Impact of Haloperidol Prophylaxis on Delirium Incidence in Elderly Patients After Major Non Cardiac Surgery

Thesis

Submitted for partial Fulfillment for M.D. degree in Anesthesia, intensive care and pain management

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2020

Acknowledgement

First of all, all gratitude is due to God almighty for blessing this work, until it has reached its end, as a part of his generous help, throughout my life.

Really I can hardly find the words to express my gratitude to Prof. Dr. Sherif Wadie Nashed , professor of anesthesia, intensive care and pain management, Faculty of Medicine, Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision

Really I can hardly find the words to express my gratitude to Dr. Dina Salah El Din Mahmoud, assistant professor of anesthesia , intensive care and pain management, for her continuous directions and meticulous revision throughout the whole work. I really appreciate her patience and support

Great thanks to Dr. Fady Adib Abdel Malek & Dr. Tamer Youssef Elie, assistant professors of anesthesia, intensive care and paim management, Faculty of Medicine , Ain Shams University. I will never be able to express my feelings and gratitude towards their simple words, and I wish to be able one day to return a part of what they have offered to me.

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

John Emil Riad Mina

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List of Abbreviations

Abbr.		Full term
APACHE	:	Acute Physiology and Chronic Health Evaluation
CAM-ICU	:	Confusion Assessment Method for the ICU
CYP	:	Cytochrome P
D1	:	Dopaminergic receptors 1
D2	:	Dopaminergic receptors 2
DDS	:	Delirium Detection Score
DRS	:	Delirium Rating Score
ECG	:	Electrocardiography
EPS	:	Extrapyramidal symptoms
GABA	:	Gamma-Aminobutyric acid
ICDSC	:	Intensive Care Delirium Screening Checklist
ICU	:	Intensive care unit
NMS	:	Neuroleptic malignant syndrome
PRN	:	Per required need
QTc	:	Corrected QT interval
RASS	:	Richmond Agitation Sedation Scale

INTRODUCTION

Delirium is an acute or subacute organic mental syndrome characterized by disturbance of the level of consciousness, cognitive impairment, disorientation, development of perceptual disturbance, attention deficits, decreased or increased psychomotor activity, disordered sleep-wake cycle and fluctuation in presentation. The term ‘‘delirium,’’ comes from the Latin roots de (meaning ‘‘away from’’) and lira (meaning ‘‘furrow in a field’’) and ium (Latin for singular), literally means ‘‘a going off the ploughed track, a madness’’ ***(Maldonado, 2008).***

Delirium is associated with adverse outcomes including prolonged hospital stay, increased costs, long-term cognitive impairment and increased mortality ***(Bakker et al., 2012).***

Delirium is very common in elderly and hospitalized patients. Its prevalence is 10-24% in the adult general

medicine population and 37-46% in the general surgical population. In the intensive care unit (ICU) setting, delirium has been reported in up to 87% of patients. Postoperative delirium rates vary widely, ranging from 9% to 87%, depending on patient age and the type of surgery ***(Greene et al., 2009)***.

Drugs have been associated with the development of delirium in the elderly. Successful treatment of delirium depends on identifying the reversible contributing factors, and drugs are the most common reversible cause of delirium. Anticholinergic medications, benzodiazepines, and narcotics in high doses are common causes of drug induced delirium ***(Alagiakrishnan and Wiens, 2004).***

The etiology of delirium is not fully understood and is probably multifactorial. Acute central cholinergic deficiency is one of the most widely accepted explanatory theories, decreased GABA activity, abnormalities in melatonin and serotonin pathways, noradrenergic hyper-activity,

inflammation with increased release of Interleukin-I and Interleukin-6 leading to neuronal damage, and cerebral hypoperfusion are other possible pathogenetic mechanisms ***(Hshieh et al., 2008)***.

To counteract the effect of some of these risk factors, previous studies on delirium prevention have focused on nonpharmacological interventions such as reorienting the patient, modifying the hospital environment, proactive geriatric consultation, pain treatment programs, family education, early mobilization protocol, nutritional support, and infection control measures ***(Inouye et al, 2006)***.

An analysis revealed that, on average, non-pharmacological interventions reduce the absolute risk of delirium by a mere 13% ***(Inouye et al, 2006).***

The antipsychotic drug haloperidol is widely used for the symptomatic treatment of delirium.

Haloperidol is a dopamine antagonist. Dopamine D2 receptor blockade is associated with enhanced acetylcholine release ***(Milbrandt et al, 2005)***.

As delirium is highly associated with cholinergic deficiency, it can be hypothesized that haloperidol may have an indirect beneficial effect on delirium, including that arising from anticholinergic causes ***(Milbrandt et al, 2005)***.

The researchers defined major surgery as procedures requiring at least two hours of general anesthesia and at least two days in the hospital following the operation. Those could include procedures such as cardiac, thoracic, vascular, gastrointestinal, gynecologic and urologic surgeries ***(Troy et al, 2019)***.

Old age comprises "the later part of life; the period of life after youth and middle age, usually with reference to deterioration". At what age old age begins cannot be universally defined because it differs according to the context. Various countries and societies consider the onset of

old age as anywhere from the mid-40s to the 70s. For its study of old age in Africa, the World Health Organization (WHO) set 55 as the beginning of old age. At the same time, the WHO recognized that the developing world often defines old age, not by years, but by new roles, loss of previous roles, or inability to make active contributions to society ***(Lwanga and Orzeszyna, 2000)***.

AIM OF THE WORK

The aim of this work was to study the effectiveness of Haloperidol as a prophylaxis against delirium in elderly patients after major non-cardiac surgeries in ICU.

Review of Literature

Delirium in the Surgical Elderly Patients

Dagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) defines delirium as disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention, a change in cognition or the development of a perceptual disturbance that is not better accounted for by a preexisting, established or evolving dementia.

The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day; in addition, there is evidence from the history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition ***(Meagher et al., 2014)***.

Table (1): Diagnostic elements of delirium ***(Morandi et al., 2008).***

Disturbance of	
Attention	Difficulty focusing and easy distractibility
Cognition	Disorganized thinking, incoherent speech, hallucinations or delusions
Behavior	Agitation vs. lethargy, fear, paranoia or irritability
That is	
Acute	Occurs over a few hours, sometimes with short- lived prodromes
Fluctuating	Lucid intervals between episodes, with memory of the events

Three different subtypes of delirium have been identified based on the motor symptoms exhibited by the patient: hyperactive, hypoactive and mixed:

1- **Hyperactive delirium**: is characterized by (motor) agitation, restlessness, sometimes aggressiveness, attempting to remove catheters, and emotional liability.