC BRAIN INJURY: OUTCOME IN PATIENTS WITH DIFFUSE BRAIN INJURY WITHOUT SURGICAL LESION MANAGED IN HOSPITAL SULTANAH AMINAH, JOHOR BAHRU – AN OBSERVATIONAL STUDY

Background:

Severe traumatic brain injury has been one of the major causes of death in Malaysia. There has been limited numbers of intensive care facilities to cater for the escalating numbers of severe traumatic brain injury patients. Due to the limitation, not all the patients in this group been managed strictly according to the recommendations given by the Brain Trauma Foundation, especially those who did not warrant any neurosurgical intervention such as a craniotomy.

Objective:

The aim of this research was to compare the outcome of the severe traumatic brain injury with diffuse brain injury without surgical lesion treated with different treatment modalities, namely ICP-CPP-targeted, ventilation and intubation groups. This research also aims to assess the usefulness of routine serial head computed tomography (CT scan) in severe traumatic brain injury patients with diffuse brain injury without surgical lesion. It is also aims to identify factors influencing the outcome of severe brain injury patients with diffuse brain injury without surgical lesion and to determine the hazards risk of severe traumatic brain injury patients with diffuse brain injury without surgical lesion.

Research procedure:

This was a prospective observational study of severe traumatic brain injury patients admitted with diffuse brain injury without surgical lesion as defined by Marshall's Classification for Diffuse Injury, to Neurosurgical Intensive Care Unit (NICU), Hospital Sultanah Aminah, Johor Bahru. The study was conducted between 1st December 2006 and 31th May 2008 with a total of 72 patients included in the study. The patients' recruitment period was from 1st December 2006 to 30th November 2007. The follow-up was done at the third month and sixth month from the date of discharge of the recruited patients, which ended on 31th May 2008. All patients were with severe traumatic brain injury patients of both sexes, with the admission GCS of eight or below and sustained blunt head injury without surgical or mass lesion and admitted via direct admission or transferred from other hospital within 24 hours post trauma. Surgical or mass lesion defined as any high or mixed-density lesion of more than 25 cc, as defined by Marshall's CT Classification. Patients with polytrauma which caused unstable hemodynamic status, requiring immediate non head surgical intervention and post operative ventilation support, severe underlying medical disorders such as major organ failure, endocrinological or hematological disorder, suspected drug or alcohol intoxication, mentally subnormal, or history of chronic epilepsy before the event of head trauma, or who on arrival had unilateral or bilateral fixed and dilated pupils believed to be due to ongoing herniation, clinically showing absence of brain stem reflexes, with no improvement after resuscitation or failed resuscitation upon admission and patients who had a known history of hemiparesis, or had any other condition that lowered the patient's functional status score were excluded in the study.

Data entry and analysis was done using Statistical Package for Social Sciences (SPSS) version 12.0.1 Means and standard deviations were calculated for continuous variables, and frequency and percentages for categorical variables. Pearson Chi-square Test was used for categorical data between two groups (good and poor outcome). Pearson Chi-square values were determined, however if the expected frequency of less than five were more than twenty percent of the cells, Fisher's Exact Test was applied. Chi-square was applied to assess association between binary dependent variable and three treatment variables. One-Way ANOVA was applied for numerical variables of three treatment variables after normality checking when the assumptions were met. Median and interquartile range were calculated for numerical variable if it was not normally distributed and Kruskal Wallis Test was applied. Multiple Mann-Whitney Tests were performed and interpreted if the p value was significant. The significant value was set at p value less than 0.05. The prognostic factors of diffuse brain injury without surgical lesion among severe traumatic brain injury patients were determined using Cox Proportional Hazards Regression Model. For Multiple Cox Proportional Hazards Regression Model, forward stepwise was applied. Log-minus-log plot, hazards function plot and partial residuals were applied to check the model assumption.

Result

Seventy two patients with severe traumatic brain injury with diffuse brain injury without surgical lesion treated in NICU, Hospital Sultanah Aminah, Johor Bahru between 1st December 2006 and 30th November 2007 were studied. The age of patients were ranging from eight to 64.8 years old, with median age at 34.1 years old, mean age of 34.2 years

old and standard deviation of 14.7 years old. Majority of patients were male, with 61 patients (84.7%) and remaining 11 patients were female. From a total of 72 patients admitted for diffuse brain injuries, without any surgical lesion, 41 (56.2%) were just treated with intubation for airway protection, and given oxygen via oxyvent device with continuous oxygen saturation monitoring. A total number of 16 patients were treated with ventilation support due to various reasons, which include cerebral resuscitation without ICP-CPP guided management. There were only 15 (20.8%) patients who were treated with standard ICP-CPP guided cerebral resuscitation. Eleven patients died during hospitalization (15.3%). Out of remaining 61 patients, only 49 patients (80.3%) were follow-up during first three months (with three deaths) and 45 out of 58 patients (77.6%) were follow-up during subsequent three months (with no death detected). On first third month follow-up, seven (15.2%) were still severely disabled, with moderate disability reported in four patients and 29 (63%) patients with good recovery. On the next sixth month follow-up, there were left with only one patient with severe disability, while the rest of 44 (97.8%) patients were improved with either moderate or good recovery. Outcome was worse in the ICP-CPP targeted group with median(IQR) GOS score of 2.00(2) compared to intubation group with median (IQR) of 4.00(1) and 3.00(1) in ventilation group upon discharge. This finding was statistically significant for a worse outcome in ICP-CPP targeted group than intubation group. ($p=0.001$). This difference was also seen during first three months follow-up but it was between intubation group and ventilation group ($p=0.012$) with lower median GOS in ventilation group. At sixth months follow-up, intubation group had a better median GOS compared with ICP-CPP targeted group and ventilation group, with statistically significant p value of <0.001 and

$p=0.004$ respectively. Routine CT scans were done and our findings showed that 42 (80.8%) patients did not show any progression. None of patients where a repeat HCT showed progression without clinical deterioration was given any intervention. The analysis demonstrated that the following factors were statistically significant associated with outcome at six months follow up: Best motor response on admission ($p=0.012$); Glasgow Coma Score (GCS) on admission ($p=0.007$); Rapid eye movement ($p=0.001$) and Type of diffuse injury ($p=0.009$). There was statistically significant of the increase in the hazards of dying in ICP-CPP targeted management group compared to intubation group ($p=0.008$).

