DISCUSSION

Traumatic brain injury (TBI) is associated with primary injury (owing to the biomechanical effects of the impact) and with secondary or delayed vascular, metabolic, cellular, and molecular events that are initiated minutes after the injury and last as long as several months[18]. The secondary processes activated by the trauma interact in a complex network leading to cell dysfunction, death, and/or recovery of neurologic function[20].

During the past 10 years, the application of imaging techniques such as MRI, spectroscopy, and positron emission tomography; the use of invasive focal continuous monitoring tools such as microdialysis and probes to measure brain tissue oxygen tension (PtiO2); and advanced histologic and molecular biology techniques led scientists and clinicians to an increased understanding of the mechanisms underlying secondary neuronal damage after TBI. Topics of continuing interest and recent debate are the post-traumatic alterations in brain metabolism/oxygenation and the potential of hyperoxia as therapeutic tool for TBI[95].

We conducted a prospective study on 75 adult patients of both sex who suffered from moderate TBI. Patients were categorized into 3 groups; (group I) consists of 25 patients who received HBO in addition to the conventional therapy of TBI, (group II) consists of 25 patients who received normobaric hyperoxia (NBH)

In addition to the conventional therapy of TBI, and (group III) consists of 25 control patients who received the conventional therapy of TBI only. Theses patients were followed up for a period of 20 days. The aim of the present study was to evaluate and compare the effect of HBOT and NBH in improving brain metabolism and outcome in patients with moderate TBI.

In the present study, the three studied groups were homogenous in terms of size and demographic characteristics with no statistically significant difference among them regarding age and gender. Most of the patients enrolled in the present study were adult male patients with a mean age of 30.48 ± 7.86 years in group I, 31.88 ± 8.24 years in group II, and 29.92 ± 8.92 years in group III.

In agreement with our study, Carli et al [154], reported that the greatest number of TBIs occur in people aged 15-24. Because TBI is more common in young people, its costs to society are high due to the loss of productive years to death and disability.

In addition, Hilaire et al [155], found that the mean value of age in TBI was 38±6.01 years and most of the studied sample (78.7%) were males.

In our study, males accounted for 17 patients (68%) in group I, 15 patients (60%) in group II, and 17 patients (68%) in group III, while females accounted for 8 patients (32%) in group I, 10 patients (40%) in group II, and 8 patients (32%) in group III.

Similarly with our study, Hardman et al,[156] found that TBI rates are higher in males. Men suffer twice as many TBI as women do and have a fourfold risk of fatal head injury. Males account for two thirds of childhood and adolescent head trauma.

In the present study, the most common cause of TBI was road traffic accidents accounting for 17 patients (68%) in group I, 15 patients (60%) in group II, and 16 patients (64%) in group, followed by falling from height and alleged assault.

In agreement with our study, Kushner[157] stated that the most common causes of TBI in young people include violence, transportation accidents, construction and sports.

In our study, there was a significant improvement in the outcome of HBOT group as compared to the other two groups as presented by Glasgow coma scale and Glasgow outcome scale. The mean values of GCS at the end of the study (day 20) in HBOT group increased from (10.08±1.12) to (13.24±1.61), in NBH group increased from (10.48±1.16) to (12.28±1.81), while in the control group it increased from (10.13±0.95) to (11.08±1.80).

Glasgow outcome scale shows there was a significant improvement in the outcome of HBOT group at the end of the study. 7 patients (28%) showed full recovery (GOS 5) in group I, while only 4 patients (16%) in group II and one patient (4%) in group III showed full recovery. This was followed by GOS 4 which represents 10 patients (40%) in group I, 7 patients (28%) in group II, and 5 patients (20%) in group III.

In the study of Artru et al,[158] which included 60 patients in a prospective study to evaluate the effectiveness of HBOT as a treatment of head injury coma, they found that, the rate of recovery of consciousness at 2 weeks and 1 month was higher in HBOT groups (42% vs. 28%).

Lin et al,[159] studied 44 patients with TBI divided into 2 groups. The study randomly included 22 patients who received HBOT after the patients' condition stabilization and another 22 patients as control group. The clinical conditions of the patients were evaluated with GCS and GOS. The GCS of the HBOT group was improved from 11.1 to 13.1 in average, and from 10.4 to 11.5 for control group. Significant GOS improvement was observed in the HBOT group.

