Case Report

Death from Diamox: Three Case Reports

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Diamox –Acetazolamide is an inhibitor of enzyme carbonic anhydrase and a non-bacteriostatic sulfonamide. It is widely used in ophthalmic practice to prevent and control abnormal rise in intra-ocular pressure in glaucoma, pre-operative prophylaxis in intra-ocular surgery, prophylaxis after YAG laser, cystoid macular edema and retinal arterial occlusion etc. It is also used in non-ophthalmic practice like acute mountain sickness[1], peptic ulcer[2], idiopathic intracranial hypertension in pregnancy[3], chronic hydrocephalus[4], epilepsy[5], obstructive sleep apnea[6] etc.

Diamox is not without its adverse reactions[7-11]. Common side effects include parasthesias and GIT disturbances, while occasional side effects are transient myopia, photosensitivity, urticaria, melena / hematuria etc. Diamox has certain rare but fatal complications as well which include Steven Johnson Syndrome, erythema multiforme, toxic epidermal necrolysis, metabolic acidosis, anaphylaxis, acute delirium and depression. We report three cases, where use of diamox in an eye care setup proved fatal. The practice of pre-op diamox in cataract surgery has since been stopped at Al-Shifa.

CASE REPORTS

Case One, March 2004

A 60 years old male was admitted for cataract surgery at Pakistan Institute of Medical Science (PIMS) Islamabad. Routine systemic exam & lab profile was normal. Pre-op 500 mg of Diamox was given. Patient got restless on the morning of the operation and complained of increased micturition. In the ward, located on the first floor patient looked confused and lost. He went to toilet and "Walked out" of window and died of head injury.

Case Two – January 2006

A 65 years old female admitted for cataract surgery at Al-Shifa Trust Eye Hospital, Rawalpindi. Routine systemic exam & lab profile was normal. Pre-op 500 mg of Diamox was given. Patient got restless on operation table and surgery was postponed. In the

ward, located on the first floor patient looked confused and lost. He "Walked out" of window and died of head injury.

Case Three – July 2006
A 60 years old male underwent uneventful cataract surgery at Al-Shifa trust eye hospital. Patient got restless afterwards in the ward, looked confused and lost. The patient then attempted to "go out" of ward windows but was restrained by the ward staff. Patient recovered over night and was discharged without any complication.

DISCUSSION

In all three cases, the abnormal behavior of the patients was a result of delirium or acute confusional state as a rare adverse reaction of diamox.

Delirium[12] is defined as disturbance of consciousness or reduced clarity of awareness of the environment and occurs along with reduced ability to focus, sustain, or shift attention. There is a change in cognition (e.g., memory deficit, disorientation, language disturbance, perceptual disturbance).

14-56% of hospitalized elderly patients (10-22% at admission: and additional 10-30% of cases after admission) may develop delirium[13]. Post-op delirium in general is 5-10% and as high as 42% following orthopedic surgery[14]. Mortality from delirium has been reported from 22-76%[15].

Delirium develops over a short period (hours to days) and tends to fluctuate during the course of the day[12]. Almost any medical illness, intoxication, or medication can cause delirium. Mostly multi-factorial, medications are the most common reversible cause of delirium[15]. In studies of elderly hospital patients, drugs have been reported as the cause of delirium in 11 to 30% of cases[16]. Any drug can cause delirium but the worst offenders are Anticholinergics (Atropine, Tropicamide, etc.), Benzodiazepines (Diazepam etc.) and Tricyclic Antidepressants (Tofranil etc.)[16].

