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Incidence of anesthetics drug induced malignant hyperthermia in Lady Reading Hospital (LRH), Peshawar, Pakistan

Muhammad Tayyeb[1], Muhammad Ali[2], Sher Muhammad[3], Bashir Ul Haq[3], Arsalan Khan[3], Muhammad Qasim Jan[4], Muhammad Abbas[*5]

[1]*College of Medical Technology, Medical Teaching Institution, Bacha Khan Medical College, Mardan, Pakistan*

[2]*Department of Anesthesia, Bacha Khan Medical College, Mardan, Pakistan*

[3]*Department of Anesthesia Institute of Paramedical Science, Khyber Medical University, Peshawar, Pakistan*

[4]*Department of Anesthesia, Qazi Hussain Ahmad Medical Complex, Nowshera, Pakistan*

[5]*Department of Microbiology, Abdul Wali Khan University, Mardan, Pakistan*

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Abstract

Malignant hyperthermia (MH) is a pharmacogenetic disorder and life-threatening syndrome of skeletal muscle with exposure to potent inhalational anesthetics (Halothane, desflurane) and depolarizing muscle relaxant (succinylcholine). To determine the incidence of anesthetic drug induced malignant hyperthermia in patients in lady reading hospital Peshawar. This cross-sectional study was carried out in duration of six months (February to August 2019) in lady reading hospital (LRH) Peshawar. The intension of this study was to determine the incidence of drug induced (MH) in patients who are going for surgical procedure under general anaesthesia especially exposure to inhalational agents and Suxamethonium. Ethical approval was taken from ethical committee of Khyber Medical University (KMU) and Leady Reading Hospital (LRH) Peshawar. Informed consent was taken from Participants. Demographics details and patient's data were recorded and analysed through SPSS. Data of 424 patients were obtained in which males were 268 (63.2%) and female were 156 (36.8%). The mean age of the patients was 31.2±19.4. There was no case of malignant hyperthermia among these patients. The pinpoint incidence of malignant hyperthermia is unknown. In our study we are not find any case of malignant hyperthermia.

* **Corresponding Author:** Muhammad Abbas ✉ abbasmuhammad148@gmail.com

Introduction

Malignant hyperthermia (MH) is a pharmacogenetic disorder of skeletal muscle severe reaction with exposure of depolarizing muscle relaxant or inhalational anesthetics agent (Halothane, desflurane, Isoflurane) (Michael S. Phillips, 1994). The invention of the restorative effectiveness of dantrolene and advances in anesthesia monitoring have decreased the morbidity and mortality of MH significantly (Riazi, Kraeva, *et al.*, 2014). MH referred to as "Hidden Killer" because of high mortality rate even the susceptible patients are healthy studies have reported facts that deaths related with MH still happen, even with treatment (Rosero *et al.*, 2009). Three genes, RYR1, CACNA1S and STAC3 are related with MH vulnerability and the harsh dysfunction of skeletal muscle Ca2+ homeostasis that fallout in the clinical features of an MH response under anesthesia (Riazi, Kraeva and Hopkins, 2018). In 20th century several cases were reported related with anesthesia-related deaths correlated to peri-operative hyperthermia. However, it was not until 1960, when MH define as an independent syndrome. After introducing of dantrolene in 1975, as a particular ryanodine receptor antagonist, a causal cure became available and the death frequency for acute MH crisis reduced from around 70-80% to approximately 5% (Schneiderbanger *et al.*, 2014). In 1994 clinical grading scale was developed for MH to define standard clinical case definition and to make a comparisons between groups of patients that were defined by similar characteristics (Brady *et al.*, 2009).

Intra-operative incidence of Malignant Hyperthermia (MH) is 1:10,000 and 1:250,000 (David S Beebe, no date). Although an MH catastrophe may build up at first contact to anesthetic agents with those drugs identified to generate an MH event, on ordinarily, patients need three anesthetics agents before triggering. The incidence of MH is more frequent in males compared with females (2:1) (Rosenberg *et al.*, 2015). In World majority of population, all cultural groups are affected. The incidence of MH is high in people with low age, people with average age of 18.3 years are mostly affected. It had been establish that of all reactions 52.1% occur in children under 15 years of age (Kimberly Prather Strazis and Fox, 1993). Estimates of genetic abnormalities associated with MH susceptibility can range from 3,000 to 1 (vary from 1: 3000 to 1: 8500), and a contemporary estimation is 1 in 400 (Gonsalves *et al.*, 2013).

The Porcine Stress Syndrome was recognized as an "wakeful" MH episode in 1966.It was declared that, in animals like pigs worries such as rebellious cause a fast death. Till now debated continuously that heat-stroke as possible promotors for an MH episode. Awake" MH episodes in patients was reported by both Gronert and Den borough, according to den borough the patients also responded to dantrolene who suffered with exercise induced heat stroke (R. A. Bannister, 2012). MH can be diagnosed with lab testing and clinical sign and symptoms (clinical presentations). Main characteristics of MH are rigid muscle body, hyperthermia, acidosis, hyperkalaemia, tachycardia, and rise of end tidal carbon dioxide concentration, tachycardia. Rarely the CK value rise in MH vulnerability may be the first indication. Vitro contracture test is considered a gold standard for diagnosis of MH. Muscles biopsy used so then electric current passes through muscles biopsy and then apply caffeine and halothane. The in vitro contracture testing (IVCT) and caffeine and halothane contracture test (CHCT) are the two widely used forms of this test (Zhu *et al.*, 2004). A study of 12 million hospital discharges signify the prevalence of MH to be 1 in 100,000 among those patients scheduled for surgical procedures in the state of New York although there was no specific type of anesthesia mentioned. This study likely demonstrate an underestimate of MH in related with general anesthesia (Brady *et al.*, 2009).

