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AN OVERVIEW ON THE POTENTIAL HEALTH HAZARDS OF FORMALIN

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ABSTRACT

Formaldehyde is a colourless gaseous material which mixed with water in varying proportions gives formalin. Formalin is used predominantly in histopathological laboratories for fixation of tissues and its one of the most commonly used fixative. However formalin vapours are hazardous and when they exceeding the permissive levels which have been proposed have an effect on various systems of the body. It is classified as a carcinogen and associated with cancers of the nasopharyngeal system by the US EPA and World health organization. Although the dermal exposure is of concern the dominant exposure is from the ambient and indoor air. It is imperative to know the effects of formaldehyde so that the involved personnel can handle with hair and minimize the risk of formalin exposure and thereby reduce the health hazards. This review focuses on the effect of formalin on all the systems of the body and its management.

KEYWORDS: **Formalin, hazard, cancer, exposure, fixation.**

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INTRODUCTION

Formalin is one of the most common chemical agents employed in fixation of tissues in routine histopathological techniques. It was first discovered by a British Chemist August Wilheld Von Holfmann[1]. Formalin is a mixture of formaldehyde in soluble water and it is a colourless liquid which liberates formaldehyde vapours. It is a simple aldehyde which is obtained from its cyclic trimer trioxane and the polymer paraformaldehye[2]. It is widely used in medical field and histopathological laboratories in primary fixation of the tissues[2]. The low cost of the chemical makes it the most common fixative for microscopy and histological techniques. Formalin is a source of irritant and the primary mode of exposure is through inhalation and to a lesser extent through the skin[2]. This literature reviews have shown various effects the health in various aspects and also reports on dermatitis and asthma[3, 4]. Formaldehyde also affects various systems of the body and hence it is essential to document the physiologic changes which are induced. In view of its use in laboratories, its toxicity and volatility, the exposure of formaldehyde has a significant role in human health[5, 6]. Formaldehyde is classified by the U.S. EPA as a probable human carcinogen, and as carcinogenic by the World Health Organization[7]. Hence it is essential to understand the effects of this hazardous chemical in health and to know the suggestible permissible levels of the formaldehyde. The review also highlights the various modes of reducing the formalin exposure and thereby the risks.

Permissive levels of exposure

Formaldehyde exposure is large doses or chronic exposure of lower dose is detrimental to the health. The permissible level of formaldehyde to occupational exposure is about 3ppm in a time weight average breathing zone during an 8 hour period. A ceiling concentration of 5ppm and a maximum peak of 10ppm are also acceptable for no longer than 30 minutes during a one day shift. The toxic potential of this can be reduced with minimal quantities of sodium tetraborate to increase the pH to 7.2 and to make it alkaline. Increased levels of exposure could result in mutagenic and carcinogenic potential. The American Conference of Government Industrial Hygienist (ACGIH) has established a higher limit of 300 ppb for occupational exposure (Threshold limit value)[8]. The International Agency for Research on Cancer (IARC) classified formaldehyde as group 1 known human carcinogen in June 2004[9].

Elimination of formalin from the system

The formaldehyde is quickly broken down in the body and almost every tissue is capable of breaking down the formalin. It gets converted to a chemical called formate, which is nontoxic in nature. This is usually excreted in urine and eliminated from the body. It is also converted to carbon-dioxide and removed from the body. Retention of formaldehyde vapours in the systems can be toxic, allergenic and carcinogenic[9].

Effect of formalin on respiratory tract

The most important effect of formalin on the respiratory system is unpleasant smell[10]. Acute effects of formalin adversely effect the pulmonary system decreasing the vital capacity and other pulmonary system. This is usually attributed to the bronchoconstriction produced by formalin[11]. Constant inhalation of formalin vapours causes shortness of breath, congested breath, irritation of the upper pulmonary tract and compromised pulmonary function[12]. Inhalation of vapours in large doses or chronic inhalation in low doses results in irritation of lower respiratory tract and has posed risks of cancer particularly the upper respiratory tract. It has also been a probable cause of nasopharyngeal carcinomas[13, 14, 15].

Effect of formalin on eyes

The second most common effect of formalin on eyes is the redness of eyes with excessive lacrimation. A long term study in Belgium and India shows that chronic exposure leads to a poor vision later in life[10,16].

Effect of Formalin on central nervous system

Formalin causes deterioration of nervous system and the initial symptoms are unusual tiredness and dizziness. Formaldehyde also results in assimilation resulting in headache[10]. Patient often complains of prolonged sleeping time. Sometimes the patients also report itching or sore eyes and disturbed nocturnal sleep. A strong dose of formalin often results in syncope[12]. Long terms exposure affects the neurotransmitter system by increasing the serotonin and dopamine metabolites in the hypothalamus[17, 18].

