Cosmic Radiation Increases the Risk of Nuclear Cataract in Airline Pilots

A Population-Based Case-Control Study

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Background: Aviation involves exposure to ionizing radiation of cosmic origin. The association between lesions of the ocular lens and ionizing radiation is well-known.

Objective: To investigate whether employment as a commercial airline pilot and the resulting exposure to cosmic radiation is associated with lens opacification.

Methods: This is a population-based case-control study of 445 men. Lens opacification was classified into 4 types using the World Health Organization simplified grading system. These 4 types, serving as cases, included 71 persons with nuclear cataracts, 102 with cortical lens opacification, 69 with central optical zone involvement, and 32 with posterior subcapsular lens opacification. Control subjects are those with a different type of lens opacification or without lens opacification. Exposure was assessed based on employment time as pilots, annual number of hours flown on each aircraft type, time tables, flight profiles, and individual cumulative radiation doses (in millisieverts) calculated by a software program. Odds ratios were calculated using logistic regression.

Results: The odds ratio for nuclear cataract risk among cases and controls was 3.02 (95% confidence interval, 1.44-6.35) for pilots compared with nonpilots, adjusted for age, smoking status, and sunbathing habits. The odds ratio for nuclear cataract associated with estimation of cumulative radiation dose (in millisieverts) to the age of 40 years was 1.06 (95% confidence interval, 1.02-1.10), adjusted for age, smoking status, and sunbathing habits.

Conclusion: The association between the cosmic radiation exposure of pilots and the risk of nuclear cataracts, adjusted for age, smoking status, and sunbathing habits, indicates that cosmic radiation may be a causative factor in nuclear cataracts among commercial airline pilots.

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THE IONIZING RADIATION exposure of commercial airline pilots arises from 2 sources, solar particle events and galactic cosmic radiation and their secondary events produced in collision with air nuclei and aircraft materials.[1] Characteristic of these exposures are many high linear energy transfer components, which differ from other occupational exposures and lead to uncertainty in terms of cancer risk.[1] In studies on pilots, the most consistent finding in European[2,3] and US[4-6] cohorts has been increased incidence and increased mortality of malignant melanoma; however, malignant melanoma has only recently been related to ionizing radiation,[7,8] and no adjustment was made for exposure to UV light in these studies.

An increased incidence of chromosomal aberration in peripheral blood lymphocytes has been found in Concorde pilots,[9] commercial pilots,[10] and astronauts,[11] and is considered to be induced by exposure to ionizing radiation. For the crew members of the Mir Space Station, the frequency of aberrant lymphocytes was used to estimate cancer risk, which was 20% to 30% elevated.[11]

The biological adverse effects of pilots' radiation exposure, other than cancer and chromosomal aberration, have been the subject of only limited study. Radiogenic cataracts are, however, well-known, and early radiation-induced lesions on the ocular lens are well documented.[12] A study[13] in which information was gathered by questionnaire only indicated increased rates of cataracts among US pilots; however, the diagnoses of the cataracts were not clinically con-

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firmed. A recent study[14] among astronauts showed an association of incidence of cataracts with space radiation; the cutoff between low and high exposure was only 8 mSv. This exposure level is comparable to levels that have been used in cancer incidence studies[2] on commercial pilots.

It is, therefore, of interest to determine whether lens opacification among commercial airline pilots is related to their duration of employment and estimated exposure to cosmic radiation.

