INFLUENCE OF DRUGS AND SUBSTANCE ABUSE ON TRAUMATIC BRAIN INJURIES SEVERITY PROGNOSTIC ASSESSMENT AMONG ROAD TRAFFIC CASUALTIES

By

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ABSTRACT

Background: Road traffic crashes (RTCs) are the leading injuries-related cause of death worldwide. A clear dose-effect relationship has been demonstrated for drugs and/or substances use and traumatic brain injury (TBI).

Objectives:

The objective of this study was first to estimate the prevalence of drug and substances use in traumatic brain injuries casualties. Second to assess TBI severity by selected assessment prognostic tools.

Subject &Methods: The study was conducted from January 2014 to March 2015, where 1200 cases of both sexes were examined after RTCs. Toxicological screening and confirmatory tests were done for all cases to detect drugs and substance abuse. The initial severity of TBI was assessed by Glasgow coma score GCS and modified Marshall Classification. The clinical outcome was evaluated according to Glasgow Outcome Score (GOS), intensive care unit (ICU) & hospital length of stay (LOS).

Results: Head injuries account for (110) 9.17 % of cases. Eighty eight cases (80%) were confirmed positive for substance use after hospital admission. Severe head injuries group account for 48/54 cases while 40/56 were with less severe head injuries. At the time of crashes tramadol was positive in forty cases (36.4%), cannabis was positive in twenty one cases (19.1%), alcohol was positive in eleven cases (10%), amphetamine was positive in five cases (4.5%), cocaine and sedative hypnotics were positive in one case(0.9%) and nine cases were positive for multiple substances (8.1%). Both GCS and modified Marshall Classification revealed that there was no statistical significant different in sociodemographic characteristic. However, confirming significant difference in relation to ICU, hospital LOS and GOS, which was more evident in Marshall assessment. Visible diffuse injuries as described by Marshall was observed in 77 patients (70%). In this study, 10/110 patients had undergone neurosurgery intervention. Using sensitivity and positive predictive value; in positive drug testing group, Marshall classification giving in more and less severe head injury a sensitivity 44%, 47% and positive predictive value 57%, 34% respectively in comparative to GCS. The relation was significant (P 0.003). In the negative drugs testing group, there was complete agreement between severe GCS and Marshall. As for agreement between mild or moderate GCS and less severe Marshall .These indicated that severity of head injury was relatively more accurate using Marshall classification in comparison with GCS which was affected by drug and substances abuse. The clinical outcome of patients revealed that 93 cases (84.5%) underwent good recovery, 7 (6.4%) moderate disability, and 5 (4.5%) died in early days.

Conclusion: Drugs and Substance abuse among road traffic casualties influence the severity of TBI and clinical outcome.

Recommendations: Modified Marshall classification is more sensitive as an early prognostic tool, so it is recommended to use it for the assessment of TBI severity induced by the influence of drugs and substance abuse intoxication.

Key words: Drugs/substance abuse, Traumatic brain injuries and modified Marshall classification. ***Corresponding Author:** Heba Youssef Sayed. Address: Forensic Medicine & Clinical Toxicology

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INTRODUCTION

Cubstance use (encompassing both alcohol **D** and/or other psychoactive substances) is commonly associated with head trauma (1). Traumatic brain injury (TBI) estimated to be 36-51% on emergency admission to hospital (2) .Drug use also increases the probability of poor outcomes following motor vehicle crashes. It has been shown that risk of death following traffic accidents increases when it is secondary to substance use (3& 4). Road traffic injuries pose a significant threat to the Egyptian population. Recent estimates revealed that Egypt experiences 42 road traffic deaths per 100,000 populations, which is the highest death rate as ranked by the World Health Organization (WHO) Eastern Mediterranean Region (EMR) (5).

Drug addiction is associated with permanent drug-mediated biochemical and structural changes in the human brain. Given the presence of neuropsychiatric disorders in many drug abusers, it will be important to decipher the neuropathological substrates for the signs and symptoms that impact patients' daily activities. The accumulated evidence some suggests that drugs can cause inflammatory responses, substantial loss of neurotransmitters, as well as neuronal death in animal models when using these drugs to mimic the human conditions. (6&7). Assessment of level of consciousness by the Coma Scale (GCS) Glasgow (8) or assessment of structural brain damage revealed on neuroimaging scans such as computed tomography (CT) (9). The level of consciousness might be obscured in the acute phase due to substance use, in contrast to a more objective assessment of structural brain injury (10& 11).

Most of the studies are conducted in the USA, which may limit applicability of findings to non-American countries, "given the potential influence of cultural factors on patterns of alcohol and drug consumption" (12). In Europe, and Australia, (13) there have been a few studies on the effects of substance use on anatomical brain injury based on CT classification (14,15). It is important to study the impact of substance consumption on TBI severity in different countries because of varieties in cultural acceptance of substances use, and also in order to identify significant abuse among TBI patients and identify those who might benefit from intervention (16, 17, 18&19).Furthermore, it has been debated whether the influence of substance abuse increases (20&21) or decreases (21&23) the risk of more severe injuries, or if it has no effect (24,25 &26).

The aim of this work was first to estimate the prevalence of substance abuse in traumatic brain injuries casualties admitted to Port-said general hospitals. Second to assess the influence of substance use at the time of injury on the anatomical brain injury severity scored by modified Marshall classification.

SUBJECTS & METHODS

<u>A-</u><u>Subject</u>

The study was conducted from January to December 2015, where 110 out of 1200 patients (9.17 %) were having head injuries after road traffic crashes (RTCs) in Port Said –Ismailia –Cairo high way.

