Intraperitoneal administration of dexpanthenol inhibits the decrease in the number of leydig and sertoli cells in the wistar strain of white rat (rattus norvegicus) test exposed to monosodium glutamate

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ABSTRACT

Introduction: Free radical accumulation that goes beyond the ability of the body's defense mechanism causes oxidative stress which is one of the causes of premature aging in the testicular organs. Dexpanthenol works by increasing the levels of intracellular coenzyme A, ATP and glutathione which play a role in the defense and repair of cells against oxidative and inflammatory stress. The purpose of this study was to prove that intraperitoneal administration of Dexpanthenol inhibited the decrease in the number of Leydig cells and Sertoli cells in the testes of Wistar rats (Rattus norvegicus) exposed to Monosodium glutamate (MSG).

Methods: This research is true experimental with post-test only control group design. 32 rats were divided into two groups with each group consisting of 16 rats. The first group was the Control Group (P1) which was given a placebo aquadest twice a week intraperitoneally. The second group was the treatment group (P2) which was given Dexpanthenol 1000 mg / kgBW twice a week intraperitoneally. All groups were given 4 g / kgBB of MSG mice every day with sonde. The experiment lasted 14 days and then testicular tissue was taken be evaluated and the number of Leydig cells and Sertolinya cells were counted.

Results: The Saphiro-Wilk test results showed that the data of the number of Leydig cells was not normally distributed (p <0.05) while the data of the Sertoli cell counts were normally distributed p> 0.05. Comparative analysis of Leydig cell counts was conducted using Mann-Whitney Test while comparative analysis of Sertoli cell numbers using Independent-T Test. The results of the analysis showed that there were significant differences in the mean number of Leydig cells and Sertoli cells between groups P1 and P2.

Conclusion: This study concluded that intraperitoneal administration of Dexpanthenol inhibits the decrease in the number of Leydig cells and Sertoli cells in the testis of Wistar strain white rats (Rattus norvegicus) exposed by Monosodium glutamate.

Keywords: Dexpanthenol, MSG, Leydig cell number, Sertoli cell number

INTRODUCTION

The aging process occurs accompanied by morphological changes and decreased function of all cells and organs in the body. Aging that is accelerated or referred to as premature aging can be caused by external factors such as unhealthy lifestyle and diet, wrong habits, environmental pollution, stress and poverty. Internal factors that could contribute include free radicals, hormonal processes, glycosylation, methylation, apoptosis, decreased immunity and genetic factors.1

Early aging due to free radicals is more common because humans are often exposed to free radicals such as air and water pollution, cigarette smoke, alcohol, certain drugs, cooking processes, industrial solvent, ozone, hyperoxia, ionizing radiation and heavy metal ions. Free radical accumulation that exceeds the body’s antioxidant defense system will cause oxidative stress which is damaging to cells and organs.2,3

One compound that can induce oxidative stress is Monosodium Glutamate (MSG) which is often added to the daily diet as flavoring4. MSG is toxic to various organ cells including testicular cells with oxidative damage mediated by an increase in lipid peroxide production which damages the membrane structure and functional integrity resulting in cellular necrosis accompanied by decreased levels of tissue antioxidants needed in the body’s antioxidant defense.5,6

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Intracellular antioxidants become the first defense line in fighting free radicals are reduced glutathione (GSH), but cellular GSH levels can decrease in conditions of oxidative stress. During this time GSH reduction was corrected by giving L-Cystein, N-Acetyl Cystein or Glutation ester but the level of safety was still not satisfactory. While GSH administration become problematic due to its short plasma half-life and not all body cells can uptake GSH in intravenous administration while oral administration is constrained by recipient's digestive ability and expensive costs.

Dexpanthenol (D-panthenol; pro vitamin B5) is an analog of pantothenic acid in alcohol which is converted to pantothenic acid in tissues. Pantothenic acid then changes to Co-A, which acts to increase ATP production. With an increase in ATP, GSH cell productions will also increase. Dexpanthenol absorption is faster than pantothenic acid, has extensive safety and has been shown to indirectly increase GSH cell levels in various organs.

The effect of Dexpanthenol in preventing the decrease in Leydig cells and Sertoli cells number in the testes of white rats (Rattus norvegicus) of Wistar strains exposed to MSG until now has never been reported. The purpose of this study was to prove that intraperitoneal administration of Dexpanthenol could inhibit the decrease in the number of Leydig cells and Sertoli cells in the testes of white rats (Rattus norvegicus) of Wistar strain exposed by MSG.