METHODS

This is a case-control study in which the cases of opacification of the ocular lens were detected in surveys among pilots and in a random sample of the population in Reykjavik. The 79 pilots (all men) were 50 years or older and were recruited from a cohort of commercial pilots that has been described in a previous publication[15]; the participation rate was 73.1%. The sample from the population was originally drawn in 1996, when these persons were 50 years and older; the participation rate was 75.8%.[16] Of the survivors, 88.2% were reexamined in 2001, when the men numbered 377 and 366 of them were eligible for this study. Of the 11 persons disregarded, 6 had an artificial intraocular lens, 2 each had nondilatable pupils and a poorly completed questionnaire, and 1 had an artificial eye. All participants were white and residents of the Reykjavik area. They gave their informed consent for participation, and the study was approved by the National Bioethics Committee and the Personal Data Protection Authority. The participants underwent a detailed eye examination and answered a questionnaire on lifestyle factors, previous diseases, and medications, including smoking status and sunbathing habits, the last a surrogate of recreational exposure to UV light. All participants had their pupils maximally dilated with 1% tropicamide and 10% phenylephrine hydrochloride eyedrops before the eye examination. Two ophthalmologists (E.O. and H.S.), experienced in cataract grading, classified and graded lens opacification according to the World Health Organization (WHO) simplified cataract grading system, using slitlamp microscopy.[17] The WHO classification system includes nuclear, cortical, and central optic zone involvement and posterior subcapsular cataracts, as well as progressing grades; these 4 types constitute the cases. We also performed Scheimpflug imaging and retroilluminated photography of all lenses for documentation; these data, however, were not used for analysis in the present study.

Detailed employment information was available for 79 pilots. This included start and termination of employment and annual number of hours flown on each aircraft type. All time tables from Icelandair, domestic and international flights, from January 1, 1958, to December 31, 1996, were computerized and, together with the flight profiles of each route and aircraft type, formed the basis for the calculations of effective radiation doses (in millisieverts) per air hour for each aircraft type and year. These calculations were done using computer software (CARI-6),[18,19] as described in a previous exposure study.[20] Linking the effective radiation dose per air hour for aircraft type and year with the annual air hours flown by each pilot allowed us to calculate the individual cumulative radiation dose (in millisieverts). In the same way, the cumulative radiation dose was calculated up to the age of 50 years and separately up to the age of 40 years, omitting the exposure sustained after these age limits.

A multivariate case-control analysis was performed using a logistic regression analysis.[21] The adjusted odds ratio and exact computation of 95% confidence intervals (CIs) were calculated using a computer software package (SPIDA).[22] Case-control status was the dependent variable. For nuclear, cortical, and posterior subcapsular cataracts, the case definition was grade 1 or higher, according to the WHO classification.[17] Whether an individual was ever or never a commercial pilot was treated as a dichotomous variable. Age, the main known risk factor for nuclear and cortical cataracts, was treated as a continuous variable (expressed in years). In the population of Reykjavik (Reykjavik Eye Study), other risk factors have been identified, including smoking for nuclear cataracts[23] and outdoor (sunlight) exposure for cortical cataracts.[24] Ever/never smoked and regularly/not regularly sunbathing were treated as dichotomous variables. In different separate analyses, the length of employment (in years), the cumulative radiation dose (in millisieverts), the cumulative radiation dose (in millisieverts) to the age of 50 years, and the cumulative radiation dose (in millisieverts) to the age of 40 years were each treated as continuous variables. The analyses of the association of the different types of cataracts with the cumulative radiation dose up to the ages of 50 and 40 years were performed to allow for the possibility of induction or latency time. In yet another analysis, the cumulative radiation dose (in millisieverts) up to the age of 40 years was divided into quartiles and treated as an ordinal variable.

Table 1. Data From Logistic Regression of Nuclear Cataract Risk Among Cases and Controls According to Employment as a Commercial Airline Pilot, Age, Smoking Status, and Sunbathing Habits

Variable	Controls (n = 374)*	Cases (n = 71)*	Adjusted Odds Ratio (95% Confidence Interval)†
Age, mean, y	66.1	74.6	1.17 (1.12-1.22)
Employment			
Never a pilot‡	310	56	1.00
Ever a pilot	64	15	3.02 (1.44-6.35)
Smoking status			
Never smoked‡	250	12	1.00
Ever smoked	124	59	1.92 (0.92-3.99)
Sunbathing habit			
Not a regular sunbather‡	327	63	1.00
Regular sunbather	47	8	0.91 (0.38-2.20)

*Data are given as number in each group.
†Data have been calculated in a unique multivariate analysis, taking into account simultaneously all the variables.
‡Reference group.

