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Adopting a Local Protocol in the Management of Neuroleptic Malignant Syndrome in the University of Port Harcourt Teaching Hospital (UPTH)

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Abstract: Neuroleptic Malignant Syndrome (NMS) is a life-threatening neurologic emergency associated commonly with the use of neuroleptic agents. In view of the high rate of fatality associated with it, urgent careful and adequate management is often required. To highlight the UPTH adopted protocol for the management of Neuroleptic Malignant Syndrome. All the cases of Neuroleptic Malignant Syndrome managed between Jan, 2008–Dec, 2014 in the unit were retrieved and our adopted management protocol critically reviewed. The outcome of our locally adopted management approach of NMS has been largely successful with 100% success rate in all 7 cases managed in the last three (3) years. All our patients recovered without any neurologic sequelae and were scheduled for adequate follow – up after discharge.

Keywords: Local Protocol, Management, Neuroleptic Malignant Syndrome, UPTH

1. Introduction

Neuroleptic Malignant Syndrome (NMS) is a life-threatening neurologic emergency associated commonly with the use of neuroleptic agents and characterised by distinctive clinical syndrome which includes alteration of sensorium and consciousness, generalised rigidity, high grade fever usually above 40^0C and dysautonomia [1].

The incidence rate ranges from 0.02 – 3.0% among patients taking neuroleptic agents [2]. Mortality results directly from the dysautonomic manifestations of the disease and from systemic complications. [3] Mortality has declined from the earliest report in the 1960s of 76% and is more recently estimated between 10 and 20% [3].

It is common following the use of high potency typical oral and depo injectable neuroleptic agents [2]. It is widely believed that it is not a dose-dependent phenomenon, but delayed manifestations and occurrences of NMS in old patients who have previously being receiving other type of neuroleptics appear to have contradicted this belief. A number of risk factors including medical conditions, dehydration and head injury and abrupt withdrawal of neuroleptic have been suggested [4, 5]. It is equally known that combination therapy and high doses of typical antipsychotics e.g. Haloperidol have equally shown higher risk than those on monotherapy especially the delayed ones [4].

Neuroleptic malignant syndrome could easily be confused with conditions like serotonin syndrome, malignant hyperthermia, heat stroke and meningoencphalitis. [6-13] It affects all age groups and age has never been reported as a risk factor [14]. In most studies, men outnumber women twofold. It is often followed by a number of biochemical changes [15-18].

The syndrome presents with myriad of symptoms cutting across all the systems of the body [19]. It occurs commonly within 72hrs of commencement of medication, although there have been cases of delayed manifestations. Apart from its high risk of fatality, the disorder presents with some inherent management difficulties and this makes this condition a medical emergency [20-29].

Dehydration in Neuroleptic Malignant Syndrome is both a risk factor and a clinical feature. As a clinical feature, it is usually caused by hyperthermia, diaphoresis and in some cases tachypnea [30]. The patients are usually moderately and severely dehydrated with a loss of 3-6kg and greater 6kg of their premorbid body weight respectively. The common clinical feature include increased thirst, dry mouth, dry skin, reduced skin turgor, decreased urine output (or no urine production in severe cases), dizziness, drowsiness, lethargy, confusion, seizure, hypotension (including orthostatic hypotension), tachycardia or shock.

The dehydration is usually accompanied by-electrolyte and acid base imbalances which could be hypo or hypernatremia, hyperkalemia and metabolic acidosis. The dehydration in Neuroleptic malignant syndrome is usually corrected with the use of Ringer's lactate or Normal saline and administered through the intravenous route. As with other cases of moderate to severe dehydration, the deficit is corrected and further losses prevented with maintenance therapy.

In cases of shock, the legs of the patient is elevated and 20mls per kilogram body weight of Normal saline is given over 30minutes and the patient reassessed. This can be repeated if necessary [31]. If severely dehydrated, 30millilitres per kilogram body weight of Ringer's lactate is given over 30minutes and then followed by 70millilitres of Ringer's lactate over the next two and half hours. After this initial fluid resuscitation, maintenance with normal saline of 4millilitres per kilogram body weight for the next 10kg and over 1 millilitre per kilogram body weight for the subsequent kilogram of body weight [32].

The total is given over 1 hour and the 24hrs calculation is done and given daily. An insensible loss of 800millilitres is added to the daily maintenance fluid. The patient is assessed every 15-30 minutes until the pulse and blood pressure returns to normal and every hour subsequently. Correction of electrolytes is done using the serum electrolyte as a guide. Some cases have benefitted from the use of electroconvulsive therapy [29]. Some studies have pointed to high risk of recurrence [33-37].

However, over a period of 3 years, the Neuropsychiatric Department of UPTH has successfully managed about 7 cases of Neuroleptic Malignant Syndrome, adopting the basic principles of its management with modifications. A highlight of this locally adopted management approach forms the essence of this presentation.

2. Objective

i. To highlight the challenges encountered in the management of Neuroleptic Malignant Syndrome.

ii. To highlight the UPTH adopted protocol for the management of Neuroleptic Malignant Syndrome.