**METODS**

Monosodium Glutamate (MSG) used is pure MSG with the Ajinomoto trademark made a solution by diluting 40 g of MSG in 100 ml of aquadest.

Dexpanthenol is used in the form of a solution with the trademark Dexenol which contains 1000 mg of Dexpanthenol per 5 ml.

This research is true experimental with post-test only control group design. 32 rats were divided into Control Group (P1) and Treatment Group (P2) with each group consisting of 16 rats. All groups were given MSG 4 g / kg BW per day with sonde, Group P1 received 1 ml aquadest 1 ml 2x a week intraperitoneally and P2 was given Dexpanthenol 1000 mg / kg BW rat (1 ml) 2x a week intraperitoneally. The experiment lasted 14 days, and then testicular tissue was taken be evaluated and the number of Leydig cells and Sertoli cells were counted.

**RESULTS**

Testicular tissue damage due to MSG administration in this study showed in histological features of testis control group which showed interstitial vacuoles, disorganization of spermatogenic cells, reduced number of Leydig cells and Sertoli cells, release of germ cells from basal lamina, basal lamina became irregular and partly disintegrated (Figure 1). This evidence supports the results of previous studies. The histological features of testes after administration of Dexpanthenol 1000 mg / kgBB mice 2 times per week for 14 days were improved with a minimum vacuole in the interstitial tissue, better organization of spermatogenic cells, increased numbers of Leydig and Sertoli cells, reduced detached germ cells from basal lamina, and the basal lamina was more regular and intact than the control group (Figure 1).

Comparative analysis of Leydig cell number was conducted using Mann-Whitney Test while comparative analysis of Sertoli cell number was done using Independent-T Test as presented in Tables 1 and 2.

The results of the analysis showed that there were significant differences in the mean number of Leydig cells and Sertoli cells between the Control Group and the Treatment Group with p <0.05. The results can be seen more clearly through the histogram in Figure 2 and Figure 3.

The average number of Leydig P2 cells in Figure 2 is 43.6. It is more than the average number of Leydig cells in P1 which is 26.8. The average number of Sertoli cells in Figure 3 for P1 is 9.8 which are much smaller than P2 (20.9).

**DISCUSSION**

There are several theories regarding the mechanism of decrease number of Leydig cells and Sertoli cells due to oxidative stress induced by MSG, namely the local / direct effect due to chemical reactions with glutamate or indirectly due to an imbalance of the gonadotropin hormone.

As a precursor of coenzyme A (Co A), Dexpanthenol protects cells and all organs from peroxidative damage by increasing cell glutathione levels. After pantothenic acid / derivatives enter the body, with the help of pantothenic kinase, it will be converted to Co-A in mitochondria so that energy production and ATP synthesis would increase and induce cellular synthesis of glutathione. It can be said that Dexpanthenol plays a role in increasing Co
A, ATP and GSH levels which all play a major role in cellular defense and the repair system against oxidative and inflammatory stress.\textsuperscript{10,11} Cellular protective mechanisms (cytoprotective and membranoprotective) are believed to depend on Co A or occur through biochemical reactions involving Co A\textsuperscript{-} (acyl Co A) including increased cellular glutathione and maintenance of redox status.\textsuperscript{11,17}

The decrease in the number of Leydig and Sertoli cells in this study is inhibited by several of the mechanisms mentioned above which allow the establishment of Calcium homeostasis, decreased lipid peroxidation and maintained integrity of both cell and mitochondrial membranes. These conditions lead to oxidative balance which inhibits cell damage directly or indirectly by maintaining the Hypothalamo-pituitary-testis axis.

So the protective effect of Dexpanthenol is not related to its action as free radical scavenger but primarily as a precursor of Co A which facilitates various metabolic pathways such as glutathione biosynthesis which is one of the main systems of cell protection against oxidative stress.\textsuperscript{11}

**CONCLUSION**

This study concluded that intraperitoneal administration of Dexpanthenol inhibits the decrease in the number of Leydig cells and Sertoli cells in the testes of Wistar strain white rats (Rattus norvegicus) exposed by Monosodium glutamate.

Dexpanthenol supplementation in inhibiting the decrease in the number of Leydig and Sertoli cells related to MSG exposure is in accordance with the principles of Anti-aging Medicine that uses the latest medical science and technology for early detection, prevention, treatment and improvement to the original condition of dysfunction, disorders and diseases related to aging with the aim of prolonging life in a healthy state.

**REFERENCES**


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Figure 2. The Average Number of Leydig Cells After Treatment

Figure 3. The Average Number of Sertoli Cells After Treatment


