Anti Oxidative Stress Potential of Cinnamon (Cinnamomum zeylanicum) in Operating Room Personnel: A Before/After Cross Sectional Clinical Trial

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Abstract: Regarding role of oxidative stress in operating room personnel and the anti oxidative stress potential of Cinnamomum zeylanicum (cinnamon) in healthy subjects, the present study aimed to examine anti oxidative stress potential of cinnamon in operating room personnel. A group of 18 operating room personnel was invited to drink cinnamon (100 mg/300 mL tea) once daily for 10 days. Blood samples were obtained before and after entering the study and plasma was measured for oxidative stress biomarkers including Lipid Peroxidation Level (LPO), Total Antioxidant Power (TAP) and Total Thiol Molecules (TTM). Treatment of subjects with cinnamon induced a significant reduction in plasma LPO (5.03±2.01 vs. 3.25±1.32 nmol mL⁻¹, p = 0.016). No statistically significant alteration was found for plasma TAP (1.24±0.12 vs. 1.28±0.12, p>0.05) and TTM (0.78±0.05 vs. 0.82±0.03, p>0.05) after 10 days treatment by cinnamon. In conclusion, reduction of cellular LPO by cinnamon as a dietary supplement can be a rational protocol to control source of hazards in operating room personnel.

Key words: Cinnamon, operating room personnel, oxidative stress, lipid peroxidation

INTRODUCTION

Oxidative stress arises when there is a marked imbalance between the production and removal of Reactive Oxygen Species (ROS). It has been known that exposure to anesthetic gases in operating room personnel is the source of formation of free radicals in living systems and oxidative damage to DNA, proteins and lipids (Malekirad et al., 2005a). Anesthetic gases are able to induce oxidative stress and their harmful chronic effects on reproductive, neurological, hematological, immunological, hepatic and renal systems and induction of cancer have been previously reported. Although the pathophysiology of these adverse effects of anesthetic gases is still unknown, one hypothesis is induction of oxidative stress in vital organs (Hoerauf et al., 1996, 1997; Cohen et al., 1980; Venables et al., 1983). Despite to the fact that anesthetic gases have low solubility in blood and tissues and thus are eliminated from the body rapidly, but they have been known to be neurotoxic, hepatotoxic and carcinogenic (Lucchini et al., 1996; Franco et al., 1991; Corbett et al., 1973).

Cinnamomum zeylanicum Blume, syn C. verum, form family Laureceae namely (cinnamon) is a widely used spice and have many applications in perfumery, flavoring and pharmaceutical industries. The chemical constituents of leaf and bark essential oil of cinnamon have been determined to have strong antioxidants (Raina et al., 2001; Simic et al., 2004; Jayaprakasha et al., 2002; Singhi et al., 2007; Mancini-Filho et al., 1998; Jayaprakasha et al., 2006; Jayaprakasha et al., 2003).

Cinnamon tea that is a mixture of regular tea and cinnamon that is traditionally used in Iran. Our recent cross sectional clinical trial for the first time showed that in individuals who drink cinnamon tea, their blood lipid peroxides decrease and total antioxidant capacity and total thiol molecules increase much more than those who drink regular tea (Ranjbar et al., 2006). Since oxidative stress has been introduced as the main hazard of exposure to anesthetetic gases in operating room personnel, the present cross-sectional before-after clinical trial was undertaken to explore possible protective effects of cinnamon.

MATERIALS AND METHODS

Chemicals: Dithiobis-2-nitrobenzoic acid (DTNB), tris base, tetraethoxypropane, malondialdehyde (MDA), 2-
hiobarbituric acid (TBA), trichloroacetic acid (TCA), n-butanol and 2,4,6-tripyridyl-S-triazine (TPTZ) were used in this study. Cinnamon powder was obtained from local market.

**Subjects:** A comparative cross-sectional before after study was designed with 18 subjects in a University Hospital in Arak in summer 2006. Subjects were 11 female and 7 male in the age range of 22 to 53 years working as operating room nurse. The demographic characteristics of the subjects are shown in Table 1. None of these subjects was exposed in workplace to any hazardous agents other than anesthetic gases. They were active in work shifts weekly, starting 7:30 a.m. and ending 4 p.m. The subjects were asked to drink cinnamon tea containing 100 mg cinnamon in 30 mL boiling water daily (morning) for 10 days. Cinnamon powder is commercially available in Iran markets. Heparinized blood sample was obtained before and after treatment. The blood was centrifuged at 1700 g for 10 min and the plasma was separated and stored at -70°C until analysis.