RESULTS

According to the WHO classification, there were 4 types of cases: 71 with nuclear cataracts, 102 with cortical cataracts, 69 with central optic zone involvement, and 32 with posterior subcapsular cataracts. Those with a different type of opacification and those without opacification served as control subjects.

Table 1 shows that the odds ratio for nuclear cataracts was 3.02 for those individuals who had ever been pilots at Icelandair compared with those who had not been pilots, adjusted for age, smoking status, and sunbathing habits. Age, entered as a continuous variable, was significantly associated with the risk of nuclear cataracts, but neither smoking status nor sunbathing habits were. Of the 71 cases (mean age, 74.6 years) of nuclear cataracts, 2 (2.8%) had at any time taken systemic corticosteroids, vs 7 (1.9%) of the 374 controls (mean age, 66.1

Table 2. Age-Adjusted Odds of Nuclear Cataract Risk According to Cumulative Radiation Dose Sustained Before the Age of 40 Years, Divided Into Quartiles

Variable	Controls (n = 374)*	Cases (n = 71)*	Odds Ratio (95% Confidence Interval)
Age, y	NA	NA	1.16 (1.11-1.21)
Cumulative radiation dose			
Not exposed†	310	56	1.00
First quartile (1-7 mSv)	13	6	2.82 (0.95-8.41)
Second quartile (8-15 mSv)	18	3	2.60 (0.67-10.11)
Third quartile (16-21 mSv)	18	3	2.48 (0.64-9.70)
Fourth quartile (22-48 mSv)	15	3	4.19 (1.04-16.86)

Abbreviation: NA, data not applicable.
*Data are given as number in each group.
†Reference group.

years); 3 (4.2%) of the cases had a history of eye trauma, vs 22 (5.9%) of the controls; and 9 (12.7%) of the cases had type 2 diabetes mellitus, vs 30 (8.0%) of the controls. In addition, among the controls, there was one with type 1 diabetes mellitus. The odds ratios (95% CIs) from corresponding analyses for cortical cataracts, central optical zone involvement, and posterior subcapsular cataracts were 0.95 (0.48-1.85), 0.64 (0.26-1.60), and 0.46 (0.10-2.04), respectively.

The odds ratio for nuclear cataracts associated with continuous length of employment (in years) at Icelandair, adjusted for age, smoking status, and sunbathing habits, was 1.03 (95% CI, 1.01-1.05). When radiation exposure was considered as a continuous variable, the odds ratio for nuclear cataracts associated with cumulative radiation dose (in millisieverts), adjusted for age, smoking status, and sunbathing habits, was 1.02 (95% CI, 1.00-1.03). The odds ratios (95% CIs) for corresponding analyses for nuclear cataracts associated with cumulative radiation dose (in millisieverts) to the age of 50 years and cumulative radiation dose (in millisieverts) to the age of 40 years were 1.03 (1.01-1.05) and 1.06 (1.02-1.10), respectively; in these analyses, both exposure variables were treated as a continuous variable. The odds ratios from corresponding analyses for cortical cataracts, central optical zone involvement, and posterior subcapsular cataracts associated with length of employment (in years) at Icelandair, cumulative radiation dose (in millisieverts), cumulative radiation dose (in millisieverts) to the age of 50 years, and cumulative radiation dose (in millisieverts) to the age of 40 years were all lower than unity, with 95% CIs that included 1.

Table 2 shows the adjusted odds ratio for nuclear cataracts when the cumulative radiation dose (in millisieverts) up to the age of 40 years was divided into quartiles. The odds ratios were higher than 2.5 for all quartiles, and in the fourth quartile, the quartile with the highest exposure, the odds ratio was 4.19, adjusted for age, smoking status, and sunbathing habits.