The inclusion criteria were: (a) Patients aged 15-65 years; (b) Admitted within 24 hours of injury, (c) CT scan of the brain performed within 24 hours post-injury; and (d) residing in Port Said. The exclusion criteria were: (a) patients with co-morbidities that might interfere with assessment of TBI consequences such neurological as disorders/injuries (n = 10), (b) patients with associated other organs injuries (n = 1080), (c) penetrating or fall head trauma,(d) burns,(e) previous craniotomy prior TBI, and (f) death within 30 min of admission. Patients who needed further operative management were transferred to Suez Canal University hospital, Ismailia level-1trauma center.

B- Methods

I- <u>Toxicological Screening Tests :</u>

Cases underwent toxicological screening for urine (for detection of cannabis, opiates, cocaine, sedative hypnotics drugs such as benzodiazepines and barbiturates or multiple substance use). Urine samples were screened by enzyme linked immunosorbent assay ELISA using commercially available ELISA, Randox Toxicology kits, UK.

Expired air (breath) samples were tested to detect alcohol in breath .It was performed using breathe analyzer (Alcohol Breath Analyzer model AT-103 made in India).

II-**Confirmatory Tests:**

/substance abuse Drugs or their of metabolites were confirmed from urine samples at the central laboratory of ministry of health using Gas Chromatography Mass Spectrometry GC-MS. Total blood alcohol confirmation was level done by gas chromatography (model :Trace GC. ThermoFisher Scientific, USA).

Other drugs and substances of abuse which were screened from urine samples were confirmed in urine samples also by using (Trace GC, ThermoFisher Scientific, with MS unit, USA).

Table (1): Cutoff levels for drugs and drug metabolites by ELISA urine screening followed by GC/MS confirmatory test according to Randox and ThermoFisher Scientific companies Kits.

| Cutoff levels for di | Cutoff levels for drugs and drug metabolites in urine and blood samples | | | | | | | |
|----------------------------|---|----------------|------------------------------|--------------|--|--|--|--|
| Drug/substance or | Detection | Cutoff level | Analyte Metabolites detected | Cutoff level | | | | |
| their metabolites | time /hours | detected by | in | detected by | | | | |
| | | RIA | confirmation test | confirmatory | | | | |
| | | Immunoassay | | GC/MS test | | | | |
| | | screening test | | (ng/ml) | | | | |
| | | (ng/ml) | | | | | | |
| Marijuana metabolite | 6-18 | 50 | THCA | 15 | | | | |
| Opiate metabolites | 2.5 | 2000 | Codeine | 2000 | | | | |
| | | | Morphine | 2000 | | | | |
| | | | 6-acetylmorphine | 10 | | | | |
| | | | Phencyclidine PCP | 25 | | | | |
| | | | Methadone | 300 | | | | |
| | | | Tramadol | 10 | | | | |
| Cocaine metabolites | 1.5-4 | 300 | Benzoylecgonine | 150 | | | | |
| Barbiturates | 2-4 | 200 | Amobarbital | 200 | | | | |
| | | | Secobarbital | | | | | |
| | | | Others | | | | | |
| Benzodiazepines | 2-4 | 200 | Oxazepam | 200 | | | | |
| | | | Clonazepam | | | | | |
| | | | Zolam | | | | | |
| | | | Diazepam | | | | | |
| Amphetamine | 2-4 | 1000 | Metamphetamine | 500 | | | | |
| _ | | | Amphetamine | 200 | | | | |

The cutoff level value of a test is the minimal level of substance or its metabolites in a sample above which the result is considered positive.

Detection time / hour is the time range in hour that the substance or its metabolites can be detected in a sample after intake.

Table 1 shows the cutoff level values of ELISA urine screening test according to (Randox, Toxicology, UK cutoff values).It was performed to the studied cases to detect the presence of drugs and or substances abuse or their metabolites then confirmed by GC/MS cutoff values according to ThermoFisher Scientific, USA).

The initial severity of TBI was IIIassessed by the following methods:

Glasgow coma score GCS: The **A-**Glasgow Coma Scale or GCS is a neurological scale that aims to give a reliable, objective way of recording the conscious state of a person for initial as well as subsequent assessment. A patient is assessed against the criteria of the scale, and the resulting points give a patient score between 3 (indicating deep unconsciousness) and either 14 (original scale) or 15 (the more widely used modified or revised scale). Elements of the scale are: Eye response (E): There are four First: grades starting with the most severe: No eye opening (1). Eye opening in response to pain stimulus (2). Eye opening to speech (3). Eyes opening spontaneously (4). Second: Verbal response (V). There are five grades starting

with the most severe: No verbal response (1). Incomprehensible sounds (Moaning but no words) (2). Inappropriate words (Random or exclamatory articulated speech, but no conversational exchange or Speaks words but no sentences) (3). Confused. (The patient responds to questions coherently but there is disorientation some and confusion)(4).Oriented (5). Third: Motor response (M). There are six grades: No motor response (1).Decerebrate posturing accentuated by pain (extensor response: adduction of arm, internal rotation of shoulder, pronation of forearm and extension at elbow, flexion of wrist and fingers, leg plantarflexion extension. of foot)(2).Decorticate posturing accentuated by pain (flexor response: internal rotation of shoulder, flexion of forearm and wrist with clenched fist, leg extension, plantarflexion of foot)(3). Withdrawal from pain (Absence of abnormal posturing; unable to lift hand past chin with supra-orbital pain but does pull away when nail bed is pinched) (4). Localizes to pain (Purposeful movements towards painful stimuli) (5). Obeys commands (The patient does simple things as asked) (6). TBI is graded by GCS as follows: mild score of 13-15, moderate score of 9-12, and 3-8 as severe head injuries score.

