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Lack of association between Plasma Levels of Vitamin C and Nuclear cataract

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ABSTRACT
The purpose of this study was to investigate the relationships between plasma concentration of vitamin C and nuclear cataracts in older Iranians. The Lens Opacities Classification System (LOCS) III was utilized to grade nuclear lens opacities. In order to evaluate plasma concentrations of vitamin C, fasting blood samples were taken from 410 cases and 410 control participants. The study population comprised 393 men and 417 women between the ages of 40 and 91 years. Subjects were classified in four categories according to their age: group I (40–49 years), group II (50–59 years), group III (60–69 years) and group IV (over 70 years). An enzyme-based assay in serum stabilized with metaphosphoric acid was used to measure serum vitamin C concentration. No significant association was observed between serum concentrations of vitamin C and nuclear cataract neither between cases and controls nor between different age categories within the case group. Lack of association between nuclear cataract and vitamin C status may be resulted from the fact that blood levels of this vitamin at one point in time do not adequately reflect the past activity of ascorbic acid in the lens.
***KEYWORDS**: ascorbic acid, nuclear cataract, Iran*

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INTRODUCTION

Cataracts can be defined as the opacification of the normally transparent lens in the eye due to clumping of lens protein and coloration of the lens to a brownish shade because of smoking, age, sunlight exposure, oestrogen replacement therapy, use of oral corticosteroids and diabetes [1]. The most prevalent type of cataract among the older population is nuclear cataract, in which the central portion of the ocular lens undergoes a gradual increase in density and opacity. Light-initiated oxidative damages are hypothesized to be the underlying cause of nuclear cataract [1]. Hence, it has been postulated that antioxidant nutrients could decrease the risk of cataract formation. Ascorbic acid or vitamin C is of particular interest because it can scavenge free radicals and eliminate pro-oxidants and thereby reduces oxidative damage to lens tissues [2]. Moreover, ascorbic acid is found in high concentrations in the lens as well as in aqueous humor of the eye [2]. It has been assumed that, ascorbic acid, some antioxidant enzymes (such as superoxide dismutase, glutathione peroxidase, glutathione reductase and catalase) and some carotenoids (such as α-carotene, lutein, zeaxanthin and β-cryptoxanthin) make an elaborate antioxidant defense system in the lens against the potentially damaging stress factors [3].
Nevertheless, the relation of vitamin C to cataract is not well established. While some epidemiological studies have given encouraging evidence, a number of investigations have displayed mixed results or found no association of this vitamin with lenticular opacification (Reviewed in Weikel et al. 2014 [4]).
The current study was undertaken to examine whether serum concentration of vitamin C is associated with the risk of age-related nuclear cataract in an elderly population of Northwestern Iran.

MATERIALS AND METHODS

Study population
This was a case-control, cross-sectional study which was performed between November 2008 and March 2014. Included individuals belonged to either one of the following categories: (1) case group, comprised 410 patients (209 females and 201 males) who had nuclear cataract in at least one of their eyes and had referred to Ophthalmology Ward of Urmia Imam Khomeini Hospital for cataract surgery and (2) control

group, comprised 410 individuals (218 females and 192 males) with no sign or history of cataract. Absence of cataract in the control group was confirmed by an ophthalmologist. The studied women (aged 41-91; mean 62.26 ± 8.32) and men (aged 40-85; mean 66.80 ± 7.09) were all over 40 years of age. Subjects were classified in four groups according to their age: group I (40–49 years), group II (50–59 years), group III (60–69 years) and group IV (over 70 years). All patients (aged 40-91 mean 61.88±8.59) and control subjects (aged 40-88; mean 66.34±7.59) were from the same geographical region and had a similar socioeconomic background. All the cases were informed about the study's objectives and only those who provided an informed consent were included in the current investigation. The study was approved by the Ethics Committee of Urmia University of Medical Sciences and adhered to the guidelines in the Declaration of Helsinki and subsequent revisions. Gastrointestinal and rheumatological diseases, vitamin C supplementation, past and current smoking, diabetes mellitus, prior ocular trauma, evidence of other ocular diseases except for refraction errors, alcohol consumption and previous eye surgery were all considered as exclusion criteria. Medical histories and demographic characteristics were obtained using a standardized questionnaire. Individuals with systolic/diastolic blood pressures higher than 140/90 mmHg or subjects who were using antihypertensive medications were considered as hypertensives.

