Original research article

Effect of exposure to formaldehyde on the total erythrocyte and leucocyte counts of first year medical students

Dr. Dipak Kumar Dhar

Name of the Institute/college: Himalayan Institute of Medical Sciences

Corresponding author: Dr. Dipak Kumar Dhar

Abstract

Introduction: Exposure to formaldehyde occurs in a doctor's life in the phase of medical education and training during the first year, which is a form of occupational hazard as formaldehyde is a toxic substance and known to cause both acute and chronic effects. Adverse effects on blood and cellular level changes in various occupationally-exposed populations are widely reported in medical literature. The present study was therefore conducted to evaluate its effect on the total erythrocyte count and total leucocyte count of first year medical students.

Methods: A longitudinal, descriptive study was conducted with 80 randomly selected first year students. Their total erythrocyte count and total leucocyte count was recorded once at the beginning and once at the end of the academic year. Descriptive statistics and paired "t"-test were used for analysis. A p-value < 0.05 was considered statistically significant.

Results with conclusion: Decline was noted in both the parameters. It was more marked in total leucocyte count. The change in total erythrocyte count of female students was statistically significant. The decrease in total cell counts reflects its detrimental effect on cells of blood and also the process of haemopoiesis in a broader context.

Key words: total erythrocyte count, total leucocyte count, formaldehyde

Introduction

A doctor is exposed to various occupational hazards throughout his professional life. One of such instances is during the period of education and training in medical schools, when budding doctors are exposed to formaldehyde. It is commercially available as formalin and is used as a component of embalming fluids in anatomy. Chemically, formaldehyde (HCHO) is an aldehyde which is produced by the oxidation of methyl alcohol. At room temperature, it exists as a gas which has noxious and irritating properties and a strong pungent odour. Formalin is 37% aqueous solution of formaldehyde [1]. In the field of medical science, formalin is used for various purposes like disinfection and sterilization of instruments, preservation of biological specimens and embalming of cadavers.

A medical student learns about the basics of the body's anatomy by scrupulous dissection of cadavers. Instructors and students routinely handle the cadavers which are embalmed with the help of formalin. Therefore, there is a consistent exposure to formaldehyde in the gross anatomy dissection classes for the entire first year. Studies suggest that often the exposure rates are high [2,3]. Inhalation and skin contact serve as the portals of exposure.

Medical literature is replete with reports which suggest that formaldehyde can be toxic, allergenic and even carcinogenic [4, 5]. Apart from acute effects like symptoms of mucosal irritation, effects on lung functions [6,7] and skin [6] formaldehyde also has chronic effects on blood. The available research done on different communities who are regularly exposed to formaldehyde for a long-term like staff working in the anatomy department, healthcare professionals and workers employed otherwise, shows a declining tendency in the total counts of almost all cell-lineages of blood [8-14]. Some studies assessing the effect of

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chronic occupational exposure to formaldehyde have even suggested a likely role in causation lymphohaematopoietic malignancies, especially myeloid leukaemia in humans [5, 15-17] which are accompanied by changes in the total leucocyte and erythrocyte counts, apart from their characteristic changes.

Medical students are exposed to formaldehyde for the entire first year, which too is a considerable duration of time. However, studies assessing the effect of this exposure on total cell counts are scarce. The present study was intended to delve into this aspect. In the context of occupational exposure, the estimation of total erythrocyte and leucocyte counts would reflect its probable effect on haemopoiesis.

Aims & Objectives

The aim of the study was to assess the longitudinal effect of exposure to formaldehyde during gross anatomy dissection classes on the total erythrocyte count and total leucocyte count of first year medical students.

