

## Effect of Pentoxifylline on Correction of Anemia of Chronic Disease in Rheumatoid Arthritis

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### ABSTRACT

Rheumatoid arthritis is autoimmune disease prevalence. This study aimed to evaluate the effect of pentoxifylline on anemia of chronic disease in rheumatoid arthritis clinical trial study on 70 patients with rheumatoid arthritis and anemia in Zahedan in 2013 was Permutations of sample blocks were divided into two groups .Group receiving pentoxifylline and hemoglobin levels, iron profile and TNF $\alpha$  in the two groups were compared after 4 months. Data were analyzed using T-test Mean age of patients was 42.7 $\pm$  113.1 . Hemoglobin levels increased in both groups Of 0.6 mg / dl was Of mg / dl 0.6 was (P = 0.741) changes in serum ferritin, serum iron and SI / TIBC in the pentoxifylline group, -3.7 g $\pm$  63.4 / , 2.8 mg $\pm$  30.2 dL / dl in the placebo group and 1.0 2.6  $\pm$  60.3 / g per deciliter, 28.8  $\pm$  0.7 / micrograms per deciliter .

**KEYWORDS:** pentoxifylline, anemia of chronic disease, the effect

### INTRODUCTION

Anemia is a common blood diseases in industrialized countries the average prevalence of %18 and% 56 have been reported in developing countries. WHO defines anemia as a hemoglobin of less From 13mg / dl Drayman and less than12 mg / dl refers to the ladies. Anemia of chronic disease, anemia is Often in patients with infectious diseases, inflammatory or neoplastic seen for more than 1 or 2 months and is characterized reticuloendothelial iron in the presence of adequate supplies. The cause of this anemia is multi-factorial and include mild decrease in red blood cell lifespan, direct prohibition, relative erythropoietin deficiency and a reduced intake of iron transport. Review of the past decade, the role of inflammatory cytokines in each of these factors has proved The  $\gamma$ -IFN, TNF $\alpha$ , IL $_6$  is the most important cytokine. (RA or Rheumatoid Arthritis ) Is one of the most common autoimmune disease that affects about% 1 of the world population are 3 ptx chemicals called methylxanthines derivatives 1-(5-oxohexyl)-3, 7-dimethylxanthine The effects of endogenous xanthine oxidase inhibits xanthine oxidase.( Hammerman , 1999: 69-80)

cells through the formation of damaging free radicals . (Cross AR, 1991: 281-98)

PTX due to different biochemical properties and capillary blood flow and oxygenation Nts oxidant capable of improving tissue . (Hammerman , 1999: 69-80)

It also increases flexibility and reduces blood cells by preventing the formation of blood viscosity, fibrinogen and platelet aggregation is. (Noyan T, 2003; 21(1): 49-54)

in experimental models of pentoxifylline, production, TNF-alpha by monocytes and production gamma by T cells inhibits 8 and 7 Various studies the role of pentoxifylline in reducing these cytokines, particularly TNF $\alpha$  proven These studies can be John Marcus and colleagues at the University of Essen and the Ruhr German doctor in 1999, the Department of Immunology and Biotechnology, Department of Nephrology, Medical University of Lodz, Netherlands, Belgium in 1992 and in 2009, noted . (Schandene L, 1992:30-4) , (Taha H, 2009:3-12)

On the other hand, several studies on the effect of pentoxifylline in the treatment of anemia of chronic renal failure has been performed: including a study by the Department of Renal medicine at King's college Hospital London in 2004 and studied the Department of Nephrology, Ahvaz, in these studies the effect of pentoxifylline correction of anemia in CKD is ok, but so far no studies on the impact of chronic illnesses has been done. (Cooper A, 2004:1877-82)

However, although several studies on the effect of pentoxifylline in the treatment of anemia of chronic kidney disease have been done, but so far no studies on the impact of chronic illnesses has been done. (Cooper A, 2004:1877-82)

On the other hand pentoxifylline derivative and spent many years as a vasodilator in the treatment of disorders vessel is used, oral and easily absorbed, that is, without the dangerous side effects and long term problems due