Effect of formalin on skin

Contact with formalin causes eruption on the skin and sore skin with itching[10]. It has been known to produce an allergy, contact dermatitis, eczema, irritation and inflammation of the mucous membranes[19]. Animal experiments have shown that erythema and epidermal hyperplasia results due to chronic exposure of formaldehyde.

Effect of formalin on hematopietic system

Whether formalin has an effect on hematopoietc system is not very clear. However there have been few studies reported in literature which reports intravascular coagulopathy, alteration in red cell count and haemoglobin concentration[17]. A high dose of formalin also results in development of myeloid leukemia[20, 21, 22].

Effect of formalin on Gastrointestinal tract

Formaldehyde causes gastrointestinal disturbances and initial symptoms include nausea and gastric upset[10]. Formaldehyde has a considerable effect on liver of human beings. Congestion of hepatic parenchyma and increased levels of hepatic enzymes occurs resulting in hepatic damage. This is directly proportional to the levels of exposure of formaldehye[24,26,27].

Effect on renal system

Chronic exposure to formalin over a long period of time has shown alterations in the renal metabolism resulting in anuria and papillary necrosis resulting in renal failure.

Effect of formalin on immune system

Formaldehyde binds with endogeneous proteins present in the body and thereby elicit an immune response. Chronic exposure of formalin has been associated with immunological hypersensitivity. This is suggested by a rise in the circulating antibodies IgG and IgE to serum albumin. The formaldehyde-specific immunoglobulin IgE antibody production leads to alteration in the immune response as suggested by decrease in the proportion of T cells[28,29,30].

Formalin ingestion

Ingestion of formaldehyde in large quantities could be fatal. Toxic administration of formalin produces inflammatory lesions in the oropharynx, soft palate, pharynx, epiglottis, esophagus and stomach. Later it may result in loss of memory, seizures, altered behaviour and consciousness. This finally ends up in coma and death of the patient[12]. These are due to the contact of the irritant with the mucosa and due to the corrosive nature of the formaldehyde. They result in ulceration and necrosis of the tissues resulting in complications. Clinically, it is manifested in the form of abdominal cramps, vomiting, haematemesis, malena and altered gut motility[17, 18, 19]. This results in complete renal shutdown due to disruptions in the metabolism. Experiments on animals have shown renal papillary necrosis, polyuria and increased blood nitrogen[31].

Management

Formaldehyde being a hazardous chemical causes numerous health challenges and so handling of this chemical needs to be understood. Certain measures should be adopted to reduce the risk of this exposure. The use of protective equipments, laboratory coats, gloves and masks is essential to prevent the contact of formalin with the skin. It is also essential to have an effect ventilator system to get the toxic chemicals rid off the grossing zone. Reducing the concentration of the chemical, proper storage of the product and closing the lids after use reduces the risk of exposiure[32].Further, it is imperative that lung function tests, x –rays, allergy testing and

examination of eyes be done on a periodic basis. The concentration of formalin in air should also be monitored and being an inflammable material needs proper handling as any spill or contact with n ignitable material results in risk.

CONCLUSION

Formalin is a hazardous element employed in routine histopathology laboratories for tissue fixation. Knowledge on the hazards of the formalin enables the personnel's in the lab to be precautious thereby reducing the risk of their health hazards.

Conflict of Interest

Conflict of interest declared none

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REFERENCES

1. Dixit D, Role of standardized embalming fluid in reducing the toxic effects of formaldehyde. Indian J Forensic Med Toxicol, 2 :33-39, (2008)
2. Maibach H, Formaldehyde: Effects on animal and human skin. In: Gibson J, ed. Formaldehyde Toxicity. New York: Hemisphere Publishing. 166-74, (1983)
3. Hendrick DJ, Lane DJ, Occupational formalin asthma. Br J Ind Med, 34: 11-8, (1977)
4. Owen CM, Beck MH, Occupational allergic contact dermatitis from phenol-formaldehyde resins. Contact Dermatitis, 45:294-5,(2001)
5. Bardana EJ, Montanaro A. Formaldehyde: an analysis of its respiratory, cutaneous, and immunologic effects. Ann Allergy, 66:441–52,(1991)
6. Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2- ol, IARC Monographs on the Evaluation of Carcinogenic Risks to Humans 88, Lyon, France: International Agency for Research on Cancer, 2006. pp.39–325.
7. Smedje, G., D. Norback.. "Incidence of asthma diagnosis and self-reported allergy in relation to the school environment--a four-year follow-up study in schoolchildren." Int.J.Tuberc.Lung Dis. 5(11):1059-1066, (2011)
8. American Conference of Industrial Hygienists (ACGIH).Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices (TLVs ® and BEIs)..Agents Classified by the IARC Monographs, Volumes 1–100, (2010)
9. Toxicological profile for formaldehyde. Agency for toxic substance and disease registry. Public Health Service.1657, (1999)
10. Onyije FM, Avwioro OG. Excruciating effects of formaldehyde exposure to students in gross anatomy dissection laboratory. Int J Occupat Environ Med, 3:92-95, (2012)
11. Farah Khaliq, Praveen Tripathi. Acute effects of formalin on pulmonary functions in gross anatomy lanoratory. Indian J Physiol Pharmacol. 53 (1):93-96, (2009)
12. Wantke F, Focke M, Hemmer W, et al. Exposure to formaldehyde and phenol during an anatomy dissecting course: sensitizing potency of formaldehyde in medical students. Allergy, 55:84-7, (2000)
13. Blair A, Saracci R, Stewart P et al. Epidemiologic evidence on the relationship between formaldehy exposure and cancer. Scand J Work Environ Health. 16:381-393, (1990a)
14. Partanen T. Formaldehy exposure and respiratory cancer. A meta analysis of the epidemiologic evidence. Scand J Work Environ Health. 19:8-15, (1993)
15. Garry VF, Oatman L, Pleus R et al. Formaldehy in the home: Some environmental disease perspectives. MinnMed. 63:107-111, (1980)
16. Appelman LM, Wouterson RA, Zwart A et al. One year inhalation toxicity study of formaldehy in male rats with a damaged

