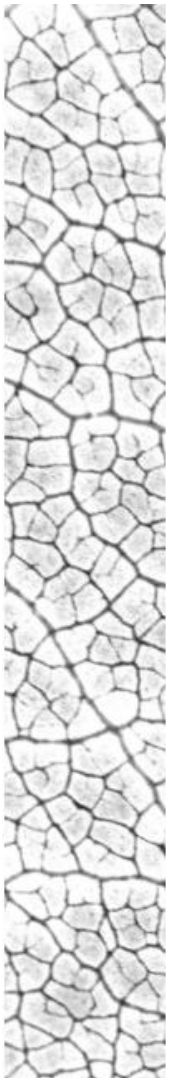

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Therapeutic effect of Vitamin A on severe COVID-19 patients

Mahmood M. Al-Sumiadai [1*], Hazim Ghazzay [2], Wisam Zabin Saleh Al-Dulaimy [3]

[1] DCH, Ministry of Health, Anbar Health Directorate, Ramadi City, IRAQ
[2] F.I.C.M.S, Internal Medicine, Department of Medicine, College of Medicine, University of Anbar, IRAQ
[3] CIB, Ministry of Health, Anbar Health Directorate, IRAQ
*Corresponding author: alsumaidaidrmah@gmail.com

Abstract
Objective: To find the effect of administration of vitamin A on patients with severe COVID-19.
Material and Methods: A cross-sectional and retrospective study was done on two groups of patients with severe COVID-19 in isolation centers in Anbar governorate. The first group was patients with severe COVID-19 given two doses of vitamin A (200,000 I.U.) for two days from the first day of admission and three doses per day of salbutamol and budesonide nebulizers.. Data about the respiratory rate and SPO2 were collected after 48 and 96 hours from the administration in addition to the death rate among those patients. In a second group, the data was collected from files of patients with severe COVID-19 previously admitted to isolated centers and not receiving vitamin A.
Results: A significant improvement in SPO2 and respiratory rate among severe COVID-19 patients given vitamin A as compared to those not given vitamin A. A lower death rate was recorded among severe COVID-19 patients who received vitamin A from those not received.
Conclusions; A great benefit of the using of vitamin A in patients with severe COVID-19. Adding vitamin A to the regime COVID-19 therapy is recommended.

Keywords: severe COVID-19, Vitamin A, therapeutic effect

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is defined as the disease that occurs from a type of viruses called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV), which was discovered firstly in Wuhan City, Hubei Province, China (CDC, 2019) It was initially reported to the World Health Organization (WHO) on December 31, 2019. On January 30, 2020, the WHO regards COVID-19 as an outbreak and a global health problem (WHO,2020; Ramzy et al.2020). On March 11, 2020, the WHO regards COVID-19 as a pandemic (WHO,2020).

Common manifestations of COVID-19 including fever, cough, fatigue, difficulty in breathing, and loss of smell and taste, The symptoms start from (1-14) days after exposure to the virus, Most patients have mild clinical features, but part of them develop acute respiratory distress syndrome (ARDS). ARDS can be precipitated by cytokine storms (Ye et al. 2020). multi-organ failure, septic shock, and blood clots. Patients are treated with supportive therapy, including replacement of fluid, oxygen therapy, and supporting other affected vital organs (Fisher and Heymann, 2020; Liu et al. 2020; Wang et al. 2020).

Vitamin A is one of the fat-soluble retinoids that include retinol, retinal, and retinyl esters Johnson et al. 2010; Ross, 2006; 2010). Vitamin A is important in the immune system of the body, vision, and cellular proliferation (WHO, 2005; Solomons et al. 2006; Johnson et al. 2010). The recommended dose in children over one year and in adults in patients with xerophthalmia (vitamin A deficiency) is (200,000 IU) giving for two days.(WHO, 2005).Toxicity in adults is uncommon in these doses, however; symptoms of acute toxicity if occur may include gastrointestinal discomfort, headaches, blurred vision, and vertigo (Olson, 1995).

Vitamin A plays an important role in enhancing the immune system, especially in T cell differentiation and proliferation (Mora et al. 2010; Ertesvag et al. 2002). Vitamin A induce the proliferation of T cells by an indirect mechanism through increasing of Interleukin-2 (Ertesvag et al 2002). Vitamin A, potentiate the differentiation of T cells (Mucida et al. 2007; Sun et al. 2007; Cabezas-Wallscheid et al. 2017).

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Hematopoietic stem cells are responsible for the production of all types of blood cells, including the immune cells. Dormant hematopoietic stem cells can self-renew, differentiate, and produce new blood cells as the body require. Vitamin A is essential for the regulation of hematopoietic stem cell dormancy (Cabezas-Wallscheid et al. 2017).

Vitamin A even plays a role in T cell homing to the intestine, affects dendritic cells, and increasing of IgA secretion, which is necessary for immune response in mucosal tissues (Ertesvag et al. 2002; Ross, 2012).

Vitamin A, also necessary in the morphological formation of the epithelium, epithelial keratinization, and functional maturation of epithelial cells which are regarded as the first-line defense against pathogen invasion (Fuchs and Green, 1980).

