Original Research Paper

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Correlation of Outcome of Diffuse Axonal Injury with Reference to Magnetic Resonance Grading

Medical Science

KEYWORDS : Brain stem, Consciousness, Diffuse axonal injury, MRI

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ABSTRACT

Introduction: *Diffuse axonal injury is defined as prolonged post-traumatic coma over 6 hours following injury without demonstrable mass lesion.It can be diagnosed using clinical signs and radiological evidence on MRI.*

Objective: *This study was conducted to investigate the correlation between brain magnetic resonance imaging (MRI) grading for diffuse axonal injury and the time interval to recovery of consciousness and outcome in patients with diffuse axonal injury.*

Methods: *Forty patients at our hospital from January 2015 to 2016 June who had been diagnosed with diffuse axonal injury and underwent MRI was included in this study. We retrospectively investigated the patients' medical records and radiological findings. We divided the patients into three groups according to the grade of MRI finding: grade I, small scattered lesions on the white matter of the cerebral hemisphere; grade II, focal lesions on the corpus callosum; and grade III, additional focal lesions on the brain stem.*

Result: *Out of 40 patients grade one injuries noted in 10 (25%) patients. Their mean GCS score at the time of admission was7.6, and mean time interval to awake status was 3.7 days. Grade two injuries noted in 16 (40%) patients. Their mean GCS score at the time of admission was 7.56 and mean time interval to awake status was14.5 days. Grade three injuries were noted in 14 (35%) patients. Their GCS score at the time of admission was 6.28 and mean time interval to awake status was 38.35 days. Patients' GCS scores in the grade I and II groups began to improve soon after admission as compared to grade III group that did not improve until 1 month after injury.*

Conclusion: *This study shows a correlation between the time intervals to recovery of consciousness in patients with diffuse axonal injury and the degrees of brain injuries seen on MRI,. Patients with diffuse axonal injuries with small hemorrhagic lesions on the hemispheric white matter or corpus callosum (Grade 1 and 2) recovered consciousness within 2 weeks. In contrast, patients with additional lesions on the brain stem (grade 3) did not recover consciousness within 2 months. Outcome better in female compared to male.*

INTRODUCTION

Diffuse axonal injury is defined as prolonged post-traumatic coma over 6 hours following injury without demonstrable mass lesion[3]. There is widespread tearing of axons and small vessels in the white matter of the brain, instead of occurring in a specific area. Diffuse axonal injury is caused by acceleration-deceleration effects of the mechanical input to the head upon shaking of the brain within the skull. This results in shearing or stretching of nerve fibers with consequential axonal damage. Automobile accidents, sports-related accidents, violence, falls, and child abuse such as Shaken Baby Syndrome are common causes of diffuse axonal injury.

It was first defined by Strich[17] in a study of patients with severe post-traumatic dementia in 1956. The time course of the pathological changes was established by Adams et al[1]. Diffuse axonal injury can be diagnosed using clinical signs and radiological evidence. Brain magnetic resonance imaging (MRI) is known to be the most sensitive method to diagnose diffuse axonal injury, especially in gradient echo image[10]. Numerous studies have been performed on the outcome of and the searching for the prognostic factors of diffuse axonal injury. This study aimed to investigate the correlation between the degrees of injuries based on MRI findings and the mean time intervals to recovery of consciousness in patients with diffuse axonal injuries.

MATERIALS AND METHODS

Forty patients who had been diagnosed with diffuse axonal injury and underwent MRI at our hospital from January 2015 to June 2016 were included in this study. We Follow up period was 2 to 6 months. We had excluded patients with secondary hypoxic brain damage on admission or who had undergone cranial operation during treatment from this study. All the Patients details and radiographic findings were reviewed prospectively and include all those patients who full fill our inclusion criteria in during study period. Patients were divided into three groups according to the location of lesions on MRI findings (grade I, II, and III) as classified by Gennarelli et al[7]. An MRI finding of scattered small hemorrhagic lesions on hemispheric white matter was classified as grade I, a finding of additional focal lesions on the corpus callosum was classified as grade II, and a finding of additional focal lesions on the brain stem was classified as grade III (Fig. 1).

