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Sustained Lower Incidence of Thyroid Cancer in West Cumbria, UK

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Abstract

Background: In recent years, incidences of thyroid cancer have increased in developed countries; one of the known risk factors for thyroid cancer is exposure to radioiodine. Previous research by Bowlt and Tiplady [5] has shown an inverse link between radioactive iodine levels contained in thyroid tissue of deceased inhabitants and the distance they lived from the Sellafield nuclear facility in Cumbria, UK.

Objectives: The present study aimed to determine what thyroid cancer incidences were in the regional localities in Cumbria for the last decade.

Methods: An ethics-approved retrospective cohort study in which age-standardised incidence of thyroid cancer per 100,000 population was compared between localities within Cumbria and with UK average figures.

Conclusions: The present study shows that the apparent lower incidence of thyroid cancer in West Cumbria has persisted, although due to the limited number of thyroid cancers diagnosed, a statistically significant difference was not observed. Further research – potentially involving populations living near sources of radioiodine emission - is indicated to investigate if there are any mechanisms that underlie this apparent trend.

Keywords Thyroid cancer; Epidemiology; Incidence; Radioiodine; Radiation homeostasis; Radiation hormesis

Introduction

Thyroid cancer is the 18th (UK) and 5th (US) most common cancer in women and the 20th most common cancer in men in the UK [1,2]. Treatment usually involves surgical removal of the thyroid and long-term treatment with levothyroxine. The incidence of thyroid cancer has increased by as much as 69% over the last decade, and a total of 2,727 new cases were diagnosed in the UK during 2011 [2]. This recent increase in incidence is at least partly due to improved diagnostics. However, another important factor may be the growing popularity of a 'Western' diet high in fat and sugar. A recent study has linked obesity to an elevated risk of thyroid cancer in women, although a similar association was not seen in men [3]. Adequate intake of iodine is essential to human health and development, and small quantities obtained from the diet are actively concentrated within the thyroid gland. For these reasons, exposure to the radioactive iodine isotopes 129I and 131I is an important risk factor for the development of thyroid cancer. The effect of exposure to very high doses of radioiodine has been demonstrated clearly following the Chernobyl nuclear accident in 1986. Children from the most highly contaminated regions of Ukraine, Belarus and Russia were shown to have a 7 to 9-fold increase in their risk of thyroid cancer [4].

The health effect of lower doses of radioiodine is less clear. Data from between 1969 and 1986 have shown an incidence of thyroid cancer in the districts of Copeland and Allerdale in Cumbria, UK, that is below the national average [5,6]. This was despite an increased exposure to radioactive 129I discharged from the Sellafield nuclear facility and measured in tissue samples from deceased Cumbrians [5]. More recent environmental data published by Sellafield Ltd. confirms that measurable levels of I129 and I131 continued to be released by the facility over the last decade, although these levels are considered to be within safe limits [7]. This increased environmental exposure occurring over decades, combined with the effect of fallout from Chernobyl in 1986, means that the population of West Cumbria are of particular interest regarding thyroid cancer risk. The aim of this present study was to analyse new epidemiological data from the period 2003-2013 and to ascertain whether lower thyroid cancer incidence in West Cumbria have persisted.

Methods

Study design and patients

This retrospective cohort study was reviewed and approved by both the National Research Ethics Service (NRES), ref. 14/LO/1734 and the NHS Trust in which the research took place and the thyroid cancer patients were diagnosed and treated. Any patient diagnosed with thyroid cancer between the period 1 Jan 2003 and 31 Dec 2013 was included. Patients treated for thyroid cancer at West Cumberland Hospital or Cumberland Infirmary, but being a resident outside the four localities covered in this project (Carlisle, Eden Valley, Allerdale and Copeland) were excluded from analysis.

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Statistical analysis

Data was collated in Microsoft Excel 2007, and further analysed and interpreted using Excel and SPSS Statistical Package for Social Sciences (SPSS) version 17.0 (SPSS Inc. Chicago, IL, USA, 2007). Thyroid cancer cases were categorised by local authority. For each locality, age-standardised incidence rates (with 95% confidence intervals [CI]) were calculated using Office of National Statistics methodology and the European Standard Population. Standard quinary age distribution tables for Carlisle, Eden Valley, Allerdale and Copeland for the year 2008 – midpoint for period covered - were obtained from ONSOffice for National Statistics (ONS). UK age-standardised incidence rates were taken from the year 2011 (http://www.cancerresearchuk.org/cancer-info/cancerstats/types/thyroid/mortality/uk-thyroid-cancer-mortality-statistics). Difference in age at diagnosis between localities was assessed through one-way ANOVA testing.

Results

A total of 124 patients were diagnosed with thyroid cancer between 2003-2013 in the four Cumbrian localities of Allerdale, Copeland, Carlisle, and Eden Valley, included in this study. Table 1 shows age-standardised incidence rates for thyroid cancer in said four different Cumbrian localities and the for the UK. The youngest person to be diagnosed with thyroid cancer in the period covered was 23 years of age. Importantly, children were not included in this analysis because they fall under the care of surgeons in a tertiary health centre in Newcastle, rather than the local surgical team. The mean age at diagnosis for patients in the different localities indicates a pattern that suggests that thyroid cancer may occur earlier in life in West Cumbrian patients. However, ANOVA analysis demonstrates that this is a non-significant finding with the sample size (Table 2).

