A Study of Anesthetic Agents Induced Genotoxicity: Kasr El Aini Hospitals' Experience

Thesis

Submitted for fulfillment for the Medical Doctorate degree in Forensic Medicine and Clinical Toxicology

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2015

Abstract

Exposure to waste anesthetic gases carries significant health hazards; genotoxicity is an identified risk among others. This study was conducted to evaluate the possible genotoxic effects of waste anesthetic gases on exposed medical personnel working in Kasr Al Aini hospitals. Sister chromatid exchanges (SCE) and micronucleus tests (MN) were performed on 31 exposed and 32 non exposed subjects. Both SCE and MN showed significant difference between the two groups. SCE was correlated to MN in the exposed group. SCE and MN significantly increased with age and duration of work. However no effect of smoking or sex was observed.

Comet assay was performed on 32 operation room (OR) personnel and 35 non exposed. The study revealed significantly increased comet parameters (mean comet tail length and moment) in peripheral blood lymphocytes of OR personnel in comparison with control individuals.

Furthermore, significant difference was observed as regard the age and duration of work in the exposed group, however no significant difference was observed as regard the gender or smoking.

In conclusion, our study points to the risk of DNA damage in medical personnel exposed to waste anesthetic gases.

Key words: (Anesthetic gases, occupational exposure, genotoxicity, Sister chromatid exchange, Micronucleus test, comet assay)

Acknowledgement

First of all greatest thanks and merciful to Allah, the great creator and the source of all man's knowledge.

I would like to express my great indebt to Dr. Dina Ali Shokry; Professor and Head of Department of Forensic Medicine and Toxicology, Faculty of Medicine, Cairo University, for her efficient and indispensable help, faithful guidance and willing efforts to facilitate the difficulties during this work.

My deep appreciation and thanks to Dr. Hala Saeed Zaghlool; Professor of Forensic Medicine And Toxicology, Faculty of Medicine, Cairo University, for her great support and valuable guidance to this study with all possible means.

Great thanks to Dr. Abeer Ahmed Zayed; Professor of Forensic Medicine and Toxicology, Faculty of Medicine, Cairo University, for her help and kind supervision.

Many thanks to Dr. Alaa Mohamed Shehab; Lecturer of Forensic Medicine and Toxicology, Faculty of Medicine, Cairo University, for his kind supervision and encouragement.

Great thanks and appreciation to Dr. Rania Ahmed Zayed; Professor of Clinical Pathology , Faculty of Medicine, Cairo University for her willing and useful participation in this study.

I wish also to express my gratitude and special thanks to my professors and colleagues in Department of Forensic Medicine and Toxicology, Faculty of Medicine, Cairo University, for their unlimited support and help.

It’s my pleasure to acknowledge all colleagues in the department of Anaesthesia for their active participation and cooperation throughout my work.

My greatest thanks and admiration have to be mentioned to all my dear friends for their support and love in the good and bad days.

And last but not least great thanks to my late father, my mother , my husband and all my family who loved and supported me throughout my whole life and till this very moment.

Azza Rady

2015

Table of contents

Title	Page
List of abbreviations	i
List of figures	ii
List of tables	iv
Glossary	vi
Introduction and aim of work	1
Review	
1. Genetic toxicology	3
2. Occupational Exposure to Anesthetics	21
3. Overview of Inhalational Anesthetic Agents	29
4. Sister Chromatid Exchange	32
5. Micronucleus Test	37
6. Comet Assay	45
Patients and methods	50
Results	57
Discussion	83
Conclusion and recommendations	90
Summary	92
References	94
Arabic summary	

List of Abbreviations

ASTM	American Society for Testing and Materials
ACGIH	American Conference of Governmental Industrial Hygienists
CA	chromosomal aberrations
CBMN	cytokinesis block micronucleus test
COSHHR	Control of Substances Hazardous to Health Regulations
DNA	deoxyribonucleic acid
FGF	fresh gas flow
FISH	fish fluorescent in situ hybridization
ICU	intensive care unit
HBM	human biomonitoring
MN	micronucleus test
NAS	national academy of sciences
NBUD	nuclear budding
NFPA	National Fire Protection Association
NIOSH	National Institute for Occupational Safety and Health
NPB	nucleoplasmic bridge
NRC	national research council
OCED	Organization for Economic Co-operation and Development
OEL	occupational exposure limits
OR	Operation Room
PACU	Post anesthesia care unit
ROS	reactive oxygen species
RPMI	Royal Park Memorial Institute culture medium
SCE	sister chromatid exchange
SCGE	single cell gel electrophoresis
UDS	unscheduled DNA synthesis
WAG	waste anesthetic gases