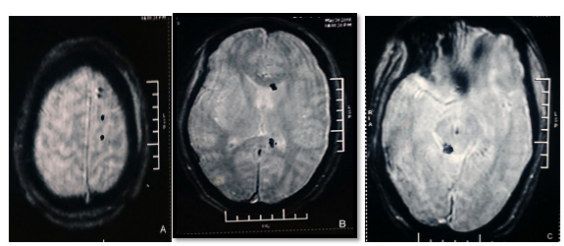

Fig 1: Magnetic resonance images show multiple small hemorrhagic foci on the hemispheric white matter (A), corpus callosum (B), and brain stem (C).

Various clinical parameters such as sex, age, initial Glasgow Coma Scale (GCS) score, follow-up GCS score, time interval from injury to recovery of consciousness (awake status), and Glasgow Outcome Scale (GOS) were investigated. Recovery of consciousness was defined as opening eyes to verbal stimulus and obedience to command. Outcome was assessed by GOS as GR (good recovery), MD (mild disability), SD (severe disability), PVS (persistent vegetative state), and death.

Statistical analysis was conducted with the SPSS (version 20.0) (Trial Version). The Variation between the MRI grade and the mean time interval to recovery of consciousness was evaluated by one-way analysis of variance (ANOVA). Statistical significance was defined as $p < 0.05$.

RESULT

We evaluated 40 patients of Diffuse Axonal injuries. Among these 24 patients 60%were male and 16 patients 40 %were

female. Male to female ratio was 3:2. Mean age was 25.68 years. Cause of head injuries in these patients were road traffic accident in 22(55%) patients, fall from height in10 (25%) patients, sports injury in 3 (7.5%) patients, accidental hit by animal in 5(12.5%) patients. These patients had several coincidental injuries such as rib fracture long bone injuries maxillofacial injuries and soft tissue injuries in body. These patients also has scanty amount of intra cranial hemorrhage, contusion and cranial bone fracture but for these they not require surgery. No other surgical procedure done on them except tracheotomy and stitching of superficial skin wound. Tracheotomy was performed in eight patients due to developed respiratory tract infections. Average GCS score of all patients on admission was 6.9 and mean follow up period was 9.33 months. By using GOS to classify outcome 19 patients were assessed as GR, 12 Patients were assessed as MD, 4 patients were assessed as SD and 5 patients were assessed as PVS. Among 40 patients grade one injuries noted in 10 (25%) patients. Their mean GCS score at the time of admission was7.6, and mean time interval to awake status was 3.7 days. In these patients GR was noted in 6 (60%) patients, MD in 4(40%) Patients. No patients develop SD or PVS. Grade two injuries noted in 16 (40%) patients. Their mean GCS score at the time of admission was 7.56 and mean time interval to awake status was14.5 days. In these patients GR was noted in11 (68.8%) Patients, MD in 4 (25%) Patients SD in one (6.2%) Patient No patients had death or PVS. Grade three injuries were noted in 14 (35%) patients. Their GCS score at the time of admission was 6.28 and mean time interval to awake status was 38.35 days. In these patients GR was noted in 2 (14.3%) patients, MD in 4(28.6%) Patients, SD in 3 (21.4%) Patients PVS in 5(35.7%) patients. Fig. 2 shows the Sequential changes in the mean GCS scores of each grade over time. Patients' GCS scores in the grade I and II groups began to improve soon after admission; those in the grade III group did not improve until 1 month after injury.

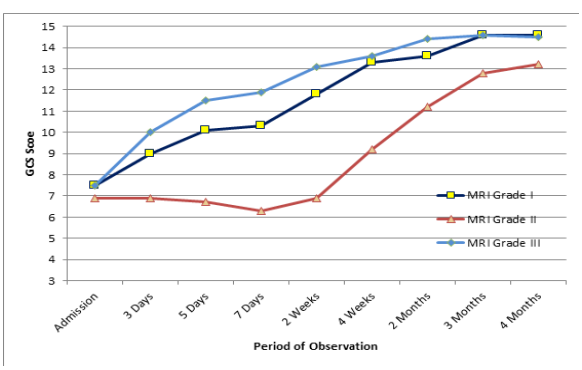

Fig 2: Sequential changes in the mean GCS scores of each grade over time

Statistical analysis was performed for comparison of the mean time interval to awake status of each grade (Table 1). The mean time interval to awake status between the grade I and II groups did not show significant difference; however, there were statistically significant differences between the grade I and III groups (p = 0.004) and the grade II and III groups (p = 0.030) (Table 1).