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to the the role of cytokines known drug effective in reducing anemia of chronic disease, we examined the drug's effect in correcting anemia in patients with rheumatoid arthritis. (Maksymowych WP, 1995:625-9)

## METHOD

In this clinical trial is a research study population, the patients in the stable phase of the disease known as rheumatoid arthritis and anemia of chronic disease patients referred to the rheumatology clinic of Ali ibn Abi Talib (AS), which Zahedan in vitro evaluation of anemia it was rejected for other reasons , Due to the fact that so far no studies had been done in this area, we refer to it and The study patients were reviewed at a high trailclinical and did not hit the books, 35 In both cases and controls had. RA patients in the stable phase of the disease Randomly divided into two groups according to age and sex, so that they were relatively uniform Randomized block permutation in both intervention and control groups were placed .This study identified 70 patients with rheumatoid arthritis and anemia of chronic disease patients in stable phase involved Five people (%7/1 ) Man of sixty-five ( %92/9 ) Females, mean age By Company  $42/7 \pm 13/1$  Years .

### Gender of many patients

Comparison of Hb before and 4 months after receiving pentoxifylline , In the present study, the pre-intervention group, the mean hemoglobin mg / dl  $7/0 \pm 2/11$  and 4 months after receiving pentoxifylline mg / dl  $6/0 \pm 8/11$ , respectively. This difference was statistically significant. ( $0/25/0 = P$ )

Table 4-1. Hb compared before and 4 months after receiving pentoxifylline test Paired t-test

p-value	After intervention	Before intervention	
0/025	$0/09 \pm 11/8$	$\pm 11/2$	Hemoglobin Rate

### 2 - Comparison of mean hemoglobin before and 4 months after receiving placebo

In this study, the mean hemoglobin in the control group before the intervention mg / dl  $9/0 \pm 9/10$  and 4 months after receiving placebo mg / dl  $0/1 \pm 5/11$  respectively. This difference was also statistically significant. ( $0/0360 = P$ )

Table 4-2. Hb compared before and 4 months after receiving placebo tests using Paired t-test

p-value	After intervention	Before intervention	
0/036	$11/5 \pm 1/0$	$\pm 10/9$	Hemoglobin

### 3 - Comparison of Hb before and 4 months after the intervention group receiving pentoxifylline and placebo

The amount of hemoglobin in both groups, the rate of mg / dl  $0/6$ , which was not a statistically significant difference. ( $0/741 = P$ )

### 4- Comparison of Hb before and 4 months after the intervention group receiving pentoxifylline and placebo using the Independent t-test

p-value	Placebo	Pentoxifylline	
0/741	$0/6 \pm 1/0$	$0/6 \pm 0/7$	Theamountof hemoglobin

### 5 - Comparison of iron profile (including serum ferritin, serum iron and serum iron compared to TIBC) before and 4 months after receiving pentoxifylline

Ferritin levels before the intervention  $\mu\text{g} / \text{dl}$   $4/70 \pm 124$  and later  $\mu\text{g} / \text{dl}$   $5/56 \pm 5/120$ , serum iron levels before intervention  $\mu\text{g} / \text{dl}$   $1/31 \pm 9/78$  and the subsequent  $\mu\text{g} / \text{dl}$   $3/29 \pm 7/81$  and the ratio of serum iron to TIBC before the intervention,  $09/0 \pm 21/0$  and then  $0/1 \pm 23/0$ , which was not found any significant difference. ( $0/50 < P$ )

### 6 - Comparison of iron profile (including serum ferritin, serum iron and serum iron compared to TIBC) before and 4 months after receiving pentoxifylline test Paired t-test

p-value	After intervention	Before intervention	Iron profiles
0/121	$120/5 \pm 56/5$	$124/2 \pm 70/4$	Ferritin
0/156	$81/7 \pm 29/3$	$78/9 \pm 31/1$	Iron Serum
0/545	$0/23 \pm 1/0$	$0/21 \pm 0/09$	Ratio of iron to TIBC

