A Study of Non Traumatic Coma with Respect to Etiology and Outcome

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ABSTRACT

Introduction: Coma is among the most common and striking problems in general medicine. Because coma demands immediate attention, the physician must employ an organized approach.

Material and methods: A prospective observational cohort study was undertaken in 50 randomly selected patients of non-traumatic coma admitted to a tertiary care hospital over a period of one year. The selected patients were evaluated by detailed history, clinical examination and relevant investigations.

Results: Intracranial causes (50%) consisting of cerebrovascular accident and neuroinfection were responsible for the majority of cases followed by metabolic causes (44%) and drug/poisoning induced (6%). Mortality was highest (40%) in intracranial causes group. Drug induced coma showed the best recovery.

Conclusion: Intracranial lesions (cerebrovascular accident and neuroinfection) is the most common etiology of non traumatic coma and is associated with the worst prognosis.

Keywords: Glasgow coma scale, Cerebrovascular accident, Neuroinfection.

INTRODUCTION

Coma is a state of unarousable unconsciousness without any psychologically understandable response to external stimuli or inner need. The patient may appear to be asleep but is incapable of responding normally to external stimuli other than by showing eye opening to pain, flexion or extension of limbs to pain, and occasionally grunting or groaning in response to painful stimuli. It occurs when there is damage to the reticular activating substance in the upper midbrain or its projections, bilateral damage to large areas of the cerebral hemispheres, or suppression of reticuloencephal function. Non traumatic coma is among the most challenging problems faced by the physician. Non traumatic coma is caused by a wide variety of conditions, some of which are more common than the others. Some of the causes of non-traumatic coma are cerebrovascular accidents, drug intoxication, metabolic disturbances, post seizure states, status epilepticus, meningitis, encephalitis, brain tumour, brain abscess.¹ The prospect of a patient in coma recovering is totally dependent upon the cause and duration of the coma; coma due to metabolic causes, endocrine disorders, hypothermia or drug intoxication is most often reversible if treated rapidly and appropriately. Clinical signs that are important for prognosis include the motor component of the GCS, the duration of coma (which is really a duration of lack of eye-opening) and other signs of brainstem damage.²

The cause of non-traumatic coma is not always evident at presentation. Knowledge about the various etiologies of non traumatic coma can guide the initial evaluation of the patient and hence facilitate an early etiological diagnosis and prompt treatment. Hereby we present a study with the aim and objective to examine the etiologies of non traumatic coma in a tertiary care hospital and to study the outcome of the patients with respect to etiology. This study also aims to determine the relationship between the Glasgow coma scale score and the outcome of the patient with non traumatic coma.

MATERIAL AND METHODS

A prospective observational cohort study was undertaken in 50 randomly selected patients of non-traumatic coma admitted to B.M. Hospital, Mysore, over a period of 1 year, who were diagnosed and evaluated by detailed history and clinical examination. Institutional ethical committee clearance was obtained to conduct the study. Informed consent was obtained from relatives / attenders of the patients.

Patients above the age of 18 years presenting in a comatose state for more than 6 hours were included in the study. Patients presenting with traumatic causes of coma were excluded from the study.

All patients on admission were evaluated by detailed history, clinical examination, Glasgow Coma Scale scoring. Laboratory investigations included complete haemogram, serum electrolytes, blood glucose levels, renal function tests, liver function tests, arterial blood gas analysis. Other tests included urine examination, ECG, X-ray chest, CSF examination (in suspected cases of meningitis), CT scan brain in suspected cases of stroke and when needed.

Patients were evaluated neurologically on a daily basis, and the progress was monitored with Glasgow Coma Scale scoring. All patients were followed till the time of death in the hospital or discharge.

STATISTICAL ANALYSIS

Statistical methods applied were descriptives, frequencies and percentages, Chi square test and cross tabs. P value was identified by crosstabs (P value <0.05 is significant). Computer software used were MS Word and MS Excel.

RESULTS

50 cases of non-traumatic coma formed the study group. In these cases age-wise distribution, sex-wise distribution, and etiological distribution of coma was analyzed. The etiological factors were...

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compared with the final outcome. Other independent variables were also entered into comparison model.

The age group ranged from 21 years to 71 years. In the age group between 21-40 years mortality was lower than in the age group of 41-70 years as shown in table-1. Thus in this study younger patients had a more favorable outcome when compared to older patients. In older patients added risk factors like hypotenston (HTN), Type2 Diabetes Mellitus (DM), ischaemic heart disease (IHD), previous cerebrovascular accidents (CVA), and chronic renal failure (CRF) all added to the mortality. There was no significant relation between the age group and the outcome (P=0.725). However, patients with age more than 40 years were more likely to have a poor outcome as compared to those in the younger age group.

Out of 50 patients 33 were males and 17 were females, giving male to female ratio of 1.94:1. Among the 19 patients who died 12 were males (63.2%) and 7 were females (36.8%). The difference in morality rates among males and females was not statistically significant (P=0.740).