Table 1: comparison of the mean time interval to awake status of each grade

(I) MRI GRADE	(J) MRI GRADE	Mean Difference (I-J)	Std. Error	Sig.
I	II	-10.80000	9.87228	0.524
	III	-34.65714*	10.13987	0.004
II	III	-23.85714*	8.96246	0.030

In our study we also noted that out of 4 female patients of grade 3 injuries, 3 (75%) patients had good outcome (Good recovery and mild disability). As compared to male where Out of 10 male patients of grade 3 injury only three patients (30 %) had only good outcome. (Table 2)

Table 2: outcome in grade 3 injuries patients

Sex (No of patients)	Good recovery	Mild disability	Sever disability	Persistent vegetative state
Male (10)	1	2	2	5
Female (4)	1	2	1	0

Chi Sq = 5.635 p value = 0.018*(S)

DISCUSSION

Diffuse axonal injury is defined as prolonged post-traumatic coma over 6 hours following injury without demonstrable mass lesion[5]. There is widespread tearing of axons and small vessels in the white matter of the brain instead of occurring in a specific area,

It was first defined by Strich in a study of patients as "diffuse degeneration of the cerebral white matter" in a series of patients with severe post-traumatic dementia in 1956.

Diffuse axonal injury is caused by acceleration-deceleration effects of the mechanical input to the head upon shaking of the brain within the skull[6]. The brain is partially fixed within the hard skull, so that the deep and the superficial part of the brain can move at different speeds. Further damage can occur in the transition between white and gray matter because the tissues have different consistency and will move differently. This results in shearing or stretching of nerve fibers with consequential axonal damage. Falx will prevent movement of the hemispheres across the midline, but since corpus callosum is the connection between the more moving hemispheres, believed this structure and other midline structures to be particularly susceptible to shear forces Mostly. Automobile accidents, sports-related accidents, violence, falls, and child abuse such as Shaken Baby Syndrome are common causes of diffuse axonal injury that produce long acceleration comparatively. Determination of its severity is based on the direction, magnitude, and speed of the head motion during the injury sequence. Gennarelli et al. reported a high correlation between the direction of the head motion in acceleration and the duration of coma in an experimental animal model study. Although diffuse axonal injury could occasionally occur when the head was accelerated in a sagittal or oblique direction, it was most readily produced by coronal acceleration of the head. In mild injury the lesions are localized within fronto-temporal cerebral white matter, stronger injury of rotatory acceleration caused additional lesions on corpus callosum and upper brain stem. Gennarelli et al. reported severe injury has a tendency to cause deeper lesions.

The time course of the pathological changes has been established by Adams et al. In humans, instantaneous injury occurs to numerous axons in the white matter of the brain, manifested by axonal retraction balls visible on microscopic examination. Gross lesions associated with severe diffuse axonal injury in humans consist of hemorrhagic tears in the corpus callosum and in the dorsolateral quadrant of the rostral brain stem. Several days later, microglial clusters appear and the axonal retraction balls start to disappear. Months after the injury, the bulk of the white matter is reduced and long tract degeneration can be demonstrated.

Diffuse axonal injury can be diagnosed using clinical signs (level of consciousness and neurological deficits) and radio-

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logical findings. Pupillary dilatasjon not caused herniation, can be seen in severe diffuse axonal injury Furthermore, increased sympathetic activity, such as hypertension, tachycardia, increased sweating and fever, occur due to damage in the brain stem and in the hypothalamus Lesions affecting pyramid courses in the internal capsule and brainstem may cause paresis and spasticity

Typical CT findings of diffuse axonal injury is small, punctiform bleeding in the transition between gray and white matter of the cerebrum and less frequently in the corpus callosum, blood in the ventricle and blood in the subarachnoid space around the mesencephalon . Non-hemorrhagic lesions are difficult to detect by CT. CT will therefore underestimate the incidence and extent of the diffuse axonal injury. Patients with such an injury can have normal CT.

Brain magnetic resonance imaging (MRI) is known to be the most sensitive method to diagnose diffuse axonal injury, Diffusion MRI is a relatively new technique that shows thermal motion of water molecules in tissue. By diffuse axonal injury, the decrease in water diffusion when collapse of the cell structure occure. Areas of the brain tissue with reduced diffusion indicates an irreversible cell injury that will lead to tissue necrosis. Newer studies such as Diffusion tensor imaging are able to demonstrate the degree of white matter fiber tract injury even when the standard MRI is negative. Zimmerman et al reported the first study of radiological diagnosis of diffuse axonal injury that includes small hemorrhagic lesions on the corpus callosum, upper brain stem, corticomedullary junction, parasagittal area, and basal ganglia.