### 7 - Comparison of iron profile (including serum ferritin, serum iron and serum iron compared to TIBC) before and 4 months after receiving placebo

Ferritin levels before the intervention  $\mu\text{g} / \text{dl}$   $6/59 \pm 119$  and later  $\mu\text{g} / \text{dl}$   $7/62 \pm 1/122$ , serum iron levels before intervention  $\mu\text{g} / \text{dl}$   $9/27 \pm 6/79$  and subsequent  $\mu\text{g} / \text{dl}$   $4/30 \pm 3/80$  and the ratio of serum iron to TIBC before intervention  $1/1 \pm 24/0$  and then  $09/0 \pm 22/0$ , which was not found any significant difference. ( $0/50 = P$ )

8- Comparison of the iron profile (including serum ferritin, serum iron and serum iron compared to TIBC) before and 4 months after receiving placebo tests using Paired t-test

p-value	After intervention	Before intervention	Iron profiles
0/231	122/1±62/7	119/5±59/6	Ferritin
0/493	80/3±30/4	79/6±27/9	Iron
0/274	0/22±0/09	0/24±1/1	Serum

9 - Comparison of mean Rail profile (including serum ferritin, serum iron and serum iron compared to TIBC) before and 4 months after the intervention group receiving pentoxifylline and placebo .

Changes in ferritin, serum iron and serum iron, TIBC than in the pentoxifylline group, respectively  $\mu\text{g} / \text{dl}$   $4/63 \pm 7/3$ -,  $\mu\text{g} / \text{dl}$   $2/30 \pm 8/2$  and  $0/1 \pm 02/0$  and in the placebo group, respectively  $\mu\text{g} / \text{dl}$   $3/60 \pm 6/2$ ,  $\mu\text{g}/\text{dl}$   $8/28 \pm 7/0$  and  $09/0 \pm 02/0$ , which was not statistically significantly different from each other. ( $0/50 = P$ )

10 - Comparison of the average profile of iron before and 4 months after the intervention group receiving pentoxifylline and placebo using the Independent t-test

p-value	Placebo	Pentoxifylline	Iron profiles
0/569	2/6±60/3	-3/7±63/4	Ferritin
0/211	0/7±28/8	2/8±30/2	Iron
0/854	0/02±0/09	0/02±1/0	Serum

11 - average compared to  $\text{TNF}\alpha$  before and 4 months after receiving pentoxifylline

$\text{TNF}\alpha$  levels in the groups before the intervention  $\text{pg} / \text{dl}$   $7/7 \pm 1/12$  and 4 months after receiving pentoxifylline  $\text{pg} / \text{dl}$   $6/3 \pm 3/4$  of which were statistically significant. ( $0/190 = P$ )

12 - average compared to  $\text{TNF}\alpha$  before and 4 months after receiving pentoxifylline test Paired t-test

p-value	After intervention	Before intervention	
0/019	4/3±3/6	12/1±7/7	Rate $\text{TNF}\alpha$

13 - Medium compare  $\text{TNF}\alpha$  before and 4 months after receiving placebo

$\text{TNF}\alpha$  levels in the control group before the intervention  $\text{pg} / \text{dl}$   $5/5 \pm 1/9$  and 4 months after receiving placebo  $\text{pg} / \text{dl}$   $1/10 \pm 5/12$ , which was not statistically significant. ( $0/128 = P$ )

Table 4-8. Compared to  $\text{TNF}\alpha$  before and 4 months after receiving placebo tests using Paired t-test

p-value	After intervention	Before intervention	
0/128	12/5±10/1	9/1±5/5	RATE $\text{TNF}\alpha$

14 - Medium compare  $\text{TNF}\alpha$  before and 4 months after the intervention group receiving pentoxifylline and placebo.