COMMENT

Our calculations show a significant association between length of employment (measured in years), cumulative radiation dose (measured in millisieverts), and cumulative radiation dose sustained before the ages of 50 and 40 years and risk of nuclear cataracts, adjusted for age, smoking status, and sunbathing habits among commercial airline pilots. For these exposure variables, the odds ratio was highest for cumulative radiation dose sustained before the age of 40 years, which is compatible with a long latency time for the induction of nuclear cataracts. Despite the few cases, the odds ratios were high in the quartile analysis and the 95% CIs did not include unity in the quartile with the highest exposure. Our observed association is supported by the evidence from the study in which US pilots were questioned[13] and the incidence study on US astronauts,[14] in which subjective methods were used to categorize cataracts, and findings from a preliminary study on a multinational group of astronauts and cosmonauts,[25] suggesting a causal association of the nuclear cataract risk with the cosmic radiation exposure of the pilots.

According to the literature, posterior subcapsular and nuclear cataracts have been associated with ionizing radiation exposure in studies on patients with cancer,[26,27] atomic bomb survivors,[28] and patients without cancer.[29] The experience from these previous studies is, however, difficult to apply to the results of our case-control study involving pilots, primarily for 2 reasons. First, the classification of the cataract varies between studies and through time; and second, the nature of the radiation exposure that the pilots sustain in their occupation is particular and perhaps more comparable to the exposure of astronauts.[14] In the study on astronauts,[14] nuclear cataracts were the only single type significantly associated with space radiation. Posterior subcapsular cataracts are rare in the population of Reykjavik,[16] and the numbers are too small to allow us to draw conclusions.

Civil aviation safety requires commercial pilots to be in good general health, to have intact sight and hearing ability, and to undergo regular medical checkups. According to the questionnaire, the occupationally active pilots had had eye examinations twice a year. The present cross-sectional survey on lens opacification is an addition to these thorough medical examinations. The selection process for the occupation, and the ongoing medical scrutiny of pilots, suggests that they may be healthier than the general male population. Thus, a low prevalence of cataracts is perhaps to be expected among pilots, as the low odds ratios for cortical cataracts, central optic zone involvement, and posterior subcapsular cataracts may indicate.

The main modifying factor (age) is adjusted for in the analyses. The raw data in Table 2 suggest little or no association between piloting and nuclear cataract, but the odds ratios are 2.5 or higher in all quartiles, indicating that pilots are getting the cataract at a younger age than nonpilots. The most important possible confounding factors for cataracts are adjusted for in the study. These are smoking habits for the risk of nuclear cataracts and sunbathing (UV radiation) for the risk of cortical cataracts. The association between smoking habits and nuclear cataract was nonsignificant, presumably because of lack of power, as the strength of this association was similar in magnitude to that found in the Reykjavik Eye Study.[23] The UV radiation exposure of pilots on board aircraft is minimal, according to measurements in the cockpit.[30] The use of systemic corticosteroids and history of eye trauma were rare and in similar magnitude among cases of nuclear cataracts and controls. All types of diabetes mellitus combined was not a significant risk factor for cataracts in the Reykjavik Eye Study,[23,24] and in the present study, the proportions of persons with diabetes mellitus were similar among cases of nuclear cataracts and their controls; thus, it is unlikely that use of corticosteroids, history of eye trauma, and diabetes mellitus are confounding the results.

The systematic use of the WHO cataract grading system diminishes the risk of misclassification of cases and controls.[17] The authors performing the slitlamp microscope classification and grading were masked as to the exposure levels of the pilots. The use of the comprehensive population census strengthens our study. This allowed us to draw a random sample from the male population in Reykjavik and to ascertain the vital status and addresses of the pilots and individuals of the sample. The information on smoking and sunbathing habits and health and lifestyle factors was obtained by trained interviewers applying a questionnaire; the interviewers were unaware of the case-control status of the participants, as were most of the participants themselves. The primary information on employment time and annual air hours per aircraft type for an individual pilot was collected for administrative purposes at the airline company before formulating the hypothesis of the study and diagnosing the cases, which eliminates the possibility of recall bias concerning the exposure variables. The small size of the study did not allow us to separate out the possible effects of calendar time or to analyze the degree of seriousness of the lens opacification in relation to exposure.

To our knowledge, this is the first published case-control study of lens opacification involving commercial pilots, adjusted for age and individual risk factors for cataracts. Our results indicate that cosmic radiation may be a causative factor in nuclear cataract among commercial airline pilots.

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