CLINICAL STUDY

Antioxidants Taken Orally prior to Diagnostic Radiation Exposure Can Prevent DNA Injury

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ABSTRACT

Purpose: To evaluate efficacy of oral antioxidant treatment given to patients before radiologic procedures in reducing x-ray-induced DNA damage.

Materials and Methods: In a single-center prospective controlled trial, antioxidant treatment with 2 g ascorbate, 1.2 g *N*-acetylcysteine, 600 mg lipoic acid, and 30 mg beta carotene was given to 5 consecutive participants before undergoing clinically indicated technetium-99m methylene diphosphonate (^{99m}Tc MDP) bone scans for cancer staging. These participants were compared with 5 participants without antioxidant treatment. DNA damage was visualized in peripheral blood mononuclear cells (PBMCs) before and after bone scans using three-dimensional microscopy and fluorescently labeled gamma-H2AX protein. Wilcoxon rank sum test was used to determine whether there was a statistically significant difference in the radiation received between the control and antioxidant groups, the number of foci/cell before and after bone scan within groups, and foci/cell after bone scan between groups.

Results: There was a significantly higher number of gamma-H2AX foci/cell after ionization radiation in the control group compared with the antioxidant group ($P = .009$). There was no statistically significant difference in number of gamma-H2AX foci/cell before or after exposure in the antioxidant group; the number of gamma-H2AX foci/cell was statistically significantly higher ($P = .009$) in the control group after exposure to ^{99m}Tc MDP.

Conclusions: In patients undergoing ^{99m}Tc MDP bone scans, treatment with oral antioxidants before scanning significantly prevented DNA damage in PBMCs. Antioxidants may provide an effective means to protect patients and health care professionals from radiation-induced DNA damage during imaging studies.

ABBREVIATIONS

DSB = double-strand break, FCS = fetal calf serum, IQR = interquartile range, NAC = *N*-acetylcysteine, PBMC = peripheral blood mononuclear cell, PBS = phosphate-buffered saline, ^{99m}Tc MDP = technetium-99m methylene diphosphonate

The oncogenic effect of ionizing radiation is clearly established and is understood to occur as a result of improper DNA repair processes with resultant molecular changes in the DNA, such as single-strand and double-strand breaks (DSBs), cross-links, and sugar/ribose alterations (1). Although the direct link between modern diagnostic radiation exposure and increased cancer incidence has not been proven, the oncogenic risk of radiation-based imaging modalities is widely postulated and has been calculated (2,3). For every 10-mSv of low-dose ionizing radiation, there is a 3% increase in age-adjusted and sex-adjusted cancer over a mean follow-up period of 5 years (3).

The oncogenic potential of these imaging modalities is of concern to medical imaging professionals, specifically interventional radiologists, interventional cardiologists, endovascular surgeons, and nursing and technologist colleagues, who are directly exposed on a daily basis. Despite risk reduction strategies, the peer-reviewed literature has shown an increased risk of cataracts, left-sided brain tumors, and radiation fibrosis in the

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clinician's hands. A 2013 case study identified 31 cases of brain cancer in interventionalists, including glioblastoma multiforme, meningioma, and astrocytoma (4). These specific tumors are known for their potential to be radiation-induced (5) and showed an 85% left-sided dominance, thought to be secondary to the more direct radiation exposure to this area during interventional procedures (6). These studies have shown that the left side of the interventionalist's head receives a dose 17 times greater than the right side of the head. Furthermore, an observational study performed on technologists working with radiation showed a 2-fold increased risk of brain cancer mortality and mild elevations in the incidence of melanoma and breast cancer compared with technologists never exposed to radiation (7).

Current risk reduction strategies involve dose reduction, minimizing unnecessary testing, shielding, and protection from scatter; however, the oncogenic potential of ionizing radiation from common medical imaging modalities persists. Antioxidant-based radioprotection has been proposed and tested in vitro and in vivo/in vitro with bench top cell irradiators (8,9). Antioxidants exert their effect by scavenging hazardous free radicals that are created by the interaction between ionizing radiation and water molecules before the free radicals can interact with, and damage, DNA (10). An oral antioxidant medication administered before exposure may reduce the degree of DNA damage in patients undergoing these procedures. Oral antioxidant treatment may also be of benefit to medical professionals exposed to radiation and DNA damage, including interventionalists and their teams exposed to radiation and DNA damage every day. There are 2 potential approaches: medication before imaging for protection and upregulation of repair after exposure to bolster repair of damaged DNA. We presented our in vivo/in vitro work at the 2011 annual scientific meeting of the Society of Interventional Radiology (11). This study reports the impact of antioxidant treatment before radiation exposure performed completely in vivo in humans.

MATERIALS AND METHODS

Participants

Approval from the University Health Network Institutional Review Board was obtained, and patients were enrolled into the study after providing informed consent. Ten patients undergoing technetium-99m methylene diphosphonate (^{99m}Tc MDP) bone scans met inclusion criteria and were consecutively enrolled. All participants were men with an average age of 67 years (range, 40–82 y). Of 10 patients, 7 had bone scans for staging of prostate cancer, and 3 had bone scans for staging of pancreatic and lung cancer and for musculoskeletal pain (**Table 1**). Patients were excluded if they received radiotherapy or chemotherapy in the past 6 months, if they underwent imaging using ionizing radiation in the previous week, or if they consumed nutraceuticals used in the experimental therapy on the same day or before participation. ^{99m}Tc MDP bone scan provides a high dose of radiation to blood compared with other diagnostic examinations (12–14). The average activity of the dose injected was 798 mBq (range, 757–829 mBq); this dose was systemic, and therefore all peripheral blood mononuclear cells (PBMCs) had an equal probability of being irradiated.

Study Design and Treatment

In this single-center prospective controlled study, the first 5 consecutively recruited participants were assigned to the control group, and the next 5 were assigned to the antioxidant group. The antioxidant group received an oral antioxidant medication of 2 g ascorbate, 1.2 g *N*-acetylcysteine (NAC), 600 mg lipoic acid, and 30 mg beta carotene 15 minutes before radiotracer injection. These vitamins were selected based on a review of the literature and 5 years of research and were ingested orally (11).

In all participants, 6 mL of blood was drawn before the injection of ^{99m}Tc MDP tracer for the bone scan (average 800 mBq ± 20.3). A second 6-mL blood sample was drawn 2.5 hours later, before scintigraphic imaging was obtained. Direct comparison of the quantity of

Table 1. Characteristics of 10 Participants Randomly Assigned to Control or Antioxidant Group

Assigned Group	Patient	Age (y)	Radiation Activity (mBq)	Indication for Scan
Control	1	67	784	Prostate cancer staging
	2	74	799	Prostate cancer staging
	3	82	789	Prostate cancer staging
	4	70	814	Prostate cancer staging
	5	61	795	Prostate cancer staging
Antioxidants	6	66	800	Pancreatic cancer staging
	7	72	829	Prostate cancer staging
	8	40	757	Musculoskeletal pain
	9	76	815	Lung cancer staging
	10	69	807	Prostate cancer staging