Melatonin; An Established Radioprotective Agent Against Japan's Nuclear Disaster

[Melatonin; Japon Nükleer Felaketine Karşı Etkin Bir Radyasyondan Koruyucu Ajan]

ABSTRACT
In spite of its widespread use and the well known potential hazards associated with exposure to ionizing radiation, countries are poorly ill-equipped to protect their citizens in case of a fallout as seen in northeastern region of Japan. In case of nuclear fallout, there is no practical way to save people from the hazardous effects of ionizing radiation. Health authorities may provide potassium iodide for people to prevent thyroid cancer. Another preventive attempt would be using amifostine, a well known agent with radioprotective features. Melatonin (N-acetyl-5-methoxytryptamine) is a pineal product which is also known to have robust radioprotective features. Both human and experimental animal studies have clearly shown that it is a unique antioxidant and a DNA and chromosome protector against a variety of harmful agents including ionizing radiation.

ÖZET
Yaygın kullanımına ve iyonizan radyasyona maruziyetin iyi bilinen potansiyel tehlikelerine rağmen ülkeler, Japonya'nın kuzeydoğusunda görüldüğü gibi nükleer patlamaya bağlı salınım durumunda kendi vatandaşlarını korumak için çaresiz bir şekilde kötü donanıma sahiptirler. Nükleer patlamaya bağlı salınım durumunda insanları iyonizan radyasyonun tehlikeli etkilerinden koruyacak pratik bir yol yoktur. Sağlık otoriteleri tiroid kanserlerini önlemek için insanlara potasyum iyodür dağıtabilirler. Bir diğer koruyucu girişim radyoprotektif özellikleri ile tanınan amifostin kullanımı olabilir. Melatonin (N-asetil-5-metoksi triptamin) pineal bezden salınan, güçlü radyoprotektif özellikleri bilinen bir üründür. Melatoninin benzersiz bir antioksidan olduğu ve iyonizan radyasyonu da içeren bir çok tehlikeli ajana karşı DNA ve kromozom koruyucusu olduğu hem insan hem hayvan deneylerinde açıkça gösterilmiştir.

Ahmet Korkmaz
Dun-Xian Tan
Russel J Reiter

Dept. of Cellular and Structural Biology, The University of Texas Health Science Center at San Antonio, San Antonio, TX.

Key Words:
Melatonin, Ionizing Radiation, Protection.

Anahtar Kelimeler:
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Sorumlu yazar/ Corresponding author:
Ahmet Korkmaz
Dept. of Cellular and Structural Biology, The University of Texas Health Science Center at San Antonio, San Antonio, TX, USA.
fizyocan@gmail.com

The use of radiation has become an essential component of modern life, particularly in energy production, and has widespread applications for industrial, military and medical use. In spite of its widespread use and the well known potential hazards associated with exposure to ionizing radiation, countries are poorly ill-equipped to protect their citizens in case of a fallout as seen in northeastern region of Japan. It has been long known that ionizing radiation is a strong DNA damaging agent and carcinogen (1). It is worth emphasizing that both beneficial (e.g., cancer treatment) and harmful effects of ionizing radiation involve the similar mechanism; it readily damages DNA.

In case of nuclear fallout, there is no practical way to save people from the hazardous effects of ionizing radiation. Like in Japan, the government may provide potassium iodide for people who live around Fukushima to prevent thyroid cancer. However, ionizing radiation affects the whole body and causes DNA damage in every cell. Therefore, this preventive attempt is far from optimal to protect individuals, especially those less than 20 years of age, who are more prone to be influenced by ionizing radiation (2).

Another preventive attempt would be using amifostine, a well known agent with radioprotective features (3); however, it can be only administered intravenously (4) and is not suitable in case of large scale exposure and/or if the exposure persists at low levels for a prolonged period. Amifostine was developed by the Antiradiation Drug Development Program of the US Army Medical Research and Development Command as a radioprotective compound and approved for clinical use in the protection of dose limiting normal tissues in patients against the damaging effects of radiation and chemotherapy (5). It is expensive, not self-administrable and not suitable for prolonged use. Therefore, what is urgently needed a more feasible, relatively inexpensive, widely available drugs with negligible or no side effects to overcome such an

enormous exposure occurring in Japan and possibly in neighboring countries.

Melatonin (N-acetyl-5-methoxytryptamine) is a pineal product which is also known to have robust radioprotective features. Both human (6-8) and experimental animal studies (9-11) have clearly shown that it is a unique antioxidant and a DNA (12) and chromosome protector (13) against a variety of harmful agents including ionizing radiation (14). It was also proven that melatonin is a more efficient protector than amifostine (15) and another antioxidant, octreotide (16). Furthermore, in the human body, melatonin is not exclusively produced by pineal gland; every single cell with DNA may produce melatonin in small amounts basically to protect themselves from the harmful effects of free radicals (17). Ionizing radiation generates free radicals and also directly hit DNA. By all means, melatonin is an established radioprotector (18).

Melatonin is an amphipathic molecule and can readily enter all cells. There is no known biological barrier for melatonin including the blood-brain barrier or cell and nuclear membranes. After oral administration, melatonin rapidly passes into blood stream as well as into the cerebrospinal fluid (19), bile (20), seminal, amniotic and ovarian follicular fluid (21). Melatonin has been administered in both physiological and pharmacological amounts to humans and animals, and there is widespread agreement that it is a non-toxic and non-teratogenic molecule (22). In pregnant rats, the maternal lowest no observed effect level was found to be 200 mg/kg/day while the developmental no observed adverse effect level was 200 mg/kg/day (23). Melatonin is easily synthesized in pharmacologically pure form, is inexpensive and affordable and it also has a very long shelf life. It can be used virtually by all individuals at every age and for prolonged period (24).

Fortunately, scientists from Brookhaven National Laboratory (New York, USA), one of the leading centers for radiation biology, very recently documented that melatonin is an excellent candidate as a countermeasure against radiation exposure (25). In the current situation in Japan and possibly in the neighboring, melatonin seems to be the most feasible agent to reduce the risk of cancer and several other health problems which will be seen in decades and even in subsequent generations.

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