Glossary

- **Risk assessment:** is the process of evaluating the toxic properties of chemicals and the conditions of human exposure to ascertain the likelihood that humans will be adversely affected and to characterize the nature of the effects, which may be experienced. (Deleranko, 2014).
- **Carcinogen:** Any chemical or physical agent that increases cancer burden by increasing the incidence, altering the tissue distribution, increasing the malignant or metastatic potential, or decreasing the latency period of cancers in an individual or a population.
- **Genotoxin:** Any chemical or physical agent that directly or indirectly causes DNA damage, i.e., a covalent chemical modification to a DNA molecule.
- **Mutagen:** Any chemical or physical agent that directly or indirectly leads to a heritable alteration in the genetic sequence of bases in DNA (Hamilton, 2002).
- **Mutagenesis** refers to the ability of a virus or chemical agent to induce changes in the genetic sequences of mammalian or bacterial cells, thus altering the phenotypic expression of cell characteristics (Barile, 2008).
- **Effect biomarker**: Any change that is qualitatively or quantitatively predictive of health impairment or potential impairment resulting from exposure.
- **Exposure biomarker:** An exogenous substance or its metabolite or the product of an interaction between a xenobiotic agent and some target molecule or cell that is measured in a compartment within an organism (DeCaprio, 2006).
- **Point mutation**: Change in the genetic code, usually confined to a single base pair.
- **Aneuploidy**: An abnormal number of chromosomes in a cell or organism that is not an exact multiple of the haploid number.

- **Base substitution**: The substitution of one or more bases for another in the nucleotide sequence.
- **Clastogen**: An agent that produces structural changes of chromosomes.
- **Frameshift mutation**: A mutation in the genetic code in which one base or two adjacent bases are inserted into or deleted from the nucleotide sequence of a gene.
- **Gene mutation**: A detectable permanent change (point mutation, insertion, or deletion) within a single gene or its regulating sequences.
- **Micronucleus**: A microscopically detectable particle in a cell that contains nuclear DNA, usually one twentieth to one fifth the size of the main nucleus. It may be composed of a broken centric or acentric part of a chromosome or a whole chromosome.
- **Sister chromatid exchange**: The morphological reflection of an interchange between DNA molecules at homologous loci within a replicating chromosome.
- **Mutation**: A structural alteration of DNA that is hereditary and gives rise to an abnormal phenotype. A mutation is always a change in the DNA base sequence and includes substitutions, additions, rearrangements, or deletions of one or more nucleotide bases.
- **Adduct**: The covalent linkage or addiction product between an alkylating agent and cellular macromolecules such as protein, RNA, and DNA.
- **Alkylating agent**: A chemical compound that has positively charged (electrondeficient) groups that can form covalent linkages with negatively charged portions of biological molecules such as DNA. The covalent linkage is referred to as an adduct and may have mutagenic or carcinogenic effects on the organism. The alkyl species is the radical that results when an aliphatic hydrocarbon loses one hydrogen atom to become electron-deficient. Alkylating

agents react primarily with guanine, adding their alkyl group to N7 of the purine ring.

- **Occupational exposure limit (OEL)**: A generic term denoting a variety of values and standards, generally time-weighted average concentrations of airborne substances, to which a worker can be safely exposed during defined work periods (Deleranko, 2008).

- **Cell cycle checkpoints**: refer to mechanisms that monitor cell cycle progression and prevent premature entry into the next phase of the cell cycle. In general, activation of cell cycle checkpoints leads to the arrest of cell cycle progression in the presence of damaged DNA. If repair is successful, cell cycle proceeds. In cases where the repair fails, the cell undergoes apoptosis or becomes tumorigenic (cancer) (Encyclopedic Reference of Genomics and Proteomics in Molecular Medicine, 2006).

List of Figures

Figure 1	Causal pathway from initiation to the occurrence of disease	Page 3
Figure 2	Biomarkers of risk assessment	Page 5
Figure 3	Mechanism of action of DNA and non DNA interacting genotoxicants	Page 11
Figure 4	Visualization of sister chromatid exchanges	Page 33
Figure 5	Micronucleus formation	Page 38
Figure 6	The various possible fates of cultured cytokinesis blocked cells following exposure to cytotoxic and/or genotoxic agent	Page 42
Figure 7	Examples of comets from human lymphocytes	Page 47
Figure 8	The range of applications of the comet assay	Page 49
Figure 9	Bar chart for comparison of SCE frequency between exposed & non-exposed	Page 59
Figure 10	Bar chart for comparison of MN frequency between exposed & non-exposed	Page 60
Figure 11	Scatter plot showing the proportionate correlation between age & SCE frequency	Page 61
Figure 12	Scatter plot showing the proportionate correlation between age & MN%	Page 62
Figure 13	Scatter plot showing the proportionate correlation between duration of exposure & SCE frequency	Page 62
Figure 14	Scatter plot showing the proportionate correlation between duration of exposure & MN%	Page 63
Figure 15	Scatter plot showing the proportionate correlation between SCE frequency & MN%	Page 63
Figure 16	Bar chart for Comparison of SCE frequency regarding age groups within exposed group only	Page 65