Measurements

A quantitative assessment of nuclear lens opacities was achieved using slit lamp illumination technique according to the LOCS III [5]. The presence of nuclear cataract was defined by a grade of 3.0 on the nuclear opalescence scale.

For ascorbic acid analysis, 5 mL of venous blood samples were drawn from each subject and were collected in a Vacutainer tubes containing EDTA. The blood samples were kept at room temperature for about one hour to allow for adequate clotting. Within 2 hours of collection, samples were centrifuged at 3000 rpm at 4°C for 15 minutes and were finally transferred to a -80°C freezer. An enzyme-based assay in plasma stabilized with metaphosphoric acid was utilized to measure the total concentration of plasma vitamin C.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS ver. 17). The continuous variables were evaluated for normality by Kolmogorov-Smirnov criterion prior to statistical analyses. Chi square test was utilized to compare qualitative variables whereas two tailed Student's test was used to compare intergroup continuous parameters. To examine the independent impact of serum concentrations of ascorbic acid on nuclear cataract, a logistic regression analysis was performed for the age group IV. Additionally, another logistic regression model- with ascorbic acid quartiles as independent variable and the highest quartile as the reference - was fitted for the last age group (age group IV) to evaluate the graded effect of ascorbic acid concentrations on the risk of nuclear cataract. Respective odds ratios (OR) were computed for an unadjusted analysis as well as for an adjusted model. The adjusted model was controlled for those parameters that may contribute to the risk for nuclear cataract such as age, sex and hypertension. Two-sided P values less than 0.05 was considered statistically significant for all analyses.

RESULT

Baseline characteristics of the cases and controls are summarized in Table 1. None of the investigated parameters showed a significant difference between patient group and healthy subjects. Table 2 compares the mean levels of vitamin C between cases and controls according to the different age groups. No statistically significant difference was found between normal subjects and patients in age groups I, II and III. However, a marginal difference (P=0.042) was observed for those who had more than 70 years of age (age group IV) (Table 2).

In order to recognize effective factors predisposing to nuclear cataract, a logistic regression analysis with backward selection strategy was conducted in the subjects belonging to the age group IV. Results displayed an independent association between serum levels of vitamin C and the risk of nuclear cataract in this group (OR=1.74, 95% CI: 1.11-2.53; P =0.042). However, the statistical significance was lost after controlling for age (OR=1.13, 95% CI: 0.82-1.42; P =0.425).

Moreover, in order to determine the graded impact of ascorbic acid levels on the nuclear cataract in the last age group, we also performed a logistic regression analysis with ascorbic acid quartiles as the independent variables. In this age group 25th, 50th and 75th percentiles of ascorbic acid (ranged from min=23.50 to max=89.43 μmol/l) were 33.21, 46.48 and 57.09 μmol/l respectively. Association results between ascorbic acid quartiles and risk of nuclear cataract have been presented in Table 3 in two models including unadjusted model and a model adjusted for hypertension, age and gender. The odds ratio (OR) for nuclear cataract increases with decreasing quartiles of ascorbic acid (Ref=highest quartile) both before and after adjustment. According to the adjusted model, subjects in the first (≤ 33.21 μmol/l)

quartile is 1.69 (95 % CI, 0.75-2.03) times more likely to have nuclear cataract than those in the last quartile (≥ 57.10 µmol/l) (P<0.05). But again, statistical significance was lost after controlling for confounding parameters (OR=1.81, 95% CI: 0.89-1.92; P =0.502).

Table 1. Characteristics of the Study Participants

Characteristics	Control group (N=410)	Case group (N=410)	P value
Age [Yr], mean±SD	66.34±7.59	61.88±8.59	0.342
Males/Females [N], (%)	192/218	201/209	0.529
Hypertension [N], (%)	273/137	258/152	0.273
BMI [Kg/m2], mean±SD	26.88±4.23	25.04±3.69	0.682
Vitamin C [µmol/l], mean±SD	33.46±2.85	28.46±3.11	0.411

Table 2. Vitamin C concentrations in cases and controls according to different age groups

Age groups	Plasma Concentrations of Vitamin C (µmol/l)		P value
	Control group	Case group	
Age group I (40-50), (N=115+115)	34.24±2.32	30.03±2.53	0.425
Age group II (51-60), (N=93+93)	30.62±3.01	27.24±2.83	0.361
Age group III (61-70), (N=103+103)	31.54±2.73	26.32±2.44	0.112
Age group IV (>70), (N=99+99)	35.25.2.76	31.79±2.19	0.042

