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**ORIGINAL ARTICLE**

# Effect of Alfa-Tocopherol on Pain and Inflammation of Rats

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## Abstract

**Background:** Alfa-tocopherol (αT) is a naturally occurring lipid soluble anti-oxidant that protects our body from oxidative process. **Objective:** The purpose of the present study was to assess the effects of α-tocopherol on pain and inflammation in rats. **Methodology:** This prospective experimental study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh from January 2013 to December 2013. Ten (10) male Long Evans rats, weighing 180 to 250 grams, were collected from Bangladesh Institute of Research and Rehabilitation for Diabetic Endocrine and Metabolic Disorders (BIRDEM), Shahbag, Dhaka for this purpose. On the basis of vitamin, all the rats were divided into two (02) groups (5 rats in each group). Group A received normal saline and group B received α-tocopherol. All the groups received single dose and equal volume through intraperitoneal route. Just one hour after administrations, 5 rats of each group were subjected to formalin test followed by formalin induced paw edema test. **Results:** In early, inter and late phases, the frequencies of jerking was significantly lower in group B than that of group A. In the early and late phases of formalin test duration of flexing and licking was significantly ($p<0.05$) lower in group B than that of group. In this study, mean±SE of paw edema volume in group A (0.28 ± 0.02 ml) was higher than that of group B (0.20 ± 0.03) but the difference was not statistically significant ($p=0.070$**)**. Supplementation with single loading dose of α-tocopherol significantly ($p<0.05$) lowered the variables for nociceptive pain, central analgesic activity and inflammatory pain in comparison to normal saline treated group (control). Inflammations were also non-significantly reduced than those of control rats. **Conclusion:** From this study it may be concluded that, single loading dose of α-tocopherol have analgesic and anti-inflammatory effect. [*Journal of Current and Advance Medical Research 2018;5(1):15-18*]

**Keywords:** Pain; inflammation; α-tocopherol

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## Introduction

Pain is one of the main symptoms of many diseases, and can considerably interfere with a person's quality of life[1]. It is the most common symptom that causes people to seek out health care. It may vary in quality, intensity and duration. It has been classified into nociceptive, inflammatory, neuropathic and functional type by etiology[2]. Nociceptive pain is a vital physiologic sensation caused by stimulation of peripheral nerve fibers[3]. When something harmful or irritating affects a part of our body inflammation takes place to promote healing by removing the offending agent and it is usually accompanied by inflammatory pain.

Evans and Bishop[4] discovered vitamin E, a fat soluble vitamin and α-tocopherol is the most biologically active among its eight naturally available forms[5-7]. It is the major lipid soluble antioxidant found in human plasma, erythrocytes as well as tissues. It was suggested to perform various functions in human body including antioxidation[5] prevention of infertility, regulation of enzyme function[6] and also analgesic and anti-inflammatory effects[8-9]. Many studies showed analgesic and anti-inflammatory effects of α-tocopherol. Significant reduction of the nociceptive pain was found after supplementation of this vitamin in rats[10]. Very few data are available regarding the effect of α-tocopherol on pain and inflammation. Therefore this present study was undertaken to assess the effects of α-tocopherol on pain and inflammation in rats.

## Methodology

This prospective experimental study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, Bangladesh from January 2013 to December 2013 for a period of one (01) year. Ten (10) male Long Evans rats, weighing 180 to 250 grams were collected from Bangladesh Institute of Research and Rehabilitation for Diabetic Endocrine and Metabolic Disorders (BIRDEM), Dhaka for this purpose. On the basis of vitamin and drug administrations, all the rats were divided into two (2) groups (5 rats in each group). Group A received normal saline and group B received α-tocopherol. All the groups received single dose and equal volume through intraperitoneal route. Just one hour after administrations, 5 rats of each group were subjected to formalin test followed by formalin induced paw edema test. After the completion of experiments, all the rats were sacrificed immediately to decrease their sufferings. On the day of experiment the rat was administered by normal salaine or α-tocopherol intraperitonealy. One hour after administration, fifty (50) µl of dilute formalin (2.0%) was injected subcuteneously into the planter aspect of the rat's right hind paw. The pain behaviors (total frequency of jerking and total duration of flexing and licking) were observed for consecutive 60 minutes. Within this time the first 5 minutes (1st-5th) was considered as the early phase, middle 10 minutes (6th- 15th) as the interphase and last 45 minutes (16th-60th) as the late phase. Observation was made by counting the total frequency of jerking and total duration of flexing plus licking of the injected paw. Immediately after the completion of formalin test, the rat was sacrificed and both the hind paws were cut at their knee joints by a sharp scissor. Then the volume of both the paws was measured using a water plethysmometer. Paw volume=Height of water column after paw immersion-height of water column before paw immersion. Net edema volume=right paw volume-left paw volume. The results were expressed as mean±SE and the data were statistically analyzed by Independent Student test. In the interpretation of results p 0.05 was accepted, as the level of significant.