Materials and methods

A longitudinal, descriptive study was conducted in the Department of Physiology, Rohilkhand Medical College and Hospital among first year MBBS students in the academic year 2015-16. Approval was obtained from the Institutional Ethics Committee (vide document IEC/IRB No. IEC/27/2015). Students having no history of previous exposure to formalin by inhalational route or direct contact were considered as subjects. The exclusion criteria comprised of presence of any pre-existing haematological disorders like anaemia and leukaemia, any acute or chronic inflammatory state, residents of high altitude, diseases with an allergic component like bronchial asthma, etc all of which are known to affect the cell counts. Students those who were not willing to participate were also excluded from the study. Eighty (80) medical students (40 male and 40 female students) out of the total 150 students, who suitably fulfilled these criteria, were selected using simple random sampling technique. Informed consent was taken from every participant after explaining the nature of the study. The baseline total erythrocyte and leucocyte count was recorded at the initial part of the academic calendar when the students perform these experiments as part of their practical curriculum. Total erythrocyte count was recorded over six working days. An extra improved Neubauer's Chamber and cover slip were provided at the working tables of the selected students for the purpose of the study. RBC pipette was used to draw blood upto the 0.5 mark of the pipette followed by Hayem's fluid (diluting fluid). Dilution and charging were done as per standard procedure [18,19] and cells were counted under high-power objective of microscope. Similarly, over the next six working days total leucocyte count was recorded as per standard method [18,19]. WBC pipette and Turk's fluid were used for it and the cells were counted under low-power objective of microscope. The parameters were again recorded at the end of 10^{th} month. The baseline readings served as the control against which the follow-up values were compared. Descriptive statistics and suitable statistical tests like Paired 't' test were applied. A p-value < 0.05 was considered significant.

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Results

A decrease in both the total erythrocyte and total leucocyte counts was observed for all participants as shown in Table 1. In female students, the total erythrocyte count declined significantly after exposure (p= 0.043).

Table 1: Comparison of Total Erythrocyte and Leucocyte count of the students before and after exposure to formalin

Parameters	Baseline	After exposure	P-value
Comparison of variables of all participants			
Total Erythrocyte Count (Millions/µl of blood)	5.02 ± 0.42	4.99 ± 0.40	0.102
Total Leucocyte Count (Thousands/µl of blood)	7.85 ± 1.64	7.70 ± 1.51	0.070
Comparison of variables of male participants			
Total Erythrocyte Count (Millions /µl of blood)	5.33 ± 0.31	5.31 ± 0.24	0.663
Total Leucocyte Count (Thousands / µl of blood)	8.30 ± 1.60	8.23 ± 1.39	0.676
Comparison of variables of female participants			
Total Erythrocyte Count (Millions /µl of blood)	4.71 ± 0.27	4.66 ± 0.21	**0.043**
Total Leucocyte Count (Thousands / µl of blood)	7.40 ± 1.59	7.13 ± 1.42	0.057

The percentage of decrement in both the parameters was relatively more marked in the female students as shown in Figure 1. Leucocytes were more affected than erythrocytes.

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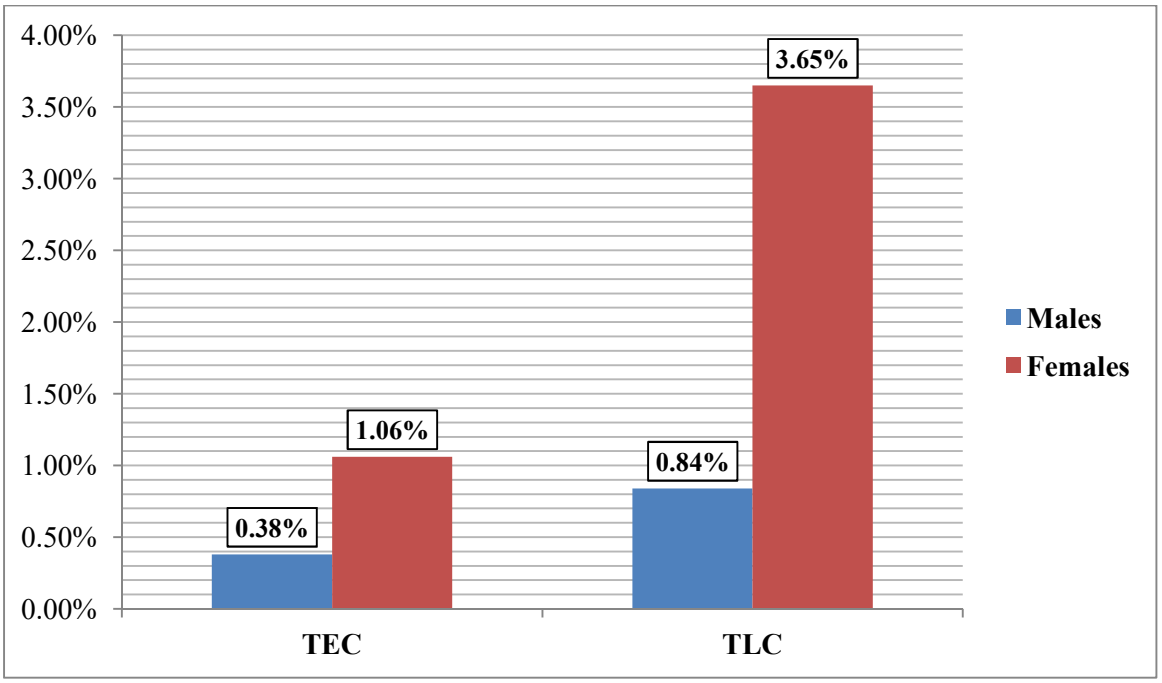
Figure 1: Percentage of decline in Total Erythrocyte and Leucocyte count of the students after exposure to formalin.



