

**SEVERE TRAUMATIC BRAIN INJURY AND ANISOCORIA: A SEARCH FOR MANAGEMENT GUIDELINES IN A SETTING WHERE FACILITIES ARE NOT AVAILABLE OR VERY LIMITED.**

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**Abstract.**

Traumatic Brain Injury (TBI) is a major cause of morbidity and mortality in all age groups. Management of Severe TBI is mainly aimed at reducing the secondary effects of brain damage, namely hypoxia, ischaemia and raised intracranial pressure. In low income countries such as in Sub-Saharan Africa, where facilities like brain computed tomography (CT) scan machines are not

readily available, neurosurgeons face challenges in decision making whether to operate or not to operate on a patient with Severe TBI and anisocoria as the latter is used as a localizing sign for a possible intracranial haemorrhage compressing the oculomotor nerve. In addition, these patients usually arrive late- a period of several hours – from referral health centres with anisocoria and no brain CT scan.

Using standard search engines, we take a look at evidence from the literature, then use this together with our own experience on two patients to suggest research driven guidelines for management of patients with Severe TBI and anisocoria (after initial resuscitation and cervical spine stabilization) in situations where an early brain CT scan is not available and the time period between the onset of anisocoria and presentation to the neurosurgical emergency unit is very uncertain.

**Key words: Severe TBI, anisocoria, management guidelines.**

## **Introduction.**

Traumatic brain injury (TBI) is a global health problem and a major cause of disability with survivors often suffering cognitive, mood and behavioural disorders leading to a substantial loss in the productive years of life and a need for lifelong services (1, 2, 3, 4, 5, 7, 11, 16). The main causes are motor vehicle accidents, falls from height and assault/violence. In the European Union, it has been estimated that 40% of TBI's are caused by motor vehicle crash events, 37% by falls, 7% by assault/violence and 16% by other causes (26). Worldwide, it is estimated that about 10 million TBI's occur annually (21). It has also been estimated that about 5.3 million people have some TBI-related disability, complaint or handicap in the USA (19).

Traumatic brain injury is classified using the Glasgow Coma Scale score (GCS) as mild (GCS 13-15), moderate (GCS 9-12) and severe (GCS 3-8) (27). The GCS is the most extensively used grading system for assessing level of consciousness (4). In Severe TBI early presentation is of utmost importance as appropriate management such as surgical intervention may lead to a good outcome. However, late presentation and the presence of anisocoria coupled with an advanced age and the presence of extracranial injuries are indicative of a poor outcome-death or vegetative state- with or without surgical intervention (1, 2, 3, 4, 5, 7, 11, 16, 29). In situations where the time interval between the onset of anisocoria and presentation to hospital is unknown or uncertain, neurosurgeons

have always been faced with the dilemma of operating or not operating, as best outcome in late presentation is a vegetative state of the patient which will lead to requirement of resources for care of the patient, impacting an economic burden to the relatives, community and the government (13). Where the period of onset of anisocoria in patients with Severe TBI is known, studies have been carried out and various researchers have stated an appropriate period of surgical intervention within this period in order to achieve a good outcome in these patients (11). Our review has three objectives. First, we intend to understand the anatomical pathway of the pupillary light reflex and causes of pupillary dilatation in TBI. Second, we look at anisocoria as a localizing sign for a possible intracranial haemorrhage (such as an epidural haematoma) and guide for surgical intervention. Third, as a result of lessons learnt from the various researchers and our own experience on two patients, we hope to suggest guidelines for management of patients with severe TBI and anisocoria, presenting late, in a setting where early brain CT scan is not available and history unreliable.

### **The Pupillary Light Reflex.**

A bright light shone on one eye sends an afferent impulse along the optic nerve to the midbrain superior colliculus. From here, a second order fibre passes to the Edinger Westphal nucleus (part of the third nerve) on the same and opposite side, which supply parasympathetic fibres to the oculomotor nerve (5, 15, 26). Efferent fibres then leave in the oculomotor nerve (third nerve) to the ciliary ganglion. From there, more fibres leave in the short ciliary nerve to the constrictor pupillae muscle (circular muscles of the iris) of the eye. With all pathways intact, shining a bright light on one eye leads to an equal degree and rate of constriction of both pupils. Dilatation of one pupil is an ipsilateral disruption of the pathways, especially constriction of the oculomotor nerve by an expanding intracranial lesion such as an acute epidural haematoma in TBI. Fibres of the oculomotor nerve subserving the pupillary light reflex are located at the periphery of the nerve and are therefore easily compressed by an expanding intracranial lesion. Ischaemic conditions such as damaged superior cerebellar artery, posterior cerebral artery, posterior communicating artery and anoxic encephalopathy may also lead to oculomotor nerve ischaemia as well as ischaemia of the pathways of the pupillary light reflex, leading to anisocoria. In addition, sympathetic storming in TBI may also lead to anisocoria without an expanding intracranial lesion (15). Although oculomotor nerve compression is often considered as the primary cause of anisocoria, some studies have shown that unequal pupillary response in early severe TBI is more due to brainstem hypoperfusion than to uncal herniation with third nerve compression (18). Other

causes of papillary dilatation are glutethimide poisoning, anticholinergics such as atropine and botulism toxin poisoning (15).