Locality	Patients (n)	Age-standardised incidence	95% CI
United Kingdom [ref 1]	n/a	3.9	3.8 to 4.1
Allerdale	30	2.7	-0.5 to 5.8
Copeland	23	2.6	-0.9 to 6.2
Carlisle	42	3.1	0 to 6.2
Eden Valley	29	4.6	-1 to 10.1

Table 1: Age-standardised incidence rate (per 100,000) of thyroid cancer per locality.

Discussion

The relative rare incidence of thyroid cancer, compared to other cancers such as prostate or breast cancer, means that this retrospective cohort study has limited power to detect significant differences in thyroid cancer incidence. Although the differences seen here are not statistically significant, based on the reported 95% confidence interval ratings, a lower age-standardised incidence rate for adults is seen for the Copeland and Allerdale counties. These results mirror those obtained by Bowlt and Tiplady, a few decades ago [5]. Following the Chernobyl nuclear accident in 1986, there was a significant increase in cases of thyroid cancer in young people in Cumbria as a whole [8]. Subsequent analysis demonstrated that the increased incidence was primarily confined to female patients [9]. It should be noted that ionising radiation fallout in Cumbria, originating from Chernobyl in 1986, was most concentrated in northern areas of the county around Carlisle [9]. Taken together, there appear to be two patterns of thyroid cancer incidence in Cumbria. One higher incidence rate involving young people and potentially related to Chernobyl, and one lower incidence rate involving adults – the focus of this study - which could possibly related to very low dose radioactive iodine uptake in the thyroid. Sellafield Ltd. discharges approximately 0.25 TBq (into Irish Sea) and 9GBq (airborne) of 129I, and 0.45GBq (airborne) of 131I each year [7]. Because of its longer half-life of 15.7 million years, 129I would remain active in thyroids for the rest of a person's life if ingested opposed to 131I with a half-life of eight days. The energy activity levels of 131I are much higher than for 129I, produces far more energy, $1.77\times10-4$ vs. 1.24×105 Ci/g.

Locality	Sex (m/f)	Mean age at diagnosis	Median age at diagnosis	95% CI
Allerdale	6 / 24	51.6	52	47.0 to 56.2
Copeland	6 / 23	52.5	48	45.4 to 59.6
Carlisle	14 / 28	56.6	56.5	51.8 to 61.4
Eden Valley	6 / 23	54.1	54.0	47.6 to 60.5
		p= 0.53 (one-way ANOVA)		

Table 2: Patients' demographics per locality.

If the linear non-threshold hypothesis for ionising radiation exposure would apply, Bowlt and Tiplady's observation of an increasing amount of 129I activity in thyroids from deceased people living nearer to Sellafield would predict an increase in thyroid cancer in Allerdale and Copeland. The linear non-threshold (LNT) hypothesis has been used to date when considering the damage that ionising radiation may incur to humans. It implies that any dose of ionising radiation is damaging and increases the risk of cancer [10]. Bowlt and Tiplady's data, together with the data presented in this present study would imply a potential role for radiation hormesis (also known as radiation homeostasis) induced by radioiodine, the phenomenon where a very small dose of ionising radiation can excert a protective effect [11,12].

The cellular mechanisms that underly radiation hormesis have been studies extensively. Epigenetic changes take place in response to (long-term) low dose radiation exposure, resulting in induction of a term coined activated natural protection by Scott [13]. In essence, a cluster of different cell defence mechanisms are activated to protect cells and DNA in particular – examples include increased antioxidants, activation of DNA repair genes, programmed cell death (apoptosis) of irreversibly damaged cells, and modulation of inflammatory pathways [13]. Taken together, these cellular processes have the potential to reduce the risk of cells becoming cancerous. The support for the radiation hormesis biomechanism appears to be getting stronger and very recently Dr C S Marcus submitted a petition to the US Nuclear Regulatory Commission to reject the LNT hypothesis [14]. In our present purely epidemiological study we can only look at an association rather than causation concerning the trend towards lower thyroid cancer incidences in West Cumbria. Nevertheless, thyroid cancer incidences do not appear to be increased despite patients in Copeland and Allerdale living in the vicinity of the Sellafield nuclear facility.

In West Cumbria, apart from higher levels of radioactive iodine emission, another factor should theoretically contribute to higher incidences of thyroid cancer. Copeland has the highest incidence in the UK of overweight and obese adults [15]. This should theoretically contribute to increased incidence of thyroid cancer – or at least counteract any mechanism for decreased incidence because obesity has been shown to contribute to an increase in thyroid cancer [3]. Other unidentified factors, not recognised due to the retrospective cohort approach taken, could also contribute such as genetic factors. Meanwhile, the incidence rate of other cancers, including colorectal and breast cancer, has gone up considerably in Copeland in the last 10 years [15].

In conclusion, age-standardised thyroid cancer incidence rates in West Cumbria are consistently lower – albeit not to statistically significant lower levels - than in the rest of Cumbria and the national UK average. Further work involving populations that live around other nuclear facilities that emit radioactive iodine could give more insight into the epidemiology of thyroid cancer and any potential relationship with very low dose radioiodine exposure.

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