One of Danish study collecting data according to age of patients and mode of anesthesia and estimated the occurrence of fulminant MH crises after the administration of volatile anesthetics as 1:84 000. If addition of succinylcholine will rise the incidence to 1:62 000 (Ording, 1996). MH can doesn't stick to specific race or gender although incidence of MH is suggested high in males and adolescents. In children the incidence of MH is estimated to be 1:15 000 and

in adolescents 1:50 000–150 000 for adults in North America and Europe (Wappler, 2001).

Thus, the main intention/aim of this study is to find out the incidence of MH in those patient scheduled for surgical procedure under general anesthesia with use of inhalational agent and depolarizing muscle relaxant.

Materials and methods

Study design, duration and setting

This descriptive cross-sectional study was conducted in different Operation theatre: Eye, Gynae and Obstetric surgery orthopaedic and ENT in lady reading hospital Peshawar Pakistan from (March to June 2018).

Sample size, inclusion and exclusion criteria

A total of 424 patients undergoing surgical procedures under general anesthesia (specially used inhalational agents and Suxamethonium Regional anesthesia and those patients who were not expose to inhalational agents and Suxamethonium are excluded from this study.

Study approval

This study was conducted after the approval of university and hospital ethical committee.

Procedure

This study was conducted after approval from hospital ethical and research committee. All enrolled patients were scrutinized with detail history and clinical examination including anesthesia fitness. The past medical record was also carefully checked in consultation with referred physician. This was done to control confounder and possible bias in study result. All patients were subjected to general anesthesia by single consultant anesthesiologist (used inhalational anesthetic and depolarizing muscle relaxant) having minimum of 5 five years' experience in department of anesthesia. The diagnosis of MH is based on clinical presentation or laboratory testing. enigmatic elevation of end tidal carbon dioxide (ETCO) concentration, muscle spasticity/rigidity, tachycardia, acidosis, hyperkalemia and hyperthermia are the dominant diagnostic characteristic of MH. The CK measurement is consider more prominent for MH susceptibility.

Clinical grading scale

In order to assist in clinical diagnosis of MH larach and his colleague develop clinical grading scale. Factor of this caliber are in Table. 1. Different range and value are mentioned to each manifestation of each clinical finding. The scale dearth of sensitivity however, although on no individual pre-formed test applied. To differentiate MH from other complication each clinical finding is carefully weighted and thoughted according to its importance. To find the attach of MH one Factor is consider in each manifestation . after qualifying of each factor, a score is then generated for episode of MH. We cannot rely on clinical grading scale whole sole. The value of these characteristics mainly help in identifying the more vulnerable to MH episode.

Contracture test or Laboratory diagnostic method

Currently the in vitro contracture test is "gold standard" for diagnosis of MH. The test is built on muscle fiber contraction under presence of halothane or caffeine. But we didn't used it because we didn't come across with any MH case. This Diagnostic method was not utilized in this study as there were no possible suspicion of MH in the selected/observed Samples as based on the suspicion criteria in accordance to the clinical grading scale used for MH. The principal used in clinical grading scale for prediction of Malignant hyperthermia is shown in Table 1. Adapted from (Rosenberg *et al.*, 1994), (Peng Philip W, 1995).

Data Analysis

Statistical analysis was performed on SPSS version 22.

Result

A total of 424 samples were collected among different surgical procedure. Majority of the participants were male 268 (63.2%) and 156 (36.8%) were female. Majority of the surgeries were in the other category 255 (60.1%) cardiac surgery (14.2%), ENT (11.8%), orthopaedic (9.2%), gynae and obs (2.6%) and eye surgery (2.1%). Inhaled anesthesia was reported in majority of the research participants 418 (98.6%) and majority of the patients have not previous surgical exposure 398(93.9%).

According to discharge status all the patients included in the research study were normally recovered (100%). Majority of the patients were in-patients (99.3%). Baseline characteristics of the research subjects. And there was no MH attack found in research subjects shown below in (Table 2 Table 3).

Table 1. principal/scale used in the Clinical Grading Scale for prediction of Malignant Hyperthermia.