## Results

**Jerking in the formalin test:** The mean±SE of frequencies of jerking in the early phase of formalin test was 92.2 ± 4.42 frequency/5 minutes in group A and 78.6 ± 1.86 frequency/5 minutes in group B. In the inter phase of the formalin test it was 80.4 ± 1.53 frequency/5 minutes in group A and 69.8 ± 1.11 frequency/5 minutes in group B. In the late phase of formalin test mean±SE of frequencies of jerking was 729.00 ± 5.71 frequency/5 minutes in group A and 629.8 ± 3.96 frequency/5 minutes in group B. In all the phases frequencies of jerking was significantly lower in group B than that of group A.

**Table 1: Frequency of jerking at different phases of formalin test in different groups of rats (n=10)**

| Phases | Group A | Group B | P value |
|---|---|---|---|
| **Early** | 92.2±4.42 | 78.6 ±1.86 | 0.034 |
| **Inter** | 80.4±1.53 | 69.8±1.11 | 0.001 |
| **Late** | 729.00±5.71 | 629.8±3.96 | <0.001 |

Early phase=Frequency/5 min; Inter phase=6$^{th}$-15$^{th}$ min, Frequency/5 min; Late phase=16$^{th}$ - 60$^{th}$ min, Frequency/5 min

**Flexing and licking in formalin test:** The mean±SE of duration of flexing and licking in the early phase of formalin test was 262.6±5.16 seconds/5 minutes in group A and 233.4±3.53 seconds/5 minutes in group B. In the inter phase of

formalin test it was 330.6 ± 12.99 seconds/5 minutes in group A and 317.2 ± 3.94 seconds/5 minutes in group B. In the late of formalin test the mean±SE of duration of flexing and licking was 2547.6 ± 9.3 seconds/5 minutes in group A and 2280.8 ± 11.4 seconds/5 minutes in group B. In the early and late phases of formalin test duration of flexing and licking was significantly lower in group B than that of group.

**Table 2: Duration of Flexing and Licking at Different Phases of Formalin Test in Different Groups of Rats (n=10)**

| Phases | Group A | Group B | P value |
|---|---|---|---|
| **Early** | 262.6±5.16 | 233.4±3.53 | 0.002 |
| **Inter** | 330.6±12.99 | 317.2±3.94 | 0.372 |
| **Late** | 2547.6±9.3 | 2280.8±11.4 | <0.001 |

Early phase=Frequency/5 min; Inter phase=6$^{th}$-15$^{th}$ min, Frequency/5 min; Late phase=16$^{th}$ - 60$^{th}$ min, Frequency/5 min

**Paw edema volume:** In this study, mean±SE of paw edema volume in group A (0.28 ± 0.02 ml) was higher than that of group B (0.20 ± 0.03) but the difference was not statistically significant.

**Table 3: Formalin induced paw edema volume in different groups (n=10)**

| Groups | Paw edema volume | P value |
|---|---|---|
| **Group A** | 0.28 ± 0.02 | **0.070** |
| **Group B** | **0.20 ± 0.03** | |

## Discussion

Pain and inflammations are unpleasant sensations occurring as a consequence of injury, disease or emotional disorder. They cause discomfort which brings the patient to physician. In addition to the body's own mechanism, there are a variety of approaches for treating pain. However, traditional analgesics have many side effects. To minimize the use of these drugs, now a days different animal study have done to assess the effects of many vitamins on pain and inflammation[9-10].

The present study has been undertaken to assess the effects of αT on pain and inflammation. For this 10 male Long Evans rats were studied and the effects of supplementation of αT were observed on nociceptive pain, central analgesic activity, inflammatory pain and inflammation. The formalin test is a useful model for the screening of both the nociceptive and inflammatory pain[11]. This test shows an early phase, interphase and late phase.

The early phase reflecting direct activation of nociceptors, the interphase shows the activation of central analgesic system and the late phase reflecting inflammation[12]. To evaluate the effects of this vitamin on nociceptive pain, frequency of jerking and duration of flexing and licking in the early phase of formalin test were assessed. In addition, to evaluate their effects on central analgesic activity, frequency of jerking and duration of flexing and licking in the interphase of formalin test were assessed. Along with this, frequency of jerking and duration of flexing and licking in the late phase of formalin test were also assessed to evaluate the effects of αT on the inflammatory pain. In this study, intraperitoneal administration of vitamin significantly lowered the nociceptive pain as well as the inflammatory pain and the enhanced central analgesic activity in comparison to that of control. These findings were also in consistent with the findings of Chen et al[13], Hong et al[14] and Majagi et al[15].

Paw edema test is an accurate and simple method for measuring inflammation as well as screening of anti-inflammatory drug in animals[8]. In this study paw edema volume was low in α-tocopherol administered group comparing control. Similar observation was also reported by Majagi et al[15] and Tahan et al[9] in animal and by Devraj et al[16].

## Conclusion

From the results of this study it may be conclude that, single loading dose supplementation of α-tocopherol (αT) have analgesic and anti-inflammatory effects. This finding can be explore in the human study for better management of pain and inflammation.

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