Modified Marshall Classification: **B**based on structural brain damages shown on a CT scan, TBI severity was defined by modified Marshall classification from grade I to VI. Diffuse injury I: where there is no visible intracranial pathology seen on CT scan. Diffuse injury II: in this grade the cisterns are present with midline shift of 0-5 mm and/or lesions densities present; no high or mixed density lesion >25 cm may include bone fragments and foreign bodies. Diffuse injury III: (swelling) cisterns compressed or absent with midline shift of 0-5 mm; no high or mixed density lesion >25 cm. Diffuse injury IV: (shift) midline shift >5 mm; no

high or mixed density lesion >25 cm. Grade V: Evacuated mass lesion, any lesion surgically evacuated. Grade VI: Nonevacuated mass lesion high or mixed density lesion >25 cm; not surgically evacuated .Patients underwent a CT head scan shortly after admission; a second CT was obtained within 6-24 hours after injury. Findings from the first and second CT scans were categorized according to diagnostic categories of types of anatomical abnormalities as classified by Marshall et al., (16) .The original Marshall classification was subdivided into two groups (23). The first group: included patients with Marshall Score <3 (less severe brain injury). The second group: included those with Marshall Score ≥ 3 (more severe brain injury with significant intracranial abnormalities) (18).

<u>IV- The Outcome</u>: was evaluated according to Glasgow Outcome Score (GOS), which use five-point scale. The outcome data collected included in-hospital mortality, ICU and hospital length of stay (LOS). The outcome was assessed 3 and 6 months after the injury.

V- Statistical analysis

Data were presented as proportions, mean \pm standard deviation or median and range. Analysis was performed to compare between groups using the Student's *t*-test for continuous variables and Pearson Chi-square test for categorical variables for categorical variables. In all tests the probability (P) was used: If P>0.05 the relation is not significant. significant. P<0.05 relation is If the Sensitivity, specificity and predictive tests were also performed to compare the degree of agreement between variables. The results of statistical analysis were then presented in tables and chart for interpretation and discussion. Data analysis was carried out using the Statistical Package for Social Sciences version 18 (SPSS Inc., Chicago, IL, USA).

| nd gas chromatography confirmatory method | | | | | | | |
|---|--|---|--|--|--|--|--|
| Alcohol | Breath analyzer | Total blood alcohol level GC | | | | | |
| measurement | 22-55 microgram of alcohol in 100 | 70-110 milligrams of alcohol per 100 | | | | | |
| | milliliters of breath | milliliters of blood | | | | | |
| Total Number | 11 | 1/110 | | | | | |
| | | 10 | | | | | |
| Percentage | | 10 | | | | | |

RESULTS Table 2: Prevalence of cases that were positive for alcohol by Breath analyzer screening test and gas chromatography confirmatory method

Table 2 shows the number and percentage of cases who were positive for alcohol detected by breath analyzer screening test followed by confirmation in blood by gas chromatography.

| Table 3 Prevalence of drugs and substance abuse after confirmation by gas chromatography |
|--|
| and gas chromatography mass spectrometry among traumatic brain injured patients exposed |
| to road traffic crashes |

| Substance and drug abuse screening results | Number | Percentage | |
|--|--------|------------|--|
| Tramadol | 40 | 36.4 | |
| Marijuana | 21 | 19.1 | |
| Alcohol | 11 | 10 | |
| Amphetamines | 5 | 4.5 | |
| Cocaine | 1 | 0.9 | |
| Sedative Hypnotics | 1 | 0.9 | |
| Multiple drugs | 9 | 8.1 | |
| Total | 88/110 | 80 | |

Table 3 shows the prevalence of drugs and substances abuse in urine and blood samples after confirmation by gas chromatography and gas chromatography mass spectrometry. Tramadol was positive in 40/110 (36.4%), cannabis (Marijuana) was positive in 21/110 (19.1%), alcohol was intoxicated in 11/110 (10%), patient used multiple drugs were nine (8.1%), amphetamine in 5/110 (4.5%), cocaine in 1/110 (0.9%), while sedative hypnotics drugs were positive in only 1/110 (0.9%) as shown in figure (1).



Figure (1): Drugs and substance abused detected by gas chromatography and gas chromatography mass spectrometry among traumatic brain injured patients exposed to road traffic crashes

Table (4): Socio-demographic and clinical variables among traumatic brain injured patients exposed to road traffic crashes in relation to Glasgow coma scale done by Student's t-test & Pearson Chi-square statistical analysis.

| Variables Severe | | Moderate | Mild | Total | P-value | | | |
|--------------------------------|----------------|--------------------------|------------------|-------|---------|--|--|--|
| | (n =45)(40.9%) | (n = 40)(36.4%) | (n = 25) (22.7%) | | | | | |
| Age | | | | | | | | |
| $Mean \pm SD$ | 38 ± 11.4 | 37 ± 8.6 | 36 ± 7.5 | | 0.87 | | | |
| Gender | | | | | | | | |
| Male | 43 | 39 | 24 | 106 | 0.89 | | | |
| Female | 2 | 1 | 1 | 4 | | | | |
| | | Marital status | | | | | | |
| Single | 14 | 10 | 10 | 34 | 0.7 | | | |
| Married | 31 | 30 | 15 | 76 | | | | |
| | | Education | | | | | | |
| Illiterate | 4 | 6 | 3 | 13 | 0.29 | | | |
| Primary school | 6 | 9 | 0 | 15 | | | | |
| High & Intermediate schools | 32 | 23 | 12 | 67 | | | | |
| Graduate | 3 | 2 | 10 | 15 | | | | |
| | | Residence | | | | | | |
| Urban | 42 | 32 | 15 | 89 | 0.95 | | | |
| Rural | 3 | 8 | 10 | 21 | | | | |
| | | Substance abuse | | | | | | |
| Positive (% in GCS) | 42 (93%) | 34 (85%) | 12 (48%) | 88 | 0.000 | | | |
| Negative (% in GCS) | 3 (7%) | 6 (15%) | 13 (52%) | 22 | | | | |
| | IC | U length of stay (days) | | | | | | |
| Mean ± SD | 9 ± 7 | 10 ± 6 | 3 ± 4 | | 0.000 | | | |
| | Length | of acute hospital stay (| days) | | | | | |
| $Mean \pm SD$ | 14 ± 11 | 18 ± 10 | 4 ± 4 | | 0.000 | | | |
| | Glasgow ou | itcome scale (GOS)at d | ischarge | | | | | |
| 1 (dead) | 3 | 2 | 0 | | 0.45 | | | |
| 2 (vegetative state) | 1 | 1 | 0 | | | | | |
| 3 (severe disability) | 2 | 1 | 0 | | | | | |
| 4 (moderate disability) | 5 | 2 | 0 | | | | | |
| 5 (good recovery | 34 | 34 | 25 | | | | | |

All values are expressed as mean and standard deviation.

