J Vet Clin Vol. 23, No. 1(Suppl.) May (2006)

Modulation by Melatonin of the Cardiotoxicand Antitumor Activities of Adriamycin

Jong-shu Kim[1], Jin-A Kim, Jin-young Lee, Hye-yun Kim, Na-eun Choi, Go-un Ju, Hae-ran Park, and Chung-hui Kim*

Department of Animal Science & Biotechnology,Jinju National University,
[1]Department of Veterinary Medicine, Gyeong Sang National University

Introduction: Melatonin is produced and secreted by the pineal gland in almost all species of animal and is best known for its ability to modulate circadian rhythms. There are numerous reports dealing with the effects of melatonin, such as the inhibition of cancer growth, stimulation of the immune system, and oxygen free radical scavenging. In this study, we investigated whether melatonin could attenuate adriamycin-induced cardiotoxicity in rats both in vivo and in vitro. We examined adriamycin-induced cardiotoxicity using various criteria, such as mortality, body-weight loss, hemodynamic dysfunction, morphologic alterations, nuclear DNA fragmentation as a measure of DNA damage, the level of malondialdehyde (MDA) as an index of lipid peroxidation, and lactate dehydrogenase (LDH) release and the level of serum creatine kinase as indices of irreversible cell damage. We also investigated whether the protective effects of melatonin are mediated by alterations in the above criteria. In addition, it was of interest to examine the effects of melatonin on the antitumor effects of adriamycin.

Materials and methods: Male Sprague-Dawley rats were used in these experiments. The mortality rate for adriamycin was studied after the administration of melatonin. For the measurement of LDH release, the heart slices were centrifuged at 1000 rpm for 5 minutes. A clonogenic assay was used to measure the ability of cells to form colonies. The following groups of rats were used to evaluate the ultrastructural alterations to the heart that resulted from adriamycin treatment.

Results: Melatonin treatment in the concentration range of 0.1-2.5 mM inhibited the growth of human breast cancer cells. In terms of oncolytic activity, the combination of adriamycin and melatonin improved the antitumor activity of adriamycin, as indicated by an increase in the number of long-term survivors as well as decreases in body-weight losses resulting from adriamycin treatment.

Clinical relevance: The results of the present study demonstrate that melatonin protects against adriamycin-induced lethality, lipid peroxidation, severe cell damage, morphologic changes, and DNA damage in rat heart and that it also inhibits the growth of the human cancer cells. These findings support the results of clinical trials that suggest the use of melatonin to prevent adriamycin-induced cardiotoxicity and to enhance the antitumor activity of adriamycin.

*Corresponding author: kimch@jinju.ac.kr