Table-2 shows the association of various comorbid conditions with the outcome in patients with non-traumatic coma. The most statistically significant disease was hypertension (P=0.029). Hypertension was present more commonly in patients with cerebrovascular disease and also was more commonly associated with mortality. The most common diseases associated with patients of coma were hypertension (34%) and diabetes (40%), which are important risk factors for the etiology of non-traumatic coma.

The table-3 shows the relation of Glasgow Coma Scale scores at the time of admission to the outcome. The scoring has been divided in two groups; 3-5 and 6-8. The group of patients who had GCS score between 3 to 5 at the time of admission had the maximum mortality, as compared to the group of patients with GCS score between 6 to 8. Thus there was an inverse relation of mortality to GCS score, with 94.7% mortality in patients with GCS 3-5, P=0.001 as shown in figure-1. There was good recovery in patients presenting with GCS score 6-8.

Table-4 shows the various etiologies of non-traumatic coma. Out of 50 cases of coma, 25 had intracranial causes like cerebrovascular accident and neuroinfections. 22 patients had metabolic causes, the most common of which were uroaic and hepatic encephalopathy. And 3 had presented with coma due to drug overdose or poisoning. Table-5 shows the broad etiological categorization of coma and its relation to the Glasgow Coma score. Amongst intracranial causes, 13 presented with a low GCS score (between 3 to 5). The etiological categorization of coma is not statistically associated with the GCS scoring with P>0.05. Graphical representation of the association of etiology with GCS Score is shown in figure-2.

Table-6 shows, the association between the etiology and outcome of non-traumatic coma. There was higher mortality in patients with coma due to intracranial causes (40%) when compared to metabolic (36.4%) and drug induced coma (33.3%) as shown in figure-3. And amongst the intracranial causes, cerebrovascular accidents were associated with higher mortality (50%) than neuroinfections (22.2%). Drug induced coma showed the best recovery.

**DISCUSSION**

Multicenter large prospective studies are being reported from developed countries to define the prognosis in coma. Studies...
are being conducted to determine the therapeutic interventions needed to improve the prognosis of coma. The overall prognosis of coma in any part of the world is usually poor as confirmed by several studies. This study is a prospective study of 50 cases of coma of non traumatic etiology. Limitations of the study are a small sample size of only 50 patients as well as lack of follow up of patients after discharge. Out of 50 cases 33 were males and 17 were females. The difference in mortality rates among males and females was not statistically significant ($P>0.05$). Analysis of age group revealed that majority of the cases appeared in the third to fifth decade.

There was no statistically significant correlation between age of the patient and mortality. However, patients with age more than 40 years were more likely to have a poor outcome compared to the other groups. According to some studies, in coma after head injury the GCS score is an important factor.
injury, age was an important determinant of outcome, but in non traumatic coma, age had no effect on outcome.\(^3\)

While analyzing the etiology of non traumatic coma, present study indicated that the intracranial causes constituting 50\% of cases were the commonest cause of medical coma followed by metabolic causes (44\%). Drug and poisoning induced coma comprised 3 cases (6\%). The results of the present study is comparable with that of other studies on coma,\(^4\)\(^-\)\(^12\) in which intracranial causes formed the major etiology of non traumatic coma, as shown in Table-7.

Some western studies\(^3\)\(^\text{13,14}\) showed hypoxic ischemic coma as the commonest cause. In the present study intracranial causes included cerebrovascular accidents (32.0\%), neuroinfections (18.0\%). All the 16 cases of cerebrovascular accidents were diagnosed by CT scan brain. Out of 16 cases, there were 4 cases of intracerebral hemorrhage, 2 cases of subarachnoid hemorrhage, 10 cases of cerebral infarctions. Out of 10 cases of cerebral infarction 1 was a case of rheumatic heart disease and had mitral stenosis with pulmonary hypertension.

Among the risk factors in CVA group diabetes was present in 8 cases and hypertension in 12 cases, and hypertension was more associated with intracerebral hemorrhage. There were two cases of subarachnoid hemorrhage and one was associated with hypertension. Among cerebral infarcts and hemorrhages, hemorrhages carried the worse prognosis. There were 9 cases of neuro-infection leading to coma out of which 2 cases were diagnosed to have tubercular meningitis, of which one was infected with HIV virus. The diagnosis was confirmed by CSF analysis. Thus HIV co-infection is a major risk factor for neuroinfections particularly tubercular meningitis.

There were 22 cases of metabolic cause of coma out of which 5 were in hepatic coma. 4 of these patients of hepatic coma were alcoholics and 3 of these presented with upper GI bleeding. Liver function tests were done in all the cases and 2 underwent upper GI endoscopy after recovery for diagnosis and management of oesophageal varices. Most of the patients presenting with hepatic coma had upper gastro-intestinal bleeding, suggesting it to be a precipitating factor of hepatic coma, as described by Sherlock S.\(^16\)

There were 5 cases of uremic encephalopathy out of which 2 had chronic kidney disease due to diabetic nephropathy. Other metabolic causes of coma included diabetic ketoacidosis encountered in 3 patients, hyponatremia (2 cases), hypoglycemic coma (3 cases) and hypoxic encephalopathy (4 patients).