All participants were provided with specific written information about the aims of the study before written consent was obtained, in accordance with the Declaration of Helsinki. The protocol of the study was approved by Institutional Review Board. Prior to blood collection, all subjects completed a structured questionnaire specifying date of birth, smoking and dietary habits, consumption of vitamin supplements and other antioxidants and use of therapeutic drugs. They were instructed not to take any multivitamin supplements or traditional herbs during the study.

**Measurement of plasma total antioxidant power (TAP):** The ability of plasma in reducing Fe³⁺ to Fe²⁺ is the principle of the method used. In brief, the medium is exposed to Fe³⁺ and the antioxidants present in the medium start to produce Fe²⁺. The reagent included 300 mmol L⁻¹ acetic buffer, pH 3.6 and 16 mL acetic acid as buffer solution, 10 mmol L⁻¹ TPTZ in 40 mmol L⁻¹ HCl and 20 mmol L⁻¹ FeCl₃, 6H₂O. The working reagent was prepared as required by mixing 25 mL acetic buffer, 2.5 mL TPTZ solution and 2.5 mL FeCl₃, 6H₂O solution. Ten microliter of H₂O diluted sample was then added to 300 μL freshly prepared reagent warmed at 37°C. The complex between Fe²⁺ and TPTZ gives a blue color with absorbance at 593 nm (Benzie and Strain, 1999).

**Measurement of lipid peroxidation (LPO):** For measuring the rate of lipid peroxidation, the TBA-reactive substances (TBARS) were measured. In this method plasma samples were mixed with TCA (20%) and the precipitate was dispersed in H₂SO₄ (0.05 M) TBA (0.2% in sodium sulfate 2M) was added and heated for 30 min in boiling water bath. TBARS adducts were extracted by n-butanol and the absorbance was measured at 532 nm. In this method, the reaction products are reported as TBARS because in addition to MDA other aldehydes react with TBA. This reaction is formed in acidic pH and high temperature and gives a maximum absorbance with a pink color at 532 nm (Satho, 1978).

**Measurement of plasma Total Thiol Molecules (TTM):** A volume of plasma (0.20 mL) was mixed in a 10 mL test tube with 0.6 mL of Tris-EDTA buffer (Tris base 0.25 M, EDTA 20 mM, pH 8.2) followed by the addition of 40 μL of 10 mM of DTNB in methanol. The final volume of the reaction mixture was made up to 4.0 mL by adding 3.16 mL of methanol. The test tube was capped and the color was developed for 15-20 min, followed by centrifugation at 3000 g for 10 min at ambient temperature. The absorbance of the supernatant was measured at 412 nm (Hu and Dillard, 1994).

**Statistics:** A detailed multiple variable database was formed. All data were collected either as dichotomous variables e.g., age and weight or as continuous variables e.g., laboratory measurements. All data were analyzed with StatsDirect version 2.6.2. Paired t-test was used to analyze the differences observed in plasma biomarkers after treatment by cinnamon. p-values greater than 0.05 were considered insignificant. Data were expressed as mean±SE.

**RESULTS AND DISCUSSION**

As shown in Table 2, TAP value was not different before and after using cinnamon tea (p>0.05, 1.24±0.12 vs. 1.28±0.12). A significant reduction in plasma LPO was observed after use of cinnamon tea (p = 0.01, 5.3±0.47 vs. 3.25±0.31 mmol mL⁻¹). TTM value was not different before and after use of cinnamon tea (p>0.05, 0.78±0.05 vs. 0.82±0.03).