Narotam and colleagues [160], studied 139 patients with traumatic brain injury to evaluate the effect of normabaric hyperoxia. They demonstrated that NBH significantly reduced mortality and improved clinical outcomes.

Martin M. Tisdall et al,[161] studied 8 adults with TBI within the first 48 hours postinjury. Inspired oxygen percentage at normobaric pressure was increased from baseline to 60% for 60 minutes and then to 100% for 60 minutes before being returned to baseline for 30 minutes. They found that NBH increase aerobic brain metabolism and has the potential to improve outcome after TBI.

In agreement with our study, sukoff and colleagues [162], in their animal model, found that HBOT decreased mortality by more than 50% relative to the non-treated injured animals.

Zhou z etal [163], found, in a rat model of moderate brain injury, that HBOT showed significant protection against neuronal loss translated into long term cognitive improvement compared to normobaric oxygen treatment.

Wang and colleagues [164], have demonstrated that multiple HBOT (3 ATA hourly for 3 or 5 days) delivered at least 2 days post injury resulted in significantly reduced overall neurological deficit and neuronal apoptosis.

In our study, HBOT group showed significant improvement in brain metabolism as compared to NBH group and the control group as measured by oxygen saturation, jugular venous lactate, and lactate oxygen index (L.O.I). In addition, there was a significant improvement regarding brain metabolism in NBH group as compared to the control group.

There was a significant increase in the jugular venous oxygen saturation ($SjvO_2$) at the end of the study in both group I (mean value increased from 67.88±4.18 to 74.80±3.94) and group II (mean value increased from 69.08±3.84 to 75.48±1.78) as compared to the control group (mean value increased from 68.40±4.92 to 69.76±4.65) indicating improvement of brain oxygenation and thereby brain metabolism but there was no significant difference between group I and group II.

Jugular venous oxygen saturation ($SjvO_2$) measures the balance between cerebral oxygen delivery and cerebral oxygen consumption. Abnormalities that increase oxygen consumption (e.g., fever or seizures) or that decrease oxygen delivery (e.g., increased ICP, hypotension, hypoxia, hypocapnia, or anemia) can decrease $SjvO_2$[54].

Claudias et al [165], measured $SjvO_2$ continuously in the ICU in 177 patients with severe head injury, jugular venous desaturation ($SjvO_2 < 50\%$) was identified at least once in 39% of the patients. Approximately half of the episodes of desaturation were due to intracranial hypertension and half were due to systemic causes. The occurrence of one or more episodes of desaturation was strongly associated with a poor outcome, suggesting that the reduction in oxygen delivery identified with the $SjvO_2$ monitoring contributed to the neurological injury. Additional data supporting the hypothesis that these secondary insults identified with the $SjvO_2$ monitoring contribute to the patient's neurological injury come from the increase of the extracellular concentrations of lactate and excitatory amino acids in the brain using microdialysis.[54] $SjvO_2$ identifies global reductions in cerebral oxygenation due to a variety of causes, and is useful as a monitor for brain metabolism in patients with traumatic brain injury.[17]

In agreement with our study, Thiagarajan et al[166], studied eighteen head-injured patients for changes in jugular venous oxygen saturation ($SjvO_2$) and arteriovenous oxygen content difference ($AVDO_2$) in response to changes in PaO_2. They found that, $SjvO_2$ values were significantly greater with PaO_2 within the range of 200-250 mm Hg than $SjvO_2$ measured at a PaO_2 of 100-150 mm Hg. They concluded that, the adequacy of cerebral oxygenation can be estimated in head-injured patients by monitoring jugular bulb oxygen saturation and the arteriovenous oxygenation content difference.

In contrast with our study, Rockswold [167] studied the effect of HBOT on 37 TBI patients who were given 100% oxygen (1.5 atm. Pressure) for 60 minutes every 24 hours (7 treatments per patient). Mortality decreased by more than 50% but there was no significant change in jugular venous oxygen content in all patients.

Nakamura [168] et al, studied 7 head injured patients who underwent HBOT after clinical stabilization. 100% Oxygen (2.7 ATA) was delivered to patients in a hyperbaric chamber for 6o minutes every 24 hours (total 5 treatments per patient). Cerebral

metabolism monitoring using jugular venous oxygen and arteriovenous oxygen content difference before and after treatment was evaluated. They found that there was no significant change in jugular venous oxygen after HBOT.