3. Methodology

All the cases of Neuroleptic Malignant Syndrome managed between Jan, 2008 – Dec, 2010 in the unit were retrieved and our adopted management protocol critically reviewed viz a viz its effectiveness and success rate.

4. Protocol

Bipolar affective disorder was the primary diagnosis in three of the seven cases, severe depression with psychotic features in two cases, while catatonic shizophrenia and acute postpartum psychosis were the primary diagnoses in the last two cases respectively.

The protocol employs basically the same principles of managing NMS, though with some modifications. It is based upon a hierarchy of clinical severity and diagnostic certainty. All our patients were managed in the ward with an option to transfer them to the Intensive Care Unit (ICU) (which is the ideal setting) if there were no observable clinical improvement within 48 hrs, following commencement of intervention.

STEPS

1. Immediate withdrawal of all anti-psychotics and other suspected offending medications were immediately withdrawn.
2. Initial overall clinical assessment including full clinical, physical and mental status examination.
3. Establishment of stable cardiorespiratory system.
4. Assessment of the state of dehydration and replacement of lost fluid with normal saline alternate with 5% dextros saline to maintain euvolumic state. The fluid replacement followed the following pattern: For the mildly dehydrated IL over one and a half hours and then 3-5 litres. For the moderately dehydrated, IL over one hour followed by 4–6 litres of fluid over 24 hours for 72 hours and for the severely dehydrated 1 litre over 30 minutes, then 6 – 8 litres 24 hourly over 72 hours. By the 75th hour, intravenous infusions were terminated and replaced by oral fluids either directly or through nasogastric tubes. The total volume was reduced to 25% of the total fluid requirement for the first 24 hours and given 6 hourly until the patient became fully conscious.
5. Reduction of temperature by regular exposure of the body, use of fans, tepid sponging, ice block packs in water bags and use of antipyretics-intramuscular Paracetamol 1gm 12 hourly for 72 hours aimed at bringing the temperature down toless than or equal to 37.4 degree C.
6. Reduction in rigidity/relaxation of the smooth muscles of respiration (bronchial muscles) with the use of aminophylline of about 125mg 12hourly for 72 to 96 hours.
7. Use of skeletal muscle relaxant (Robaxin) 500mg 8

hourly either intramuscularly or orally for four days.
8. Use of oral Salbutamol 2mg 8 hourly for one week – (smooth muscle relaxant).
9. They were managed as unconscious patients with urinary catheter and nasogastric tube in situ to monitor urine output and feeding and drug administration respectively.
10. Basic investigations included full blood count, urinalysis, liver function test, electrolytes, urea and creatinin, immediate random and later fasten blood sugar analysis were regularly done.
11. Basic life support including direct oxygen (40-60%) administration were used when clinically indicated.
12. Low dose of short acting benzodiazepam (loraxepam 1mg daily for a short duration) to control agitation whenever it occurred.
13. Oral Bromocriptin 0.125mg 12 hourly for 1 week (7 days).
14. Intravenous antibiotics cefuroxin (12 hourly for 24 hours then 1g daily for the next 4 days). This was to check any concomitant infections from aspiration particularly.
15. Electrocombustive Therapy (ECT) was administered in about 60% of cases of between 2-3 shocks over 7 days. Consideration for ECT was based on poor response after 3 days inspite of supportive care and pharmacotherapy, persistence of residual catatonia (rigidity), some level of restlessness, where respiratory rate remained 30 cycles per minute and above after 72 hours and where lethal and malignant catatonia was suspected [29].
16. Light food was introduced when patient started feeding orally and gradually adequate and regular diet was introduced.
17. Very close in-patient monitoring including regular vital signs check and adequate nursing care were ensured.
18. Neuroleptics where restarted at 2-4 weeks after recovery with the basic guideline of restarting neuroleptics, and the typical antipsychotics were all replaced.

5. Results

The outcome of our locally adopted management approach of NMS has been largely successful with 100% success rate in all 7 cases managed in the last three (3) years. All our patients recovered without any neurological sequalae and were scheduled for adequate follow – up after discharge.

6. Modifications

The UPTH protocol has largely followed the general principle of management of Neuroleptic Malignant Syndrome. However, from our results and experience, we have found the following to be useful.

1. The use of aminophyline which is a bronchodilator and a smooth muscle relaxant.
2. The use of robaxin which is both a smooth as well as a skeletal muscle relaxant. The commonly used drug is dantrolin sodium which, unlike robaxin relaxes only skeletal muscle relaxant, which is not readily available in our environment.
3. The use of oral salbutamol - another smooth muscle relaxant; also helps to relax the brochial muscles for stable cardiorespiratory functioning.
4. The use of fans, ice block to complement the regularly prescribed tepid sponging and antipyretic to reduce hyperpyrexia.

7. Conclusion

The UPTH locally adopted protocol, which still follows the basic principles of managing NMS, though with modification, has proven largely effective with 100% success rate in the last three years. It is important that we share this knowledge and information with others who have been challenged in the past with high mortality rates arising from neuroleptic malignant syndrome. It is indeed a fatal condition, requiring focused, timely and knowledgeable intervention, with withdrawal of all antipsychotics, adequate fluid replacement treatment of concurrent infections and temperature control as main stay of malignant.

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