### **Localization of an expanding intracranial lesion (epidural haematoma) using anisocoria.**

In TBI where Brain CT scan is not available, the clinical findings of coma (GCS less than or equal to 8), unilaterally dilated pupil with loss of light reflex and a contralateral motor deficit are indications for exploratory burr holes first on the same side, then on the opposite side of the dilated pupil (8, 22). Studies carried out by McKissock et al indicate that an epidural haematoma will be found on the same side of the papillary dilatation in 85% of cases (20). In another study of 100 patients undergoing transtentorial herniation or brainstem compression exploratory burr holes were positive in 56% of cases. Subdural haematoma was the most common extraaxial mass lesion- alone and unilateral in 70%, bilateral in 11% and in combination with epidural haematoma or intracerebral haemorrhage in greater than 9% (2). Chestnut et al had found out that asymmetrical pupils predict the presence of an operable mass lesion in 30% of cases (10).

Pupillary examination is done by clinically examining both pupils with a bright light in a dimly lit room for unilateral as well as consensual reaction to light. This is usually done with a pen torch, although some authors use a pupillometer for examination of the pupils and assessment of other clinical indices (17). Normally, two pupils in an individual are of equal size. A slight difference in the size might be observed in up to 20% of the population (23). Physiological anisocoria when present, remain unaltered by changing the background illumination. Pupillary examination may be difficult in the presence of orbital fractures and grossly swollen eyes, especially in patients with severe TBI (15).

### **Outcome of management of Severe TBI with anisocoria.**

Outcome assessment has been done on experimental basis in TBI animal models using histopathological indices such as cerebral perfusion, cerebral blood flow, cerebral oedema and cognition (14, 18, 24, 25). The outcome has always been poor, with some studies in rats reporting a decrease cerebral blood flow of up to 50% within 4 hours of injury (18, 25).

Clinical studies in humans have also been conducted and in a study by Zandbergen et al, an analysis of patients with anoxic ischaemic coma, unresponsive

pupils and lack of response to pain showed that there was 80% risk of death or permanent vegetative state if seen within a few hours and 100% risk of death if present at 3 days (29). In a study of 100 trauma patients undergoing transtentorial compression a mean follow up of 11 months after exploratory burr holes indicated that 70% died. However, no morbidity or mortality was directly attributed to the burr holes. Four percent of the patients had a good outcome and 4% had moderate disability (2). In Severe TBI due to diffuse axonal injury, the outcome is either death or a persistent vegetative state (1). Cohen et al analyzed 21 patients with Severe TBI (GCS <8). Anisocoria was present in 14 (67%) patients. Mortality rate was three times higher in this group than in the patients without anisocoria. None of the patients with an anisocoria-craniotomy latency of 70 minutes or less died and all of these patients had a good or reasonable outcome. Analysis of the anisocoria-craniotomy latency in ten patients revealed that a lapse of more than 90 minutes was associated with a greater mortality compared with patients with a latency of less than 90 minutes (11).

In severe TBI due to injuries in the battlefield, outcome after surgery was worse in patients with the least GCS score and anisocoria (3, 6, 7).

Other studies show that some contributory factors to poor outcome in patients with Severe TBI and anisocoria apart from late presentation are advanced age, presence of extracranial injuries such as bone fractures, genetic factors like the presence of apolipoprotein E4 allele in the patient (12, 28).

### **Experience on two patients.**

#### **Patient 1.**

A 25-year-old man was brought to the neurosurgery unit at Muhimbili Orthopaedic Institute (MOI) Dar es Salaam, after having been involved in a motor vehicle crash and sustained injury to the head about 9 hours prior to arrival. He was intubated, with a stabilized cervical spine and an abrasion on the right malar area. His GCS score was 6 (motor component=4). The right pupil was fully dilated and fixed and the left pupil was mildly dilated and sluggishly reacting to light. He was taken to the operation theatre 50 minutes later for exploratory burr holes. An epidural haematoma of about 60 ml was found on the right fronto-temporal area, over a contused and oedematous temporal lobe. The haematoma was evacuated via a fronto-temporo-parietal decompressive craniectomy and bone flap placed subcutaneously in the left iliac fossa. Three months later the bone flap was replaced by a second operation (cranioplasty) and the patient fully recovered with no neurological deficit. On follow up in the outpatient clinic at 11 months after surgery, the patient was fully engaged in his previous occupation as a petty trader.