Delirium in elderly hospital patients is a well recognized phenomenon, but delirium in eye care setting has been reported less often (Table 1). Anticholinergics and Benzodiazepines are the common drugs implicated[19-21] and are in common use in eye care setting. Other precipitating factors reported in an eye care setting are alcohol restriction[17] in heavy drinkers, sensory deprivation due to dark atmosphere of the eye ward and markedly decreased vision[18]. However diamox delirium has been reported only once and that only in non-ophthalmic literature[10]. Death from delirium in an eye care setting has been reported once before[18]. It is interesting to note that mechanism of death had been identical to that of our two reported cases. Patients walked out of window in a state of altered awareness and disorientation, probably considering the window as an exit or door and died of head injury. It is interesting to note that studies have also shown delirium to be precipitating factors for 10% of falls among older people in residential care facilities[22].

The mechanism of delirium still is not fully understood[23]. Delirium results from a wide variety of structural or physiological insults. The main hypothesis is reversible impairment of cerebral oxidative metabolism and multiple neurotransmitter abnormalities. The diamox delirium has been attributed to electrolyte imbalance resulting in metabolic acidosis[7,10]. Young patients with normal renal functions have been reported[8] to develop metabolic acidosis after treatment for glaucoma and joint pain with a combination of salicylates and carbonic anhydrase inhibitors in normal doses. Carbonic anhydrase inhibitors appear to interact with salicylates to produce serious metabolic acidosis in patients without the predisposing factors generally considered to constitute risks. That is why it is recommended that treatment combining salicylates and carbonic anhydrase inhibitors is either kept to a minimum or avoided[8].

When delirium is diagnosed or suspected, the underlying causes should be sought. Despite every effort, no cause for delirium can be found in approximately 16% of patients[12]. Components of delirium management include supportive therapy and pharmacological management[24]. Fluid and nutrition should be given carefully because the patient may be unwilling or physically unable to maintain a balanced intake. For the patient suspected of having alcohol toxicity or alcohol withdrawal, therapy should include multivitamins, especially thiamine. Environmental modifications including reorientation techniques or memory cues such as a calendar, clocks, and family photos may be helpful. The environment should be stable, quiet, and well-lighted. Support from a familiar nurse and family should be encouraged. Family members and staff should explain proceedings at every opportunity, reinforce orientation, and reassure the patient. Sensory deficits should be corrected, if necessary, with eyeglasses and hearing aids. Physical restraints should be avoided. Delirious patients may

pull out intravenous lines, climb out of bed, and may not be compliant. Perceptual problems lead to agitation, fear, combative behavior, and wandering. Severely delirious patients benefit from constant observation (sitters), which may be cost effective for these patients and help avoid the use of physical restraints. These patients should never be left alone or unattended.

RECOMMENDATIONS

1. The incidence of delirium in an eye care set-up requires greater awareness, possible changes in pre-medication, and a longer observation period in the very old.
2. Avoid poly-pharmacy and follow the principle of 'start low and go slow'. It is worth mentioning that use of diamox in patients already using aspirin may be disastrous due to precipitation of metabolic acidosis.
3. The concept of diamox as a pre-medication in cataract surgery needs to be freshly looked into. 63% of surgeons do not use any IOP lowering agents in UK[25]. Single topical doses of timolol gel or latanoprost / travoprost have been found to be equally effective as replacement of pre-operative diamox[26].
4. The concept of day care surgery in eye units must be promoted. An early return to familiar, more illuminant atmosphere at home from the dark, chilly and unfamiliar atmosphere of hospital indoors will significantly reduce the risk of delirium in elderly patients.

Table 1: Delirium in an eye care setting

Year	Ref. No	Total patients studied	No. with delirium	Precipitating factor	Out-come
1902	17	Single	One	Alcohol restriction	Lost eye
1916	18	Not mentioned	Many	Sensory deprivation	2 died/fall
1977	10	Single	Single	Diamox	Safe
1979	19	27	2	Anticholinergic	Safe
1993	11	Three	3	Not mentioned	Safe
1994	20	350	6 (1.7%)	Anticholinergic	Safe
2002	21	296	13 (4.4%)	Benzodiazepines and age	Safe
2006	Current	Three	Three	Diamox	2 died/fall

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