Aim of the study

This study was designed to show the therapeutic effect of vitamin A on patients with severe COVID 19.

MATERIALS AND METHODS

The study was done in isolation centers for severe COVID- 19 patients (respiratory rate > 30 breaths/min, or SpO2 < 90% on room air) (IMAI, 2020) in the Anbar governorate west of Iraq. Informed consent was taken from families after giving them a full explanation about the purpose of the study. Two groups of samples were taken in this study, and the patients were selected randomly from different genders, different age groups, and some of the patients were with chronic disorders in both groups.

1.First group, the data was collected from severe COVID-19 patients. Vitamin A (200,000 international unit) was given on the first day and the same dose repeated the next day added to the regime recommended from the ministry of health for COVID-19 management in isolation centers from the first day of admission. . Nebulized salbutamol and budesonide three doses per day also were added to the regime. The results which include SPO2 and respiratory rate levels were reported after 48 and 96 hours from the first dose of vitamin A.

2.Second group, the data was collected from files of previously admitted patients to isolation centers not taken vitamin A. Data collection includes respiratory rate and SPO2 level at the day of admission and after 48 and 96 hours from the regime, therapy recommended without vitamin A administration.

The death rate was recorded in both groups of patients.

Exclusion criteria;

a. Pregnant women.

b. patients with liver diseases.

Statistical analysis of the data was done by using the Statistical Package for Social Sciences (SPSS). The p-value was calculated after checking the Chi-squared test. P-value was regarded as significant if the of level <0.05.

Table 1. Mean SPO2 changes among the two groups

Variable	SPO2 on the first day	SPO2 after 48 hr	SPO2 after 96 hr
The first group with vitamin A administration	77.84	89.53	93.08
The second group without vitamin A administration	78.57	80.72	75.31

p-value < 0.05.significant

Table 2. Mean respiratory rate changes among the two groups

Variable	Mean respiratory rate on the first day	Mean respiratory rate after 48 hr	Mean respiratory rate after 96 hr
The first group with vitamin A administration	39.87	33.19	28.44
The second group without vitamin A administration	39.97	35.21	34.73

p-value < 0.05.significant

Table 3. The death rate among the two groups

Variable	Number of patients	Number of death
The first group with vitamin A administration	70	2 (2.86%)
The second group without vitamin A administration	70	14 (20%)

p-value < 0.05.significant

RESULTS

The total number of the first group of patients included in the cross-sectional study was (70) and they were given from the first day of admission two doses of vitamin A and nebulized salbutamol and budesonide three times per day. The total number of the second group of patients included in the retrospective study was (70) and that data was collected from the first day of admission and they were not given vitamin A.

Regarding SPO2 calculated from the first group of patients, the mean SPO2 was improved from (77.84) on the first day to (89.53) after 48 hours to(93.08) after 96 hours. While among the second group, the mean SPO2 recorded at admission was (78.57), and after48 hours was (80.72) and were (75.31) after 96 hours. As in **Table 1**.

Regarding mean respiratory rate changes, the mean respiratory rate improved among first group patients from (39.87) to (33.19) after 48 hours to (28.44) after 96 hours. While among the second group, the mean respiratory rate was (39.97) on the first day of admission and was (35.21) after 48 hours, and was (34.73) after 96 hours. As in **Table 2**.

Regarding the death rate among the two groups, there was two reported death (2.86%) among first group patients who were received vitamin A and nebulizers. While there was 14 reported death (20%) among the second group who was not received vitamin A. As in **Table 3**.

DISCUSSION

This study has followed another study in Anbar governorate about the role of vitamin A on the treatment of mild to moderate cases with COVID-19 patients and its prophylactic effect on contacts (Al-Sumiadai et al.2020). There are many uses of vitamin A in the treatment of infectious diseases including, tuberculosis (Alabama et al. 2017), Acquired Immune Deficiency Syndrome (AIDS)(Makinde et al. 2017), and childhood viral infections like measles, chickenpox, and infantile diarrhea (Chen et al. 2012).

In the present study, we compare the results of severe COVID-19 patients in isolation centers after adding vitamin A to newly admitted patients with another patient admitted previously not given vitamin A(data was collected from their files). There was a significant improvement in oxygen saturation (SPO2) after 48 and 96 hours among patients receiving vitamin A from those not receiving the vitamin. The improvement of respiratory rate was also significant among patients given vitamin A from those not given the vitamin.

Regarding the death rate in this study, there was a low recorded death rate among patients given vitamin A as compared to a high recorded death rate among those not given the vitamin.

The underlying mechanism of vitamin A in treating COVID-19, may due to its anti-inflammatory property that decreases the chance of occurrence of cytokine storm, enhancing the immunity of the body and by its repairing action on epithelial tissue it will maintain integrity and repair destroyed epithelium of respiratory system.

CONCLUSION

From the above results we conclude the following;

1. There was a significant improvement in SPO2 and respiratory rate among severe COVID-19 patients given vitamin A as compared with those not given the vitamin.

2. A lower reported death rate among severe patients receiving vitamin A.

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