Discussion

The findings of the present study are in consonance with many similar reported effects of formaldehyde on total counts of blood cells. A decline in total erythrocyte count was also noted by Zhang L *et al* [8] and Elshaer and NSM *et al* [9]. With regard to total leucocyte count, decrease was also observed by Zhang L *et al* [8] and Kuo H *et al* [11]. The findings were further substantiated in animal models [20] and *in-vitro* cell cultures where CFU-GM progenitor cells were harvested from peripheral blood and their colony formation was studied. It was observed that colony formation fell by 20% [8]. Elshaer NSM *et al* [9] however documented both an increase and a decrease. In their study, 6.2% of the formalin-exposed subjects had abnormally low WBC count and 18.8% had abnormally high WBC count.

Decline in the total cell counts indicates a deleterious effect of formaldehyde either directly on the cells circulating in the blood or on the process of haemopoiesis in the bone-marrow, both of which will cause a reduction in the counts. A possible toxic effect on bone marrow has been suggested by Lyapina M *et al* [10]. However, it would be premature to make any striking conclusions from an exposure duration of ten months as in the present study. Notwithstanding this fact, the changes do provide insight regarding how formaldehyde reaches the bone marrow to exert its effect on haemopoiesis inspite of its rapid metabolism in the body. Chronic formaldehyde exposure is believed to be an important causative factor in genesis of lymphohaemopoietic malignancies, especially myeloid leukaemia in the occupationally exposed individuals [5, 15-17]. These disorders are commonly associated with variations in cell counts [21]. Formaldehyde has been associated with formation of DNA-protein cross-links, DNA single-strand breaks, chromosomal aberrations, sister chromatid exchange and gene mutation in human cells in numerous *in vitro* studies [6]. A small fraction of haemopoietic progenitor or stem cells in the peripheral blood exist in a dynamic equilibrium with their reserve in the bone-marrow [8, 22]. It has been proposed that formaldehyde produces cytogenetic damage in these cells or in pluripotent stem cells present in nasal turbinates and/or olfactory mucosa by mutagenic mechanisms discussed previously. These cells then migrate to the bone-marrow by blood and induce some changes in cell formation

[23]. Apart from this, one more model of damage has also been suggested. In an aqueous solution like blood, formaldehyde is converted mostly to its diol form, methanediol [formaldehyde hydrate, $CH_2(OH)_2$, or methylene glycol]. There exists a dynamic equilibrium between formaldehyde and methanediol. Methanediol has a low molecular weight of 48 which can therefore readily penetrate into tissues and therefore travel to the marrow by the blood. After reaching the marrow, the equilibrium might shift towards generation of formaldehyde. The produced formaldehyde can react with cellular macromolecules producing toxic injury on the progenitor cells [8, 23] thereby reducing the cell counts. Reactive oxygen species and free-radical mediated oxidative stress are also factors that contribute to the detrimental effects at the cellular level.

The scope of the study can be further extended if the concentration of formaldehyde in the ambient atmosphere can also be measured. This would help in quantifying the effect objectively.

Conclusion

Decrease in the total counts of cells of blood underlines the chronic effect of formaldehyde on haemopoiesis in a broader perspective. Formaldehyde is ubiquitous in the dissection hall and its contact cannot be avoided. But its effects can be minimized if we incorporate methods to reduce the exposure. Simple steps like use of personal protective devices (goggles, masks & gloves), use of specially engineered ventilation systems & dissection beds and prevention of unnecessary spillage of formalin within the dissection hall can be beneficial in this regard. Another option explored nowadays is making suitable changes in the conventional process of embalming by use of accessory chemicals or alternative embalming fluids. Chemicals like phenoxyethanol and phenoxetol have emerged to the fore in this regard.

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