3 cases of coma due to toxin/drug overdose were encountered in this study, one due to phenobarbitone overdose, one organophosphorous compound poisoning and the other was alcohol intoxication. Intracranial causes (cerebrovascular accident and neuroinfection) is the leading etiology of non-traumatic coma in our study. Among the intracranial causes of non-traumatic coma, cerebrovascular accident was found to be the most common in our study and also in various other studies.\(^4\)\(^-\)\(^9\)

**GCS Score and outcome**

One useful guide to initial severity of coma is the depth and duration of coma, and it is to record this that the Glasgow Coma Scale evolved. In this study the severity of coma at the time of presentation has been assessed by Glasgow coma scale. The GCS scoring was done till the recovery of coma or till the death or discharge of the patient from the hospital. And the outcome was categorized as death and survival (good recovery and recovery with deficits).

The GCS score at the time of presentation was between 3 and 8 in this study. Based on GCS score patients were categorized into two groups-GCS score 3-5 and 6-8, as done in other studies.\(^5\)

There were total 23 cases with scores between 3-5 and 27 cases with scores between 6-8. Most of the cases with a score of 3 had intracerebral hemorrhage and had 100\% mortality. Among those patients with GCS score 4-5, 5 survived. There was only one mortality in the group with scores GCS 6-8. The group of patients who had GCS score between 3-5 at the time of admission had the maximum mortality, when compared to the group of with GCS score between 6-8. Thus there was an inverse relation of mortality to GCS score, with 94.7\% mortality in patients with GCS 3-5. There was good recovery of coma in patients presenting with GCS score 6-8. One patient of coma caused by hypoxic encephalopathy due to hanging who had a GCS score of 5 made good recovery and the other patients who survived with GCS score of 5 had CVA, viral encephalitis, uremia due to ARF, diabetic ketosis.

In one study, the 2 week outcome for 88 patients with initial GCS score of 3 to 5 was 85.2\% dead or in persistent coma. For those with GCS of 6 to 8, 46.9\% were dead or in persistent coma.\(^7\)

Table-8 shows other studies with their results of outcome of coma in relation to GCS scoring, which is similar to our study with 95\% mortality in the group with GCS score 3-5.\(^4\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^11\)

Thus GCS Scoring system used to assess the severity of coma and to predict the outcome of coma in this study is a valuable tool, with sensitivity of 95\% and a positive predictive value of 78\%. For the assessment of mortality, the GCS score provides the best indicator for patients with non-traumatic coma.\(^7\) An increasing probability of poor outcome with decreasing GCS has been found.\(^11\)

**Association of outcome with etiology**

Among the 25 intracranial causes, there were 16 cases of cerebrovascular accidents and 9 were due to neuroinfections like tubercular meningitis, bacterial meningitis and viral meningoencephalitis. There was higher mortality (40\%) in patients with coma due to intracranial causes as compared to metabolic (36.4\%) and drug induced (33.3\%) coma. And amongst the intracranial causes, cerebrovascular accidents were associated with more number of deaths(50\%) than neuroinfections (22.2\%). Similar results were obtained in other studies, in which cerebrovascular accident was associated with highest mortality.\(^8\)\(^,\)\(^11\)\(^,\)\(^13\)

Drug induced coma showed the best recovery of 66.7\% as compared to intracranial causes (60\% recovery) and metabolic causes (63.6\% recovery). So drug induced coma can be taken as independent predictor of outcome.\(^7\)\(^,\)\(^11\)\(^,\)\(^17\)\(^,\)\(^18\) Frosberg et al.\(^19\) and Weiss et al.\(^17\) also demonstrated lowest mortality in drug induced coma.

In one series, patients with subarachnoid hemorrhage, brain infarct, and brain hemorrhage had the worst prognosis, followed by those with hypoxic or ischemic injuries; coma due to hepatic encephalopathy or metabolic causes had the best prognosis.\(^20\)

**CONCLUSION**

This study concludes that intracranial causes(cerebrovascular
accident and neuroinfection) is the most common etiology of non-traumatic coma presenting to a tertiary care centre followed by metabolic causes and drug/toxin induced. Mortality was found to be highest in intracranial causes group, whereas drug induced coma was associated with the best prognosis. This study also concludes that a low GCS score is associated with a poor outcome and hence GCS score remains the most readily available tool for assessment of non-traumatic coma, to identify those who are likely to die and those having the greatest potential for recovery. This study also concludes that empirically based estimates of prognosis in the neurologically severely ill provides great reassurance to those involved in a decision making process, including patients, families and physicians.

Knowledge of potentially favourable outcome greatly improves the morale and associated level of care on a cost effective basis.

REFERENCES