Table 3. Association between ascorbic acid quartiles and risk of nuclear cataract

Ascorbic acid quartiles (µmol/l)	OR (Unadjusted)	OR (Adjusted)
≤ 33.21	1.69 (0.75-2.03)	1.81 (0.89-1.92)
33.22-46.48	1.04 (0.56-1.87)	0.89 (0.21-1.47)
46.49-57.09	0.76 (0.25-1.41)	0.92 (0.31-1.55)
≥ 57.10 (Reference)	-	-

DISCUSSION

Age-related cataract is regarded as the most important cause of vision loss in the world. It accounts for 17.7 million (47.8%) of the total 37 million cases worldwide [6]. The primary signs of opacity may appear anywhere within the body of the lens and according to the site of initiation, age-related cataract is classified into three major types including nuclear cataract, cortical cataract and posterior subcapsular cataract. Nuclear cataract is the most prevalent type of cataract. It begins with a gradual hardening and yellowing of the central zone, called nucleus and gradually expands to the other layers of the lens. This hardening causes light to scatter when it passes through the lens and diminishes the amount of light to the retina. At final stages, these symptoms will lead to severe vision loss that can only be restored through surgery.

L-ascorbate or vitamin C is a water-soluble essential nutrient for humans, and has been known as a strong reducing agent. Several investigations have displayed anti-cataract effect of vitamin C, wherein the underlying mechanism is primarily as an antioxidant [7]. However, anti-cataract studies on humans using vitamin C suggest that this vitamin is only efficacious against nuclear type of cataract [8]. Nevertheless, it is pertinent to note that the oxidized form of vitamin C, called L- dehydroascorbate, has pro-oxidant property and can produce free radical intermediates that are very harmful to biological tissues. Accordingly, it has been revealed that vitamin C is responsible for chemical ageing of lens crystallins [9]. Additionally, this vitamin has also the ability to produce advanced glycation end products [9] which are thought to be a strong factor in aging and some age-related chronic diseases. These effects culminate in the ascorbylation of lens crystallins, their subsequent aggregation and opacification of lenses [10]. Moreover, ascorbic acid during decomposition creates a photosensitizing chromophore, which could in turn increase the susceptibility to UV-A-induced cataract [11]. In support of this, high dose of vitamin C has been reported to increase age-related cataract in females [9], and thus, its long-term efficacy against cataract still remain unclear [12].

Association studies have found controversial results as well. For example, some investigations have revealed that high dietary ascorbic acid intakes [7], high plasma levels of ascorbic acid [13], and long-term ascorbic acid supplement use [14] associated with a decrease in the risk of cataract. However, there are also some reports which failed to detect such an association [15].

The present study was achieved to determine the relation between serum ascorbic acid level and nuclear cataract prevalence among a selected group of older Iranians. In order to minimize the impact of intervening variables, several rigorous exclusion criteria were applied which resulted in the elimination

of considerable number of case and control subjects from the dataset. We did not find a statistically significant association between nuclear cataract and serum concentration of vitamin C in this group of elderly people. It is possible that the lack of association found in the current investigation between vitamin C status and risk of cataract might have partly resulted from the size of our sample. Furthermore, the cross-sectional design of this study makes it difficult to be certain whether the evaluated concentrations of vitamin C are true reflections of concentrations in the period before cataractogenesis. But our findings are in accordance with the results of some large prospective studies [15]. In addition to the low sample size, our study has some other limitations. For example, we had no data on our participants' lifetime diets or their daily exposure time to sunlight. Moreover, the association between nuclear cataract and other antioxidant agents such as carotenoids or vitamin E has not been investigated in the current investigation. Besides, our study lacks data regarding dietary vitamin C intake and aqueous humour ascorbate concentration. Therefore, the role of vitamin C as a protective factor against nuclear cataract could not be entirely ruled out.

CONCLUSION

In conclusion, our case-control study demonstrated that, there is insufficient evidence to support a significantly inverse relationship between blood vitamin C level and risk of nuclear cataract among older Iranians. Prospective investigations of longer duration and with larger sample sizes are needed to clarify further the link between this vitamin and the development of nuclear cataract.

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CONFLICT OF INTEREST

None.