The statistical differences were done by Student's t-test. The categorical values were expressed in proportions; the statistical differences were done by Pearson Chi-square.

In all tests the 95% confidence interval and P value < 0.05 is considered significant.

Table 4 shows socio-demographic and clinical variables results and TBI characteristics in relation to Glasgow coma scale (mild, moderate, and severe head injuries). Different substances abuse serum levels were also found in patients with admission GCS scores that were higher in severe (n = 42/45), and moderate head injury (n = 34/40) than in mild one (n=12/25) at time of admission and it is statistically significant P value < 0.05. The severity of brain injuries was statistically not significance in relation to gender, residence, marital age, state. education, and GOS with P value > 0.05 as well as the two died cases were scaled as moderate by GCS. However, the severity of brain injuries was statistically significant in relation ICU, and hospital length of stay LOS with P value < 0.05.

Table 5: Socio-demographic and clinical variables among traumatic brain injured patients exposed to road traffic crashes in relation to modified Marshall classification done by Student's t-test & Chi-square statistical analysis.

| Variables | More severe TBI | Less severe TBI | Total | P-value | | | | |
|-----------------------------|-----------------------|------------------|-------|---------|--|--|--|--|
| | (n = 54)(49.1%) | (n = 50) (50.9%) | | | | | | |
| Moon SD | Age 27 + 0.4 | 28 + 0.7 | | 0.45 | | | | |
| Mean ± SD | 57 ± 9.4 | 38 ± 9.7 | | 0.43 | | | | |
| Gender | | | | | | | | |
| Male | 51 | 55 | 106 | 0.29 | | | | |
| Female | 3 | 1 | 4 | | | | | |
| | Marital sta | itus | | | | | | |
| Single | 15 | 19 | 34 | 0.49 | | | | |
| Married | 39 | 37 | 76 | | | | | |
| | Educatio | n | | | | | | |
| Illiterate | 6 | 7 | 13 | 0.98 | | | | |
| Primary school | 7 | 8 | 15 | | | | | |
| High & Intermediate schools | 34 | 33 | 67 | | | | | |
| Graduate | 7 | 8 | 15 | | | | | |
| | Residenc | e | | ÷ | | | | |
| Urban | 40 | 49 | 89 | 0.073 | | | | |
| Rural | 14 | 7 | 21 | | | | | |
| | Substance a | buse | | | | | | |
| Positive | 54 | 34 | 88 | 0.000 | | | | |
| Negative | 0 | 22 | 22 | | | | | |
| | ICU length of sta | ay (days) | | ÷ | | | | |
| Mean \pm SD | 14 ± 3 | 2 ± 1 | | 0.000 | | | | |
| | Length of acute hospi | tal stay (days) | | | | | | |
| Mean ± SD | 23 ± 7 | 4 ± 1 | | 0.000 | | | | |
| Gla | sgow outcome scale (| GOS)at discharge | | • | | | | |
| 1 (dead) | 5 | 0 | | 0.000 | | | | |
| 2 (vegetative state) | 2 | 0 | | | | | | |
| 3 (severe disability) | 3 | 0 | | | | | | |
| 4 (moderate disability) | 7 | 0 | | | | | | |
| 5 (good recovery | 37 | 56 | | | | | | |

All values are expressed as mean and standard deviation.

The statistical differences were done by Student's t-test. The categorical values were expressed in proportions; the statistical differences were done by Pearson Chi-square.

In all tests the 95% confidence interval and P value < 0.05 is considered significant.

N.B: (score \geq 3 more severe TBI, score <3 less severe TBI).

Table 5 shows the main sociodemographic and clinical variables among TBI patients exposed to road traffic crashes (n = 110) in relation to anatomical severity of TBI as measured by the modified Marshall classification (score <3 less severe, score \geq 3 more severe TBI). Most of the victims were males, and under 40 years of age. Only 1.8 % of the females were in the positive drugs test group. Eighty percent (n=88) of patients were positive in drugs test on admission to hospital.

By comparison using modified Marshall classification (score \geq 3 more severe TBI, score <3 less severe,) as shown in Table (4),it was found that all severe TBI cases 54/54 were positive to drug abuse compared to 34/ 56 in less severe TBI were positive and statistically significant with P value < 0.05. The same as GCS grouping, modified Marshall severity grading of TBI was statistically not significance in relation to age, gender, education, residence, and marital state with P value >0.05 except for Glasgow outcome score (GOS) and all dead cases were scored severe. Also significant values in relation intensive care units (ICU), length of hospital stay (LOS) as in table (3).

From tables 4 and 5 it was evident that there were no statistical significant difference socio-demographic characteristic in in comparison between groups in GCS or Marshall, therefore they were controlled or neutralized as a confounder factors affecting prognostic categorizing difference, the confirming the true difference in relation to ICU, hospital LOS and GOS, which is more evident in modified Marshall severity assessment.