The present results indicated the positive potential of cinnamon in decreasing plasma TBARS to an extent of 34%. This means that the level of free radicals and their damaging effects on the cells have been markedly
Table 2: Oxidative stress biomarkers before and after treatment by cinnamon tea

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Before</th>
<th>After</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAP (μmol mL⁻¹)</td>
<td>1.24±0.12</td>
<td>1.38±0.12</td>
<td>0.70</td>
</tr>
<tr>
<td>TBARS (μmol mL⁻¹)</td>
<td>5.30±0.47</td>
<td>3.25±0.31</td>
<td>0.01</td>
</tr>
<tr>
<td>TTM (μmol mL⁻¹)</td>
<td>0.76±0.05</td>
<td>0.82±0.03</td>
<td>0.60</td>
</tr>
</tbody>
</table>

Reduced. In the meantime, the present results indicate that plasma TAP and TTM did not change by cinnamon meaning that other non-thiol antioxidants, such as uric acid, transferrin, ceruloplasmin, albumin and vitamin antioxidants e.g., α-tocopherol and ascorbic acid might have been stimulated to maintain antioxidant balance at normal state (Malekinejad et al., 2005a; Rahimi et al., 2005; Shahriari et al., 2006).

As mentioned earlier, numerous substances have been suggested to act as antioxidants in cinnamon. Various phenolic antioxidant such as flavonoids, Rosmarinic Acid (RA), tannins, coumarins, xanthones and more recently, procyaminoids have been shown to scavenge radicals in a dose dependent manner (Czinner et al., 2000; D’Amelio, 1999). Flavonoids and RA have been introduced as the main constituents of Cinnamon (Altschuler et al., 2007). Diabetes is one of diseases that the balance of body antioxidants/antioxidants is very important parameter in its pathophysiology and also complications of the disease (Rahimi et al., 2005). In a clinical trial in patients with poorly controlled type 2 diabetes, cinnamon lowered plasma glucose (Pham et al., 2007). In another study in diabetic patients, cinnamon reduced insulin resistance (Wang et al., 2007). In another clinical trial, intake of 6 g cinnamon with rice pudding in healthy subjects reduced postprandial blood glucose and delayed gastric emptying without affecting satiety (Hlebowicz et al., 2007). There is evidence that cinnamon moderately reduces fasting plasma glucose in diabetic patients with poor glycemic control (Mang et al., 2006). The intake of 1, 3 or 6 g of cinnamon/day reduced serum glucose, triglyceride, low-density lipoprotein cholesterol and total cholesterol in people with type II diabetes (Khan et al., 2003). Animal studies indicate that dietary cinnamon inhibits hepatic HMG CoA-reductase activity, resulting in lower hepatic cholesterol content as well as suppressing lipid peroxidation via the enhancement of hepatic antioxidant enzyme activities (Shobana and Naidu, 2000; Lee et al., 2003).

It is well known that people working in hospital-operating theaters are often exposed to anesthetic gases (Abdollahi et al., 2003). Starting from the 1960s, adverse health effects were observed in medical personnel, mainly nurses, who had been working with anesthetic gases particularly nitrous oxide and halothane (Lopez, 2005). The present study confirmed existence of oxidative stress in blood of operating room personnel and radiology staff (Malekinejad et al., 2005a,b). Genotoxicity is one of the key outcomes of oxidative stress (Abdollahi et al., 2004; Shadnia et al., 2005). In the body, antioxidants act as free radical scavengers and thus protect cells from being exposed to free radicals and further cellular damage. This is the mechanism by which they protect the human body from several diseases attributed to the reactions of radicals. Genotoxic effects such as micronuclei formation, sister chromatid exchange, or chromosome aberrations of occupational exposure to volatile anaesthetics have been shown to increase in operating room personnel. In addition, increased frequencies of spontaneous abortion and birth defects have been reported in operating room personnel (Nilsson et al., 2005; Abdollahi et al., 2003). In conclusion, exposure to anesthetic gases in the operating room personnel cannot be neglected and therefore reduction of cellular LPO can be a rational protocol to control source of hazards that is free radicals. Supporting this idea, a recent clinical trial showed that occupational exposure to anaesthetic gases induces oxidative DNA damage and supplementation of them with vitamin C and vitamin E for 12-weeks resulted in a significant decrease in the DNA damage (Sardas et al., 2006). Regarding existence of flavonoids in cinnamon, it should be noted that flavonoids existing in herbal products have equal potential to vitamin E in reduction of oxidative stress in vivo (Mehdipour et al., 2006). Taking all findings collectively, the present study indicates that cinnamon can protect body from increased LPO. Further studies with higher doses and higher duration of treatment are proposed to elucidate this effect more efficiently. At this stage, use of cinnamon as a dietary supplement for operating room personnel is a rational recommendation.

REFERENCES