Figure 17	Bar chart for Comparison of MN regarding age groups within exposed group only	Page 66
Figure 18	Comparison of SCE frequency regarding duration of work within exposed group only	Page 67
Figure 19	Comparison of MN regarding duration of work within exposed group only	Page 68
Figure 20	Bar chart for comparison of tail length between exposed & non-exposed	Page 72
Figure 21	Bar chart for comparison of tail moment between exposed & non-exposed	Page 73
Figure 22	Scatter plot showing the proportionate correlation between tail length & duration of work	Page 74
Figure 23	Scatter plot showing the proportionate correlation between tail moment & duration of work	Page 75
Figure 24	Scatter plot showing the proportionate correlation between tail length & tail moment	Page 75
Figure 25	Bar chart for comparison of tail length regarding age groups within exposed group only	Page 77
Figure 26	Bar chart for comparison of tail moment regarding age groups within exposed group only	Page 78
Figure 27	Bar chart for comparison of tail length regarding duration of exposure within exposed group only	Page 80
Figure 28	Bar chart for comparison of tail moment regarding duration of exposure within exposed group only	Page 80

List of tables

Table 1	Examples of biomarkers of exposure to mutagenic agents in human populations.	Page 6
Table 2	Examples of biomarkers of early biological effects from exposure to mutagenic agents in human populations.	Page 7
Table 3	Overview Of Some Genetic Toxicology Assays (Mammalian Assays)	Page 14
Table 4	Approaches to minimize occupational exposure to inhalational anesthetic agents	Page 25
Table 5	Biodegradation of volatile anesthetics in humans	Page 31
Table 6	Comparison between exposed & non exposed groups regarding demographic data	Page 57
Table 7	Comparison between exposed &non exposed groups regarding SCE frequency and MN %	Page 59
Table 8	Correlation of SCE frequency & MN with age & duration of work within exposed group only	Page 61
Table 9	Comparison of SCE frequency & MN regarding sex within exposed group only	Page 64
Table 10	Comparison of SCE frequency & MN regarding age groups within exposed group only	Page 65
Table 11	Comparison of SCE frequency & MN regarding smoking within exposed group only	Page 66
Table 12	Comparison of SCE frequency & MN regarding duration of work within exposed group only	Page 67

Table 13	Comparison of SCE frequency regarding occupation within exposed group only	Page 68
Table 14	Comparison of MN% regarding occupation within exposed group only	Page 69
Table 15	Comparison between Exposed & Non-exposed groups demographic data	Page 70
Table 16	Comparison between exposed & non exposed groups regarding tail length and tail moment of the exposed and non exposed groups	Page 72
Table 17	Correlation of Tail length & moment with age & duration of work within exposed group only	Page 74
Table 18	Comparison of Tail length & moment regarding sex within exposed group only	Page 76
Table 19	Comparison of Tail length & moment regarding age groups within exposed group only	Page 77
Table 20	Comparison of Tail length & moment regarding smoking within exposed group only	Page79
Table 21	Comparison of Tail length & moment regarding duration of work within exposed group only	Page 79
Table 22	Comparison of Tail length regarding occupation within exposed group only	Page 81
Table 23	Comparison of Tail moment regarding occupation within exposed group only	Page 82

Introduction & Aim of Work

Anesthesia represents one of the most important medical advances in history, and nowadays, it can be widely considered safe, thanks to the discovery of new drugs and the development of modern technologies. Nevertheless, anesthetic practices still represent cause for concern regarding the consequences they produce (Schifilliti et al, 2011). During surgery under general anesthesia there is inevitable pollution of the theater by vapors of wasted anesthetic gases. It is found that the highest concentration around the anesthesia machine is maximum at the area for anesthesia staff then less at the area for surgeons and scrub nurses (Aldrieny et al, 2013).

The question of whether or not exposure to anesthetics is associated with health risks and genotoxic effects for patients or clinical staff has been the subject of continuing debate (Schifilliti et al, 2011). The potential genotoxicity of anesthetic gases have also been investigated in patients before and after anesthesia and have yielded conflicting results (Chandrasekhar et al, 2006).

A survey of literature on the genotoxicity resulting from the exposure of health professionals to waste anesthetic gases revealed scanty studies from the Egyptian hospitals (Aldrieny et al, 2013).

Data from one study in one particular occupational setting cannot be used to judge the genetic risk in another occupational setting. This justifies this study (and other studies as well), despite the availability in the literature of investigations of this kind (but on different populations, with different exposures) (Chandrasekhar et al, 2006).

The Aim of the present work:

To assess the genetic damage in OR personnel exposed to waste anesthetic gases during their work in one of the major Egyptian hospitals.