Table (6) Number and Percentage of visible diffuse traumatic brain injuries as described by modified Marshall grading observed in initial computerized tomography scan of 110 patients.

| Modified Marshall Grade | No of patient | Percent |
|-------------------------|---------------|---------|
| Ι | 33 | 30 |
| П | 23 | 21 |
| III | 10 | 9.8 |
| IV | 25 | 23 |
| V | 9 | 8.2 |
| VI | 0 | 0 |
| Total | 110 | 100 |

Table 6 shows the number and percentage of visible diffuse TBI as described by modified Marshall classification observed in initial CT scan of 77 patients (70%) and 33 patient (30%) had no visible pathological changes on CT. In those 77 patients; 23/110 patients with diffuse injury grade II (presentation of cisterns, shift 5 mm or less and/or presentation of lesions, but no high/mixed density lesions >25 ml), 10/110 patient with diffuse injury III (compressed or absent cisterns with a shift of 0–5 mm; no high or mixed density lesion > 25 ml), 25/110 patients diffuse injury IV (shift > 5 mm; no high or mixed density lesion > 25 ml), and 9/110 patient showed evacuated mass lesion (8/110 epidural hematoma, 1/110 subdural hematoma).

Figures (2, 3, 4 &5) in this study showed different Marshall grades. In 10/110 patients had surgery, one of them for elevation of depressed fracture. All those patients transferred to Suez Canal University hospital. CT finding was statistically significant in relation to substance abuse with p value (0.003). Forty-nine percent of patient (n=54) had severe anatomical injuries on initial and follow up CT scan. Table (5)







Figure (2): (A) A male patient 24 years old presented with head trauma. CT brain revealed left subgalial hematoma, a mild brain edema with effacement of quadregeminal cistern and lateral ventricle. (B) Bone window revealed left temporal fissure fracture. Grade I: modified Marshall classification (less severe).



Figure (3): A male patient 34 years old presented with left and right tempro-parietal brain contusion. CT brain revealed bilateral brain hemorrhagic contusion left more than right with balanced midline. There is a small left subgalial hematoma denoting the right lesion is countercoup brain trauma. The patient treated conservatively. Grade II : Modified Marshall classification (Less severe).







Figure (4): A male patient 16 years old presented with severe head injury and cistern and ventricle were severely compressed (A). CT brain follow up after treatment of 4 days revealed opening of the cistern, despite the presence of , right frontal and mild subarachnoid hemorrhage with a skull fissure below it (B). The patient treated conservatively. He was classified as mild head injury considers GCS but in Modified Marshall classification he was Grade III: (more severe).



Fig (5A)



Fig (5B)

Figure (5): (A) A male patient 40 years old presented with acute subdural hematoma. CT brain revealed left huge subdural hematoma, a marked midline shift up to one cm. There is effacement of the same lateral ventricle. The patient had surgical evacuation but he died five days later, evacuated mass lesion in Marshall Classification. Grade V modified Marshal classification : (more severe).

Table 7: Comparison between Marshall and Glasgow coma scale(GCS) groups using sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) statistical analysis in positive drugs tests cases.

| Positive drugs test | | Marshall | | | |
|---------------------|-----------------|------------------|------------------|-------|----------|
| | | Less severe | More severe | Total | |
| CCS | Mild & moderate | 16 | 30 | 46 | NPV = 57 |
| GCS | Severe | 18 | 24 | 42 | PPV = 34 |
| Total | | 34 | 54 | 88 | |
| | | Specificity = 47 | Sensitivity = 44 | | |

Table 8: Comparison between Marshall and Glasgow coma scale groups using specificity, and negative predictive value (NPV), statistical analysis in negative drugs tests cases.

| Negative drugs test | | Marshall | | | |
|---------------------|-----------------|------------------|-------------|-------|-----------|
| | | Less severe | More severe | Total | |
| CCS | Mild & moderate | 19 | 0 | 19 | NPV = 100 |
| GCS | Severe | 3 | 0 | 3 | |
| Total | | 22 | 0 | 22 | |
| | | Specificity = 86 | | | |

 Table 9: Comparison between Marshall and Glasgow coma scale groups in both positive and negative drugs tests using sensitivity test

| Drug / substance | | GCS severity score Marshall severity score | | Total | | |
|------------------|-------|--|-----------------------|------------------|------------------|------------|
| abuse | | | | Less severe | More severe | |
| confirmation | | | | (n = 56) (50.9%) | (n = 54) (49.1%) | |
| test | | | | | | |
| | | mild | N (% within Marshall) | 9 (26.5%) | 3 (5.6%) | 12 (13.6%) |
| Docitivo | GCS | moderate | N (% within Marshall) | 7 (20.6%) | 27 (50%) | 34 (38.6%) |
| rositive | | severe | N (% within Marshall) | 18 (52.9%) | 24 (44.4%) | 42 (47.7%) |
| | Total | | N (% within Marshall) | 34 (100%) | 54 (100%) | 88 (100%) |
| | | | | | | |
| | | mild | | 13 (59.1%) | | 13 (59.1%) |
| | GCS | | N (% within Marshall) | | | |
| | | moderate | | 6(27.3%) | | 6 (27.3%) |
| Negative | | | N (% within Marshall) | 0(27.570) | | 0(27.570) |
| | | covoro | | 3(13.6%) | | 3(13.6%) |
| | | Severe | N (% within Marshall) | 5 (15.0%) | | 5 (15.070) |
| | Total | | N (% within Marshall) | 22 (100%) | | 22 (100%) |
| | | mild | N (% within Marshall) | 22 (39.3%) | 3 (5.6%) | 25 (22.7%) |
| | | moderate | N (% within Marshall) | 13 (23.2%) | 27 (50.0%) | 40 (36.4%) |
| Total | GCS | | N (% within Marshall) | | | |
| | | severe | | 21 (37.5%) | 24 (44.4%) | 45 (40.9%) |
| | Total | | N (% within Marshall) | 56 (100%) | 54 (100%) | 110 (100%) |