#### **Patient 2.**

A 23-year-old man was brought to the neurosurgery unit at MOI, about 6 hours after being involved in a motor vehicle crash. He was in mild respiratory distress and had a GCS score of 7 (motor component=5). His right pupil was fully dilated and fixed and the left pupil was normal in size, sluggishly reacting to light. He was taken to the operation theatre for exploratory burr holes and a right temporo-parietal epidural haematoma (about 50ml) was found overlying a non-oedematous brain. The haematoma was evacuated and bone flap replaced. At a follow up visit six months after surgery, the patient fully recovered without any neurological deficit.

**Suggested management guidelines for patients with Severe TBI and anisocoria in settings where brain CT scan is not available and the time period between pupillary dilatation and arrival to hospital is uncertain.**

From the forgoing brief review of the literature and experience, we found that patients with severe TBI and anisocoria most often have a poor outcome after late presentation. However, poor outcome depends on some factors such as advanced age, other associated injuries, apolipoprotein E4 and some studies have found exploratory burr holes beneficial in patients with severe TBI (12, 22, 28,). This coupled with the fact that no morbidity or mortality is directly attributed to the burr holes (2), patients with severe TBI and anisocoria should be given the chance of exploratory burr holes, provided they are fit for surgery. Therefore, suggested guidelines for management of patients with severe TBI and anisocoria, presenting late, in settings where brain scanning facilities are not available, are simply:

Exploratory burr holes should be done to all patients provided they are haemodynamically stable and fit for surgery.

Those who are not stable or fit for surgery should not be subjected to exploratory burr holes (see figure 1 below).

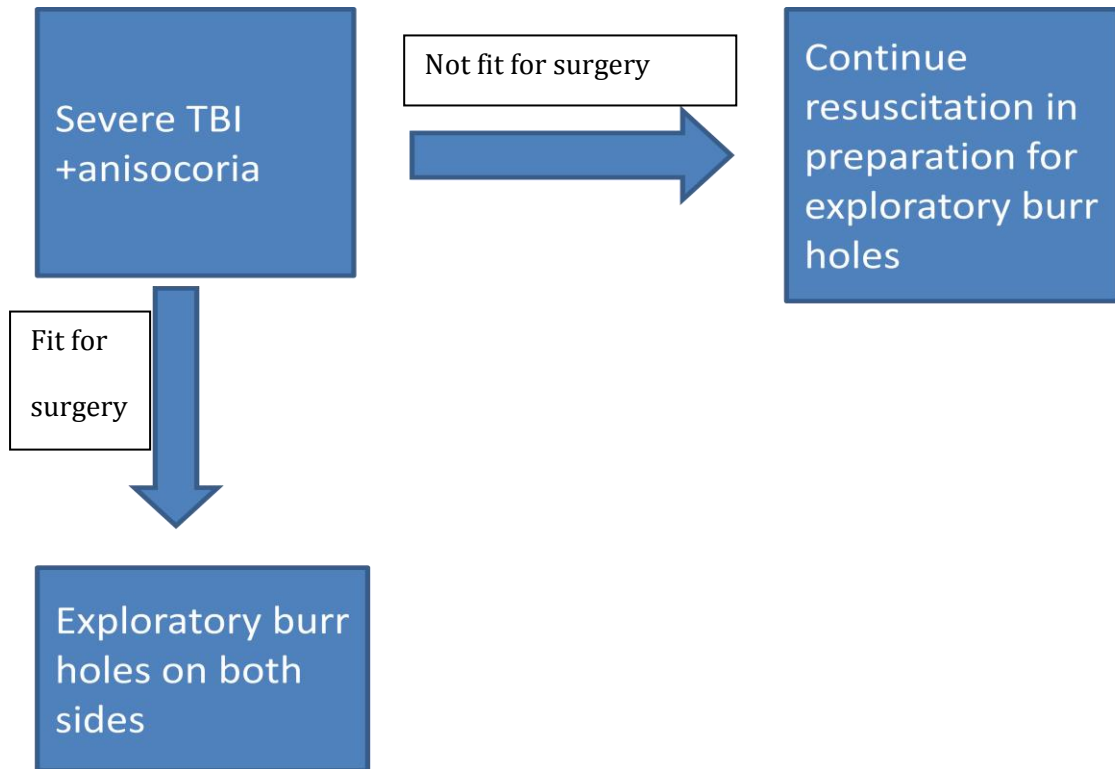


Figure 1. Flowchart of guidelines.

### Conclusion

Patients with severe TBI and anisocoria, presenting late in a setting where brain scanning facilities are not available, may benefit from exploratory burr holes which should be done if they are fit for surgery. Further studies are needed to throw more light on the management of these patients in circumstances where resources are not available or very limited.

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