REFERENCES

1. Chang, J.R., Koo, E., Agrón, E., Hallak, J., Clemons, T., Azar, D., Sperduto, R.D., Ferris, F.L. & Chew, E.Y. (2011). Age-Related Eye Disease Study Group. Risk factors associated with incident cataracts and cataract surgery in the Age-related Eye Disease Study (AREDS): AREDS report number 32. Ophthalmology.,118(11):2113-2119.
2. Mody, V.C., Kakar, M., Elfving, A. & Löfgren, S. (2008). Drinking water supplementation with ascorbate is not protective against UVR-B-induced cataract in the guinea pig. Acta. Ophthalmol., 86(2):188-195.
3. Georgakopoulos, C.D., Lamari, F.N., Karathanasopoulou, I.N., Gartaganis, V.S., Pharmakakis, N.M. & Karamanos, N.K. (2010). Tear analysis of ascorbic acid, uric acid and malondialdehyde with capillary electrophoresis. Biomed. Chromatogr., 24(8):852-857.
4. Weikel, K.A.,Garber, C.,Baburins, A. & Taylor, A. (2014). Nutritional modulation of cataract. Nutr. Rev., 72(1): 30-47.
5. Grewal, D.S., Brar, G.S. & Grewal, S.P. (2009). Correlation of nuclear cataract lens density using Scheimpflug images with Lens Opacities Classification System III and visual function. Ophthalmology., 116(8):1436-1443.
6. Mathew, M.C.,Ervin, A.M.,Tao J. & Davis, R.M. (2012). Antioxidant vitamin supplementation for preventing and slowing the progression of age-related cataract. Cochrane. Database. Syst. Rev., 6: CD004567.
7. Yoshida, M.,Takashima, Y.,Inoue, M.,Iwasaki, M.,Otani, T.,Sasaki, S. & Tsugane, S. (2007). Prospective study showing that dietary vitamin C reduced the risk of age-related cataracts in a middle-aged Japanese population. Eur. J. Nutr., 46(2): 118-124.
8. Shui, Y.B.,Holekamp, N.M.,Kramer, B.C.,Crowley, J.R.,Wilkins, M.A.,Chu, F.,Malone, P.E.,Mangers, S.J.,Hou, J.H.,Siegfried, C.J. & Beebe, D.C. (2009). The gel state of the vitreous and ascorbate-dependent oxygen consumption: relationship to the etiology of nuclear cataracts. Arch. Ophthalmol., 127(4): 475-482.
9. Fan, X. & Monnier, V.M. (2008). Inhibition of crystallin ascorbylation by nucleophilic compounds in the hSVCT2 mouse model of lenticular aging. Invest. Ophthalmol. Vis. Sci., 49(11): 4945-4952.
10. Avila, F.,Friguet, B., Silva, E. (2010). Simultaneous chemical and photochemical protein crosslinking induced by irradiation of eye lens proteins in the presence of ascorbate: the photosensitizing role of an UVA-visible-absorbing decomposition product of vitamin C. Photochem. Photobiol. Sci., 9(10): 1351-1358.
11. Fan, X.,Xiaoqin, L.,Potts, B.,Strauch, C.M.,Nemet, I. & Monnier, V.M. (2011). Topical application of L-arginine blocks advanced glycation by ascorbic acid in the lens of hSVCT2 transgenic mice. Mol. Vis., 17: 2221-2227.
12. Thiagarajan, R. & Manikandan, R. (2013). Antioxidants and cataract. Free. Radic. Res., 47(5): 337-345.
13. Ferrigno, L., Aldigeri, R., Rosmini, F., Sperduto, R.D., Maraini, G. & Italian-American Cataract Study Group (2005). Associations between plasma levels of vitamins and cataract in the Italian-American Clinical Trial of Nutritional Supplements and Age-Related Cataract (CTNS): CTNS Report #2. Ophthalmic. Epidemiol., 12(2):71-80.
14. Christen, W.G., Glynn, R.J., Manson, J.E., MacFadyen, J., Bubes, V., Schvartz, M., Buring, J.E., Sesso, H.D. & Gaziano, J.M. (2014). Effects of multivitamin supplement on cataract and age-related macular degeneration in a randomized trial of male physicians. Ophthalmology., 121(2):525-534.

15. Rautiainen, S., Lindblad, B.E., Morgenstern, R. & Wolk, A. (2010). Vitamin C supplements and the risk of age-related cataract: a population-based prospective cohort study in women. Am. J. Clin. Nutr., 91(2):487-493.

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