Tables 7, 8 and 9 clarify a comparison between GCS as an inspection test and Marshall as an radiological investigatory test in predicting severity of TBI casualties under the influence of drugs /substance abuse positive and negative tests. For the positive drugs testing groups revealing an agreement between severe GCS and Marshall in 24 cases

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and 30 truly severe in Marshall while it is mild or moderate with GCS, giving sensitivity 44% and positive predictive value 57%. As for agreement between mild or moderate GCS and less severe Marshall were found in 16 cases out of 18, giving specificity 47% and negative predictive value 34%. And the relation was significant with P value 0.003. On the contrary, for the negative drugs testing groups revealing complete agreement between severe GCS and Marshall. As for agreement between mild or moderate GCS and less severe Marshall were found in 19 cases out of 3, giving specificity 86% and negative predictive value 100%. This indicated that severity of head injury is relatively more accurate using Marshall in comparison with GCS by which 56% of truly severe cases were under the influence of drug and substances abuse.

II- <u>Clinical Outcome:</u>

Out of 110 patients included in this study, 93 cases (84.5%) were classified into the good recovery, 7 cases (6.4%) moderate disability, and 5 cases (4.5%) died in early days. Using Marshal Definition of severe head injuries showed significance with the outcome 0.001 in comparison to GCS 0.06 comparison to the outcome.

DISCUSSION

National data concerning drugs and substance abuse in Egypt is lacking. The revealed current study prevalence of tramadol, cannabis, alcohol and multiple drugs and substances abuse among drivers involved in road traffic causalities. The classification of a severe TBI was originally defined for traumatically injured patients as coma (GCS<7) for at least 6 hours, either immediately after injury or following lucid interval (16). This six hours of coma duration was chosen to exclude patients who might temporarily be in coma because of factors other than the head injuries most notably hypoxia, hypotension, drugs and substance abuse intoxication (17&18), medical sedation and paralysis (10&11).

In the present study the mean GCS score didn't differ significantly between positive and negative abusers. Agreeing with results reported by Sperry (19) and Andelic et al (11) .In contrast, assessment of structural brain damage by computerized tomography CT scanning is not influenced by state of consciousness. Therefore the severity of TBI in this study was assessed by modified Marshall classification. There is evidence that CT-scan can assist in discriminating less severe from more severe TBI (11 &13).

Socio-demographic results and injuries characteristics in studied cases (n=110) showed that most of cases were males, drivers and under the age of forty years.

These results were in agreement with many studies which showed such relation between adult males and injuries under the effect of drugs and substance abuse (2, 9, 11 & 20).

In the current study eighty eight (80%) of cases were positive for substances abuse on hospital admission .Substance abuse prevalence was 48/54 in severe head injuries and 40/54 in less severe head injuries group .It was strange that the prevalence of substance abuse was relatively high since most of studies revealed prevalence ranges from 40% to 70% (1,8,11& 21).

The explanation of such high prevalence was further analyzed in this study and revealed that TBI was not statistically significant in relation to age, gender, education, residence but do for substance abuse, ICU, LOS and GOS.

Many studies found such relation (11,15,20 &22) ,however in other studies factors like education, residence may attributed to such high frequency , illiterate and high school account for 63.6% of cases (1,11 &21).

The number of studied cases who were at school in the present study was 82%. This highlighted the importance of school education programs about the effects and dangers associated with drugs and substances abuse as "a Key component in preventing substance abuse in population "(6 &27).

The effect of positive drug /substance abuse on the central nervous system and acquired brain injuries were extensively studied .Carcuel et al showed that the patients with acquired frontal cortex brain injuries and drug addiction share a range of neuropsychiatric dysfunctions including apathy, poor self – control, and poor executive control as evaluated by the Frontal System Behavioral Scale. It was shown that the abusers subjects, along with traumatic brain injuries, exhibited greater impairment than negative control subject (24).

A similar study was conducted by Lange et al, in which 104 patients with mild TBI were compared to 104 substance abuse patients. It was shown that there were no difference between neuropsychological tests performance of TBI and addicted patients on cognitive measures of visual and verbal memory and executive functioning (28) .It was suggested that patients suffering either acquired brain injury to frontal cortex or drug addiction support the link between frontalsubcortical system injury and risk taking behaviors (29).

In the current study the prevalence of drugs and substances abuse in urine and blood samples after confirmation by gas chromatography and gas chromatography mass spectrometry revealed that tramadol was positive in 40/110 (36.4%), cannabis (Marijuana) was positive in 21/110 (19.1%), alcohol was intoxicated in 11/110 (10%), patient used multiple drugs were 9/110 (8.1%), amphetamine in 5/110 (4.5%), cocaine in 1/110 (0.9%), while sedative hypnotics drugs were positive in only 1/110 (0.9%).

The distribution of drug/substance abuse worldwide were different according to religious, ethnic and work habit. In most of Europe and United States, alcohol is usually the most frequent substance used (11,20,22&

30) . The proportion of patients with TBI found to be under the influence of alcohol was found in 12% to 56% of total TBI sample (11& 27).

These results was in contrast to the present study results where the distribution of drugs and substance abuse in the current study revealed that tramadol was the most prevalent one followed by cannabis , multiple drug abuse then alcohol. This could be due to culture and religious difference between Egyptian versus European and American societies where alcohol is a common beverage . Alcohol and TBI has been discussed in many studies. Few studies reported neuroprotective effect of ethanol (30). Ethanol induced inhibition of N-methyl –D aspartate (NDMA) mediated excitotoxicity. Dose dependent effects are also reported, with better outcome in animal obtained with low and moderate ethanol dose as compared to negative and high –ethanol groups (31,32,33 &34). In contrast many studies described adverse effects of ethanol on head trauma (18, 33, 34 & 38), especially in severe head injury (36, 37 ,39 &40).