Clinical Finding	Max. score	Indicator
Rigidity	15	Generalized muscular rigidity. Sever spasm of masseter muscle.
Muscle breakdown	15	Rise in creatine kinase greater than 20,000 IU after induction with general anesthetic drugs included depolarizing muscle relaxant.in perioperative period cola coloured urine, excess amount of myoglobin in urine and in serum (>60 µg/L, >169 µg/l) respectively. Serum potassium greater than 5.9 mEq/L (without any co-existing diseases).
Respiratory Acidosis	15	$ETCO_2$ greater than 54mmHg and Arterial PaCO2 > 60mmHg
Hyperthermia	15	Sudden rise in temperature greater than 38.9 °C (101.8 °F)
Cardiac Involvement	03	a. Inappropriate/unexplained sinus tachycardia, ventricular tachycardia or ventricular fibrillation
Family history	15	Inheritance autosomal dominant

Adapted from (Rosenberg *et al.*, 1994), (Peng Philip W, 1995).

Table 2. Baseline characteristics of the research subjects.

		Count	Column N%
Gender	Male	268	63.2%
	Female	156	36.8%
Type of surgery	Eye surgery	9	2.1%
	ENT	50	11.8%
	Cardiac surgery	60	14.2%
	Orthopaedic surgery	39	9.2%
	Gynaecology	11	2.6%
	Others (Neurosurgery, Thoracic and emergency surgery)	255	60.1%
Type of Anaes-thesia	Inhaled anaesthesia	418	98.6%
	Suxamethonium	0	0.0%
	Inhaled anaesthesia and suxamethonium	6	1.4%
Previous surgical exposure	No	398	93.9%
	Yes	26	6.1%
Discharge status	Normal recovery	424	100.0%
	Malignant Hyperthermia Exposure	0	0.0%
Patient type	Outpatient	3	0.7%
	Inpatient	421	99.3%

Table 3. show that there was no MH attack found in research subjects

	Frequency	Percent	Percentage	Cumulative Percentage
Valid No	424	100.0	100.0	100.0

The Fig. no. 1 shows the age wise distribution of the research subjects, the mean age of the research subjects was 31.15 with standard deviation of 19.4. (Fig. 1).

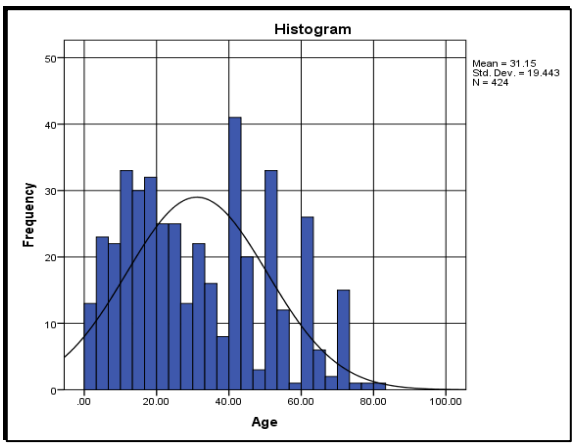

Fig. 1. Age wise distribution of research participatent.

Discussion

A total of 424 sample were collected in which the mean age of the research participatent was (31.15) with standard deviation of (19.443). although there is no single case of MH due to anesthetic agent among surgical patients, because malignant hyperthermia is a rare genetic condition linked to volatile anaesthetics and succinylcholine. Although MH is still a important risk factor for susceptible individuals scheduled for general anesthesia under the use of volatile anesthetic. Expected prevalence of MH susceptibility related to genetic defects can be as high as one in 3000 individuals (range 1:3000 to 1:8500), with an additional current approximation being 1 in 400 individuals (Robinson *et al.*, 2006). In young people the highest incidence of MH is observed with mean age of all patients 18.3 years (K. P. Strazis and Fox, 1993). In all ethnic groups MH episode were reported and often the ratio is high in male compared with female (Riazi, Larach, *et al.*, 2014)(Brady *et al.*, 2009).

Even though extensive inconsistency has been described. A new statement recommended that in 1:2000-3000 of the French population the MH vulnerable [MHS] quality may be exist (Bachand *et al.*, 1997). In the state of New York, a study carried out and according to this study about 12 million individuals who discharge from hospital established the occurrence of MH to be one in 100,000 surgeries even though the type of aesthetics was not specified. This possibly denotes a miscalculate of malignant hyperthermia In relationship with General Anesthesia (Rosero *et al.*, 2009).

In daily life many MHS individuals remain asymptomatic, therefore the true incidence of MH remains unknown. The expected prevalence related genetic is reported to be one in 2,000, while there are regional variations in the incidence of clinical MH episodes from one in 5,000 to one in 100,000 (Brady *et al.,* 2009, Monnier *et al.,* 2002, Fiege *et al.,* 2002). In our population is no episode of MH in all surgical patients under general anesthesia with exposure of provoking factor like inhalational agents and depolarizing agents.

Conclusion

Malignant hyperthermia is life threatening disorder of skeleton muscle show high metabolic response to volatile agents and depolarizing muscle relaxant. Although the mortality due to MH is decrease because of dantrolene administration from 80% to 1.4% This research study reported no case of malignant hyperthermia, whereas in literature it was very rarely reported. Hence, MH can be controlled by taking certain precautionary measures

For future researcher

As in this study there were no cases to suspected about malignant hyperthermia among these population. There is limitation in term of sample size and location It is suggested that, for future research the sample size should be increase from this study sample and study should be multicenter.

Conflict of interest

Authors declare no conflict of interest.

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