Sarah B. Rockswold et al,[106] studied sixty nine patients who had sustained severe TBIs (mean GCS 5.8). Patients were prospectively randomized to 1 of 3 groups within 24 hours of injury: 1)HBO_2, 60 minutes of HBO_2 at 1.5 ATA; 2)NBH, 3 hours of 100% of inspired oxygen at 1 ATA; and 3)control, standard care. Treatment occurred once every day for 3 consecutive days. Brain tissue PO_2, microdialysate lactate and intracranial pressure were continuously monitored. In comparison with values in the control group, the brain tissue PO2 levels were significantly increased during treatment in both the HBO2 (223 ± 29 mm Hg) and NBH (86 ± 12 mm Hg) groups ($p < 0.0001$) and following HBO2 until the next treatment session ($p = 0.003$). Brain tissue PO2 levels 200 mm Hg were reached in 51% of the HBO2 treatment sessions and 5% of the NBH treatments. There was a significant improvement in brain metabolism, cerebral blood flow and intra cranial pressure when the mean brain tissue PO2 level was ≥ 200 mmHg.

At the end of our study, there was a significant decrease in the jugular venous lactate in HBOT group (decreased from 35.44±6.84 – 21.86) and in NBH group (decreased from 34.04±6.43 – 25.80±3.56) as compared to the control group (decreased from 33.52 ±5.58 – 28.56±4.03). There was also also a significant decrease in jugular venous lactate in HBOT group as compared to the NBH group.

As regarding lactate oxygen index there was a significant improvement at the end of the study in HBOT group (decreased from 0.059 ±0.01 to 0.029±0.006) and NBH group (decreased from 0.058 ±0.013 to 0.042±0.009) as compared to the control group (decreased from 0.057±0.014 to 0.043±0.008). There was also a significant improvement in L.O.I in HBO group as compared to NBH group.

In agreement, Nakamura [168] et al, studied 7 head injured patients who underwent HBOT after clinical stabilization. 100% Oxygen (2.7 ATA) was delivered to patients in a hyperbaric chamber for 6o minutes every 24 hours (total 5 treatments per patient). Cerebral metabolism monitoring using jugular venous lactate level before and after treatment was evaluated. They found that jugular venous lactate decreased significantly after HBOT and concluded that HBOT significantly improved brain metabolism in TBI patients.

Rockswold et al,[106] in their clinical study compared the effect of HBOT and NBH on brain metabolism in severe TBI patients. They showed that both HBOT and NBH significantly decrease ventricular CSF lactate, indicating improved aerobic metabolism and tissue hypoxia. In addition, lactate pyruvate ratio significantly decreased post-treatment in patients in the HBO2 group and, to a lesser extent, in those in the NBH group indicates a shift toward a better brain metabolism after hyperoxia treatments.

Tisdall et al,[161] have stated that global oxidative cerebral metabolism and cerebral blood flow CBF were significantly improved (about 30 %) for 6 hours after HBOT but not after NBH treatment, as compared with levels following standard care. Cerebral blood flow and cerebral metabolic rate of oxygen ($CMRO_2$) are closely coupled and respond to cellular activity, that is, mitochondrial function recovery. A concurrent measurement of improvement in the mitochondrial redox state further supports this finding. These data

showed that increased tissue oxygen delivery is capable of driving an increase in oxygen utilization, leading to improved cerebral aerobic metabolism.

Sarah B. Rockswold et al [169], studied the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intracranial pressure, and clinical outcome in severe traumatic brain injury clinical article. Forty-two patients who sustained severe TBI (mean Glasgow Coma Scale [GCS] score 5.7) were prospectively randomized within 24 hours of injury to either: 1) combined HBO_2/NBH (60 minutes of HBO_2 at 1.5 atmospheres absolute [ATA] followed by NBH, 3 hours of 100% fraction of inspired oxygen [FiO_2] at 1.0 ATA) or 2) control, standard care. Treatments occurred once every 24 hours for 3 consecutive days. Intracranial pressure, surrogate markers for cerebral metabolism, and O_2 toxicity were monitored. Clinical outcome was assessed using Glasgow Outcome Scale (GOS) score. In comparison with values in the control group, brain tissue partial pressure of O_2 (PO_2) levels were significantly increased during and following combined HBO_2/NBH treatments in both the noninjured and pericontusional brain ($p < 0.0001$). Microdialysate lactate/pyruvate ratios were significantly decreased in the noninjured brain in the combined HBO_2/NBH group as compared with controls ($p < 0.0078$). The combined HBO_2/NBH group's intracranial pressure values were significantly lower than those of the control group during treatment, and the improvement continued until the next treatment session ($p < 0.0006$). There was an absolute 26% reduction in mortality for the combined HBO_2/NBH group ($p = 0.048$) and an absolute 36% improvement in favorable outcome using the GOS ($p = 0.024$) as compared with the control group.