The results of current study proved that the commonest abused drugs among cases exposed to road traffic crashes was tramadol . This could be explained by the fact that tramadol is a commonly used opioid like analgesics used to treat moderate to moderately –severe pain in adults. Tramadol abuse can affect the driving behavior of the victim via depression of central nervous system activity thus reduce vigilance, increase reaction times and increase errors associated with decision making and speed control . Seizures are one of the known complications of overdose of tramadol use. (41).

A recent study on patients who developed seizures due to tramadol use (either therapeutic or overdose) showed that the traumatic injuries occurred in around 25% of these patients (34). Patients with TBI who received tramadol are more likely to develop agitation, undergo tracheostomy and have longer hospital stay LOS (42). However its neuroprotection or adverse effects in head trauma was not clear in literature .

Cannabis and its metabolites are central nervous system stimulants substance of abuse which tend to reduce driving performance on divided attention tasks, cause tunnel vision and increase risk taking .They can also cause rebound fatigue, inattention and hyper somnolence when the stimulatory effects wear off (31).

Cannabis dependence and its influence on TBI cases was discussed in a Canadian study which estimated that 16.8% of adults were cannabis positive. Cannabinoids compromise three classes of compounds. The active components of marijuana (cannabis sativa) as well as endogenous and synthetic derivatives. To date , two distinct cannabinoid receptors (CB1 &CB2) have been discovered but the evidence for further receptors types has been brought forward (36). The CB1 receptors also

confers neuroprotection in various experimental models of striatal damage (31). during cerebral In contrast ischemia /reperfusion injury while activation of CB2 receptors was found to be protective, the greatest degree of neuroprotection was obtained by combining a CB1 inhibitor with agonist (32). For nervous system CB2 disorders, cannabinoids may be useful by modulating neurotransmission and calcium homeostasis as well as by anti-inflammatory and anti-oxidant actions. Some cannabinoids can also trigger cell death, which may be of therapeutic benefit in the treatment of malignant tumors. A number of both in vitro and in vivo models have provided promising but diverse evidence for cannabinoid protection in glutamate – mediated excitatory , hypoxia and glucose and multiple sclerosis (43).Neurotoxicity cannabinoid of estimated due to increase density of CB1 receptors which in turn increase CB signaling . It is hypothesized that CB signaling plays a role in the ultimate expression of various types of neurotoxicity. Neurotoxicants that primarily by altering act synaptic neurotransmitters level (44). Several studies have demonstrated neuroprotective effects of cannabinoids (45) (46) (47) (48), to establish a relationship between the presence of positive toxicology screening for tetrahydrocannabinol THC and mortality after TBI found that the mortality in THC (+) group was significantly decreased compared with THC (-) group.

Multiple drugs and substance abuse was evident in 9/110 cases (8.1%) in the current study.

Using of more than one drug had been explained by many studies (49,50, 51, 52) .Converging evidence from human and animal studies points to an important modulatory influence of cannabinoid CB1 receptors in the behavioral response when become combined with other addictive agents . Combining alcohol with marijuana and tramadol results in CNS impairment even at doses which would be insignificant were of either substance alone. Moreover, anv combination of multiple psychoactive substances was associated with an increased risk of road traffic crashes (53)

Amphetamine and its metabolites were prevalent drug of abuse in the present study in five cases (4.5%) have been found to be associated with traumatic brain injury.

This could be attributed to the mechanism of action of amphetamine and its metabolites which worsen the suppression of locomotor responses and striatal dopamine turnover after TBI (54,55).

One study has indicated that 27% of trauma patients used amphetamine; these cases were associated with longer hospital stays and hospital charges (56) .However Shen H et al., (57) recommended that treatment with low-dose methamphetamine TBI elicits after severe а robust neuroprotective response resulting in significant improvements in behavioral and cognitive functions.

Cocaine is a pleotropic and psychotropic drug that has various effects on multiple organ systems .Its most pronounced effect is vasoconstriction (58). However in vitro and animal studies have demonstrated protective effects of cocaine on the neurological system are less clear and may be hard to discern with low mortality rate in the study population (59).

The present study was unable to elicit the neuroprotection or hazards of each substance, but it was found generally that the severity of TBI by CT –scan was affected by substance abuse significantly P< 0.001 and the outcome P < 0.001 respectively. However using GCS in assessing the severity of brain injury revealed it was affected by drug abuse significantly P < 0.005 and the outcome not significantly P < 0.006 respectively.

This could be explained by the fact that drug abusers were frequently affected in their conscious level in comparison with negative abusers group (7).

The results of the present study revealed that assessing TBI by GCS and anatomical modified Marshall classification indicated that the severity of head injury was relatively more accurate using modified Marshall classification in comparison to GCS which was affected by positive abuse status. The study found that the assessment of substance abusers should be studied in relation to CT brain injury using modified Marshall classification scoring as recommended by others (12&13).

Although, the mortality rate was low in the present study 4.5%, the considerable number of patients with substance use in the present study revealed that the use of tramadol, cannabis and alcohol were major risk factors for TBI (12,13,15 &63) . Apart from the study dilemma that some drugs had a neuroprotective effect (59, 60, 61 &62) the study found that patients with a history of substance abuse after TBI tend to have, poorer outcome, and late deterioration (18, 33, 63 & 64) .The study used GOS for assessment of the outcome. It is a course measurement for assessment. Measurement of GOS suffers statistically from inter-observer variation ranging from 17% to 40% in clinical practice, which needs further investigation (65) .Furthermore, low number of patients makes a relative low sensitivity of the study outcome in relation to drug abuse.

CONCLUSION

Substance abuse among road traffic casualties influence the severity of TBI and clinical outcome. The study had some limitation including use of GOS as a measurement for assessment of the outcome, and small number of cases distributed along many drugs and or substances abuse.

RECOMMENDATIONS

Modified Marshall classification for TBI should be used as an early prognostic tool for the assessment of TBI severity induced by the influence of drugs and substance abuse intoxication.