$\text{TNF}\alpha$  changes in the pentoxifylline group  $\text{pg} / \text{dl}$   $9/6 \pm 8/7$ - and placebo group  $\text{pg} / \text{dl}$   $8/8 \pm 4/3$ , which were statistically significant. ( $0/10 = P$ )

15 - Medium compare  $\text{TNF}\alpha$  before and 4 months after the intervention group receiving pentoxifylline and placebo using the Independent t-test

p-value	Placebo	Pentoxifylline	
0/01	3/4±8/8	-7/8±6/9	Rate $\text{TNF}\alpha$

In this study, the effect of pentoxifylline on correction of anemia of chronic disease, arthritis Rheumatoid investigation that the amount of hemoglobin, ferritin, serum iron and serum iron, TIBC ratio in both groups after After 4 months showed no difference. However, in the case of  $\text{TNF}\alpha$  significantly reduced. So far, no studies on the effect of pentoxifylline on anemia in rheumatoid arthritis, but few studies have been done on the effect of pentoxifylline in the treatment of anemia of chronic kidney disease has been carried out, including a study by the Department of Renal medicine King's college Hospital London in 2004 and studied the nephrology department of Ahwaz in 2005, the effect of pentoxifylline in correcting anemia in CKD approved. (Cooper A, 2004:1877-82)

The study of losartan and enalapril Ahvaz group receiving pentoxifylline pentoxifylline 400 mg daily, with a maximum possible dose and control group receiving losartan and enalapril were the maximum possible dose. Also Mortazavi et al in 2012 studied the effect of pentoxifylline on hemoglobin levels and the amount of erythropoietin on anemic patients undergoing peritoneal dialysis have been studied. In this study, 25 patients were randomly divided into two groups receiving pentoxifylline and control groups. Results of this study showed significant differences in Changes in hemoglobin and serum albumin levels Both groups showed Mortazavi concluded Anemic patients who received pentoxifylline Effect on hemoglobin levels in peritoneal dialysis No erythropoietin dose of 0 is consistent with our study. (Ferrari P, 2010:344-9)

However, some studies suggest that pentoxifylline is effective in increasing hemoglobin patients. Ferraresi and colleagues in 2010 in vitro study, hemoglobin levels were significantly increased in the pentoxifylline recipients. The study showed That pentoxifylline, interleukin-6 in the circulation decreases and increases hemoglobin. (Ferrari P, 2010:344-9)

Cooper & Associates in 2004 as a 6-month cohort study, increasing hemoglobin levels with concurrent use of rh-EPO showed pentoxifylline. The change of the second month beginning Were. The subjects before the study for at least 6 months with anemia, some of them were even forced to get blood . (Cooper A, 2004:1877-82)

Navarro and colleagues in a prospective study that was conducted in 1999, the hemoglobin level in patients with advanced kidney disease who are receiving rh-EPO-resistant anemia had been investigated. In this study, 7 of these patients were treated with pentoxifylline compared with control subjects. The results of this study, increasing hemoglobin levels in patients taking pentoxifylline showed. ( Navarro JF, 1999:121-5)

In a study by Johnson and colleagues conducted in Australia in 2008, a total of 110 patients with chronic kidney disease and anemia with a hemoglobin level less than 11 mg per deciliter were in the control group receiving pentoxifylline were compared. The results of this study, a significant increase in hemoglobin levels in patients receiving pentoxifylline showed that after 4 months. In addition, the rate of blood transfusion were significantly lower in patients than in controls. ( Johnson DW, 2008)

Nazemianpour and colleagues in a study in 2007 on patients with chronic kidney disease, the results indicate a significant increase in hemoglobin levels in patients taking pentoxifylline was. (Nazemian F, 2007:p 360)

In totally, the characterization of rheumatoid arthritis or other relevant factors, pentoxifylline failed to increase hemoglobin in patients with rheumatoid arthritis and anemia are Reform, although most studies on the impact of renal patients has been observed. Due to the lack of correction of anemia in patients can be Raised the probability that might be justified , Given that Rheumatoid arthritis is a chronic inflammatory condition and the presence of various cytokines in the pathogen, it has been suggested It is likely that these cytokines induced anemia Be patient while the patient is probably due Decreased appetite, not desirable gastrointestinal bleeding arises The correction of anemia in these patients is altered.

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