or undamaged nasal mucosa. J Appl Toxixol.8: 85-90, (1988)
17. Burkhart KK, Kulig KW, MCMartin KE. Format levels following a formalin ingestion. Vet Hum Toxicol. 32: 135-137, (1990)
18. Eells JT, McMartin KE, Black K et al. Formaldehyed poisoning: Rapid metabolism to formic acid. JAMA. J Am Med Assoc. 246: 1237 – 1238, (1981)
19. Rahul Kumar, Rakesh KumarVerma, Rakesh Kumar Dixit, Navneet Kumar, Narendra Kumar, D.K.Katiyar. Embalmiing solutions and their adverse effects: An update. Asin J Pharm Hea Sciu. 3(2): 735-738, (2013)
20. Hauptmann M, Lubin JH, Stewart PA, Hayes RB, Blair A. Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries. J Natl Cancer Inst, 95 (21): 1615- 23,(2003)
21. Zhang L, Tang X, Rothman N, Vermeulen R, Ji Z, Shen M, e al. Occupational exposure to formaldehyde, hematotoxicity, and leukemia-specific chromosome changes in cultured myeloid progenitor cells. Cancer Epidemiol Biomarkers Prev 19(1): 80- 8, (2010)
22. Suruda A, Schulte P, Boeniger M, Hayes RB, Livingston GK, Steenland K, et al. Cytogenetic effects of formaldehyde exposure in students of mortuary science. Cancer Epidemiol Biomarkers Prev 2 (5): 453- 60, (1993)
23. S Cikmaz, T Kutoglu, M Kanter, R Mesut. Effect of formaldehy in halation in rat livers. A light and electron microscopi study. Toxicol Int Health. 26(2):113-119,(2010)
24. Freestone J, Bentley A. Case of formaldehyde poisoning. Br J Pharm Pract. 11:20-21, (1989)
25. Koppel C, Baudish H, Schneider V. Suicidal ingestion of formalin with fatal complications. Intensive care med. 16: 212-214, (1990)
26. S Cikmaz, T Kutoglu, M Kanter, R Mesut. Effect of formaldehy in halation in rat livers. A light and electron microscopi study. Toxicol Int Health, 26(2):113-119, (. 2010)
27. Koppel C, Baudish H, Schneider V. Suicidal ingestion of formalin with fatal complications. Intensive care med. 16: 212-214, (1990)
28. Thrasher JD, Wojdani A, Cheung G and Heuser G. Evidence for formaldehyde antibodies and altered cellular immunity in subjects exposed to formaldehyde in mobile homes. Arch Environ Health, 42(6):347–50, (1987)
29. Wantke, F.,. "Exposure to gaseous formaldehyde induces IgE-mediated sensitization to formaldehyde in school-children." Clin.Exp.Allergy 26(3):276-280. (1996)
30. Doi, S., "The prevalence of IgE sensitization to formaldehyde in asthmatic children." Allergy 58(7):668-671, (2003)
31. Rudzki E, Rebandel P, Grzywa Z. Patch tests with occupational contactants innurses, doctors and dentists. Contact Dermatitis.20: 247-259,(1989)
32. Carrier G, Bouchard M, Noisel N, Bonvalot Y, Fradet S. Impacts on lowering the permissible exposure values for formaldehy Health impact of an occupational exposure to formaldehy;. IRSST Report. RA 13-386. (2004)