Limitations of our study were mostly due to cost and availability:

- Need to transfer patients out of hospital for HBOT sessions which carry the risk of transportation.
- Delay in starting HBOT sessions until the patient is stable for transport.
- Follow up of the patient for 20 days only. As some patients may show improvement after longer periods.
- The use of jugular venous samples. Continous jugular venous oxygen saturation is more accurate. As well as the use of cerebral microdialysis and brain tissue oxygen tension.

SUMMARY

Traumatic brain injury (TBI), occurs when an external force traumatically injures the brain. TBI can be classified based on severity (mild, moderate, and severe), mechanism (closed or penetrating) or other features (e.g. occurring in a specific location or over a widespread area). Head injury usually refers to TBI, but is a broader category because it can involve damage to structures other than the brain, such as the scalp and skull.

Traumatic brain injury can cause a host physical, cognitive, emotional, and behavioural effects. The outcome of TBI ranges from complete recovery to permanent disability or death. The 20th century saw critical developments in diagnosis and treatment of TBI which decreased mortality rates and improved outcome. These include imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). Depending on the injury, treatment required can be minimal or may include interventions such as medications and emergency surgery.

Hyperoxia has been used as a new method for improving brain metabolism and outcome in patients with TBI. Two methods can be used, hyperbaric oxygen therapy (HBOT) which is the use of high concentration of oxygen at a high atmospheric pressure and normobaric hyperoxia (NBH) which is the use of high concentration of oxygen at normal atmospheric pressure.

The aim of the present work was to find out and compare the effect of HBOT and NBH in treating TBI patients. These effects were evaluated through the following parameters: Glasgow coma scale (GCS), cerebral metabolism and Glasgow outcome scale (GOS).

This study included 75 adult patients with traumatic brain injury. All patients were in the age group between 18-40 years, with GCS between 9-12 (moderate brain injury). Patients were divided into three groups, each consisted of 25 patients. Group I received HBOT in addition to the standard conventional management of TBI, group II received NBH in addition to the standard conventional management of TBI, and group III (control group) which received the standard conventional management of TBI only. In HBOT group, patients received 100% oxygen at 1.5 atmospheric pressure for about one hour each day for 20 consecutive days, while in NBH group, patients received 100% oxygen at normal atmospheric pressure in the ICU for 3 consecutive hours each day for 20 consecutive days.

Our study revealed that:

- There were no significant differences among the three groups regarding age, sex, CT brain findings on admission and laboratory investigations.
- The level of consciousness improved significantly in both HBOT group and NBH group more than the control group, and in HBOT group more than NBH group.
- There was a significant improvement in brain metabolism in both HBOT group and NBH group more than the control group, and in HBOT group more than NBH group.
- There were better recovery and better prognosis in HBOT group regarding GOS more than both NBH and control groups.

We can conclude from the present study that the usage of HBOT in management of TBI patients significantly improves the cerebral metabolism and outcome of these patients. Also we conclude that HBOT is much more effective than NBH in patients with TBI.

We recommend the use of HBOT in the management of TBI patients as soon as the patient is clinically stable and fit for transport. Also we recommend the use of NBH in TBI patients who are not clinically stable for transport or if HBOT is not available.

CONCLUSION

From the present study, we can conclude the following points in relation to the effect of hyperoxia through HBOT and NBH in the management of TBI patients.

1) It improves the cerebral oxygenation and metabolism.
2) It improves the outcome as evidenced by GOS.
3) It decreases morbidity and mortality and thus ICU stay, which can be reflected as a decrease in the cost, incidence of complications and burden on ICU staff.
4) HBOT is much more effective than NBH for improving brain metabolism and outcome.
5) HBOT is safe, non invasive and with low risk of serious complications.