National awareness programs about the health effects and dangers associated with drug and or substance abuse and driving should be implemented allover Egyptian governorates.

Targeting the governmental and nongovernmental preventive efforts to reduce drug and substance use in order to minimize the number of road traffic crashes and injuries.

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تأثير المخدرات وإساءة استخدام العقاقير على إصابات الدماغ الرضية و تقييم الخطورة و النذير بين ضحايا

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الخلفية والأهداف: حوادث الطرق المرورية هي السبب الرئيسي للوفاة بسبب الإصابات في جميع أنحاء العالم. وتوجد علاقة واضحة بين الجرعة وتأثير العقاقيير و المواد المخدرة و إصابات في الدماغ الرضية . تهدف هذه الدراسة الي أولا تقدير مدى انتشار العقاققير و المواد المخدرة بين ضحايا حوادث الطرق . ثانيا تقييم شدة إصابات الدماغ الرضية عن طريق أدوات تقييم النذير المختارة .

الحالات والطرق : أجريت الدراسة خلال الفترة من يناير إلي ديسمبر 2014 ، حيث تم فحص 1200 حالة من الجنسين بعد تعرضهم لحواث طرق مرورية . وقد أجري مسح للسموم والإختبارات المبداية التأكدية لجميع الحالات للكشف عن تعاطي العققاقير و المواد المخدراة. وجرى تقييم شدة الأولية عن طريق مقياس جلاسكو للغيبوبة وتصنيف مارشال المعدل . و قد تم تقييم النتائج السريرية وفقا لتقييم مقياس حصيلة جلاسكو و فترة الاقامة بوحدة العناية المركزة وطول الإقامة في المستشفى .

النتائج: إصابات الرأس تمثل (110) 9،17% من الحالات. ثبتت إيجابية تعاطي المخدرات بعد دخول المستشفى في ثمان و ثمانين حالة (81%). كانت إصابات الرأس الشديدة 48 /54 من الحالات بينما 56/40 مع إصابات الرأس أقل شدة. في وقت التصادم كان الترامادول ايجابيا في أربعين حالة (36.4%)، وكان القنب إيجابي في واحد وعشرين حالة (19.1%)، والكحول إيجابي في أحد عشر الحالات (10%)، وكان المنشطات ايجابية في خمس حالات (4.5%)، كان الكوكابين والمنومات والمسكنات إيجابي في حالة واحدة (0.9%) وتسع حالات كانت إيجابية للمواد متعددة (3.1%). كان الكوكابين والمنومات والمسكنات وتصنيف مارشال المعدل أنه لا يوجد ااختلاف ذو دلالة إحصائية في السمات الاجتماعية والديموغرافية علي النقيض يوجد وتصنيف مارشال المعدل أنه لا يوجد الختلاف ذو دلالة إحصائية في السمات الاجتماعية والديموغرافية علي النقيض يوجد وخصوحا في تقييم مارشال المعدل . وقد لوحظ وجود إصابات منتشرة مرئية كما وصفها مارشال في 77 مريضا (70%). في وضوحا في تقييم مارشال المعدل . وقد لوحظ وجود إصابات منتشرة مرئية كما وصفها مارشال في الاسكو ، ليوابية وضوحا في تقييم مارشال المعدل . وقد لوحظ وجود إصابات منتشرة مرئية كما وصفها مارشال في 77 مريضا (70%). في والتنوية الإيجابية؛ فيم مارشال المعدل . وقد لوحظ وجود إصابات منتشرة مرئية كما وصفها مارشال في 77 مريضا (70%). في والوضوحا في تقييم مارشال المعدل . وقد لوحظ وجود إصابات منتشرة مرئية كما وصفها مارشال في 77 مريضا (70%). في والوضوحا في تقييم مارشال المعدل . وقد لوحظ وجود إصابات منتشرة مرئية كما وصفها مارشال في 77 مريضا (70%). في والوضوحا في تقييم مارشال المعدل . وقد لوحظ وجود إصابات منتشرة مرئية كما وصفها مارشال في 77 مريضا (70%). في والوضوحا في تقييم مارشال المعدل . وقد لوحظ وجراحة المخ والأعصاب باستخدام اختبار الحساسية الإحصائي والقيمة والنوئية ولايجابية؛ في مجموعة الحالات الإيجابية لامخدرات، أعطي تصنيف مارشال في الاصابات الرأس الشديدة والأقل خطورة حساسية 44%، 47%، والقيمة التنبؤية الإيجابية 55%، 34% على التوالي و ذلك بالمقارنة بمقياس جلاسكو

في المجموعة السلبية لاختبارات العققابير و المواد المخدرة كان هناك اتفاق تام بين مقياس جلاكسو للغيبوبة للحالات الخطيرة و تصنيف مارشال في حالات إصابات الرأس الاقل خطورة وأشارت هذه النتائج ان شدة إصابات الرأس وكانت أكثر دقة نسبيا باستخدام تصنيف مارشال بالمقارنة مع مقياس جلاسكو للغيبوبة وذلك لتأثرة بتعاطي العققاقير و المواد المخدرة . كشفت المحصلة السريرية للمرضى أن 93 حالة (84.5٪) معافاة جيدة، 7 (6.4٪) عجز متوسط ، و 5 (4.5٪) وفيات في الأولى. الأولى.

الإستنتاج

تعاطي العققاقير و المواد المخدرة بين ضحايا الحوادث المرورية يؤثر علي شدة إصابات المخ الرضية و المحصلة السريرية. **التوصيات**

تصنيف مارشال المعدل أكثر حساسية كأداة تشخيصية في وقت مبكر ولذلك نوصى باستخدامه لتقييم شدة إصابات الدماغ الرضية الناجمة عن تأثير التسمم بتعاطى العققاقير و المواد المخدرة