Conclusion

In diffuse brain injury without surgical or significant mass lesion, the severity of the brain injury may not be as bad compared with those with associated surgical lesion such as intracerebral hemorrhage and acute subdural hemorrhage. This is concluded based on the finding of lower hospital mortality rate (15.3%) in this subgroup of patients with severe head injury compared to most studies which included those with surgical lesion, with mortality rate between 20.7% and 37.8%. This finding may be influenced by a high number of patients with diffuse injury type I and II, which were not associated with increased intracranial pressure compared to type III and IV. In term of recommendations for management of brain trauma, specific treatment plan may be needed for patients with diffuse brain injury without surgical lesion. The devastating outcome of patients treated with the best recommended plan shown in this study may alert us if we have done more than what is required. However, the poor outcome seen in this group of patients may be

resulted from the primary brain injury itself, as most of them with more depressed level of consciousness on admission and with more severe diffuse brain injury seen in CT imaging. Based on the study, I would like to propose a more conservative management which may be suitable for a subgroup of patients with minimal CT findings of Diffuse Injury type I and II, with better admission GCS between six and eight, normal motor response and with strong evidence of rapid eye movement on admission. Otherwise they should be treated with the best available facilities as recommended by The Brain Trauma Foundation.

1. INTRODUCTION

Severe traumatic brain injury (TBI) has been one of the major causes of death in Malaysia. It is a leading cause of death in the younger generations which include children and adult younger than 45 years old (Moppett, 2007). The leading cause of traumatic brain injuries is motor vehicle accidents and head injury feature a common cause of death in road traffic accidents (RTA). It probably accounts for three quarter of the morbidity and mortality rates in RTA in the country. In Malaysia, the incidence of road traffic accident is one of the highest in the world with about 22 deaths per 100,000 populations (PDRM, 2007) There are about six thousands two hundreds deaths per annum recorded since year 2003, while almost ten thousands victims sustained severe disabilities. The figure of mortality has not taking account of those admitted with severe TBI and eventually died in the hospital. While the rate of traumatic brain injury (TBI)-related hospitalization is declining in developed countries like United States due to better injury prevention (Thurman *et al.*, 1999), there are increasing trends of such needs in developing countries like Malaysia. This has been a big financial burden to the country.

Hospitalizations of those sustained severe injuries involve the utilization of beds in intensive care unit. In Malaysia, a total of 276 ICU beds available in all government hospitals (Maskon, 2005). Hospitalization of severe injured patients occupied about 25 beds per admission per day. This is about ten percent of all ICU beds available. There are only seven general hospitals and three university hospitals in Malaysia with neurosurgical services. With such limited numbers of ICU beds and limited numbers of

neurosurgical intensive care units in Malaysia, certainly there will be shortage of facilities needed to cater for a larger number of severe traumatic brain injured patients. The recommendations given by Brain Trauma Foundation in the management of severe traumatic brain injury patients cannot be implemented for all patients with such limitation. Additional criteria are set for the selection of TBI patients who will be benefited most from the intensive neurosurgical treatment.

An impact that transfers energy to the brain at the time of injury can result in varying extent of mechanical, neuronal and axonal damage which are often difficult to salvage. This kind of brain damage is term as primary brain injury. Secondary brain damage occurs from prospectively treatable conditions such as increased intracranial pressure (ICP), intracranial bleeding, ischemia, hypercarbia, and hypoxia. Maximizing management is of critical importance to minimize secondary brain damage with objective of decreasing overall mortality and improve functional outcome. Despite active management in the treatment of severe traumatic brain injured patients, the mortality and morbidity are still very high. The presence guidelines for the management of patient with severe traumatic brain injury ($GCS \leq 8$) with an abnormal CT brain findings on admission or a normal CT scan findings on admission but fulfilling 2 out 3 clinical criteria, which include age above 40 years old, abnormal motor respond and episodes of hypotension ($SBP < 90$ mmHg) is to ICP-monitored and cerebral protected, based on cerebral perfusion pressure (CPP) and ICP guide (Anonymous, 2007).

However ICP monitoring, ICU and high dependency unit (HDU) are facilities which often limited in most general hospitals in Malaysia to meet the high demand of patients with severe traumatic brain injuries. Hospital Sultanah Aminah, Johor Bahru, is one of the hospitals in Malaysia with neurosurgical unit. However of all the severe traumatic brain injured patients admitted to the hospital, only 75% of patients managed on a standardized head injury protocol with ICP monitoring and cerebral protection. Another 25% of patients managed conservatively due to limited resources. These figures are based on all severe head injury patients, which include those require surgical intervention. However, for those with diffuse brain injuries without other significant focal lesions that certainly do not warrant any surgical intervention, there were only twenty percent of them were treated with cerebral resuscitation with ICP targeted management. Most patients were just treated by intubation for airway protection and not ventilated.

This is a prospective observational study to look into the outcome of patients categorized as severe traumatic brain injury with diffuse brain injury without surgical lesion, mainly on the mortality and morbidity rate using Glasgow Outcome Score (GOS), and the usefulness of routine serial head computed tomography (HCT) scan in lieu of proper ICP-CPP-targeted management.