Patients often have a process with three clinical phases: After a period of unconsciousness follows a period of disorientation, known as post-traumatic amnesia, and finally seen a stage of total or partial recovery of cognitive function The duration of the phases increases with the severity of the injury, so that in the most severe cases would like to see a long-drawn path. Some patients after coma go into a vegetative state and then possibly go into a so-called minimally conscious state However, we have observed that most survivors will regain consciousness and a form of communication capability, although there is extensive cognitive outcomes.

Numerous clinical prognostic factors in patients with severe head injuries have been studied, including initial GCS, abnormal motor response, hypothalamic injury sign, duration of loss of consciousness, initial pupil size, associated hypotension or hypoxia, age, and sex[12,18]

Hypoxia and hypotension have been known to be among the most important associated medical conditions with regard to outcome in severely injured patients[13.] Initial GCS in patients with head injuries strongly correlates with outcome, especially a GCS score below 5, which is associated with a poorer outcome[6,16.] Pupillary abnormalities such as anisocoria or bilateral pupil dilatation due to herniation have also been reported to correlate with poor prognosis[11,14.] The duration of loss of consciousness has been shown to be strongly related with the outcome in some reports[16,18]

The correlation between outcome and MRI findings has been studied in several reports.Kim et al[9]. reported an association between higher MRI grade and longer duration of loss of consciousness, but not statistically significant difference between MRI grade and outcome or clinical severity. Oh et al[15]. reported worse outcomes in patients with brain stem lesions shown on MRI but sizes of lesions were not consistent with outcomes. Kim et al. reported more lesions on corpus callosum and brain stem in worse outcome in patients. And Park et al[16].reported that 14.3% of patients with cerebral white matter lesions did not recover their consciousness and 50% of patients with corpus callosum lesions, 51.6% of patients with brain stem lesion did not recover their consciousness. In our study, initial GCS scores of each MRI grade were similar, but sequential changes in GCS scores looked different : the mean GCS scores of the grade I and II groups tended to improve within 5 days, but GCS score improvement was not seen in the grade III group until after 1 month (Fig. 2). We investigated the mean time interval to awake status according to the MRI grade. Patients with grade I or II injury recovered their consciousness within 2 weeks. Patients with grade III injury recovered consciousness within 2 months. Although our relatively small number of cases was a limitation, our data were statistically significant. Therefore, in case of diffuse axonal injury except secondary hypoxic brain damage, patients with lesions on cerebral white matter and corpus callosum has a tendency to recover their consciousness earlier than patients with lesions on brain stem.

Recent evidence from experimental models has shown a markedly reduced vulnerability of female brain. It has been postulated that the lesser vulnerability of female brain may be due to neuroprotactive effect of estrogen and progestron

Mechanism thought to mediate the neuroprotective effect of estrogen include;preserved vascular autoregulatory capacity, membrane stabilizing antioxidant effect attenuation of Ab production,suppression of neuronal excitability, upregulation of proapoptotic bcl-2 The findings of this research paper suggest that women had less chance of dying than men of the same age and the same TBI severity with the same etiology of trauma in the same year of occurrence. Mortality differences have also been found in a study done with stroke patients, with women having a better 1-year survival rate after a stroke . The hypothesis to explain this difference is related to progesterone's neuroprotective effect in TBI . The animal and human brain injury literature suggests a possible female gender advantage in recovery from TBI based on the theory that the presence of progesterone has a neuroprotective effect following TBI[21] . In these studies, female gender was independently associated with reduced mortality and less complications after TBI.

CONCLUSION

This study shows a correlation between the time intervals to recovery of consciousness in patients with diffuse axonal injury and the degrees of brain injuries seen on MRI, despite the limitation of a small study population. Patients with diffuse axonal injuries with small hemorrhagic lesions on the hemispheric white matter or corpus callosum recovered consciousness within 2 weeks. In contrast, patients with additional lesions on the brain stem did not recover consciousness within 2 months. Outcome better in female compared to male.

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