Cancer incidence near oil fields in the Amazon basin of Ecuador revisited.

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Abbreviations

IARC. International Agency for Research on Cancer

CDC. Centers for Disease Control.

CI. Confidence intervals

E. Expected

ICD. International classification of diseases

O. Observed

SIR. Standard Incidence Ratio

SMR. Standard Mortality Ratio

Conflict of Interest

Alejandro Arana and Félix Arellano are partners of Risk Management Resources that provides consultancy to Chevron, and oil Production Company with business in Ecuador in the past.
Risk Management Resources had a contractual agreement giving the Company complete control of the content of the manuscript as well as to the journal of choice for submission.

Abstract

Objectives

San Sebastian et al have reported an overall excess for all types of cancers in San Carlos, Ecuador (Standard Incidence Ratio (SIR) 2.26; 95% CI 0.97 - 4.46 for males) and an increased mortality due to cancers in males (Standardized Mortality Ratio (SMR) 3.6; 95% CI 1.31 - 7.81). The authors concluded that there was an excess of cancer among the villagers linked to environmental pollutants stemming from oil production activities. The publication of the 2001 Ecuador census provides population data for San Carlos and allows the revision of the San Carlos cluster of cancer cases evaluation.

Methods

Cancer cases from 1989 to 1998 were obtained from the original article. Data on cancer occurrence and mortality from GLOBOCAN from the National Cancer Registry of Ecuador, Quito (1993-1997). Population data for the village of San Carlos was obtained from the 2001 Ecuador census. Statistical analyses were based on the comparison of observed and expected numbers of cancer cases and deaths due to cancer. We calculated the expected number of cancer cases, based on standard cancer incidence rates reported for Quito by the International Agency for Research on Cancer (IARC).

Results

In males there were 8 cases observed and 8.8 expected; (SIR 0.91; 95% CI 0.42-1.72). In females, there were 2 cases observed and 8.9 expected (SIR 0.22; 95% CI 0.04 to 0.42). In males there were 6 deaths observed and 6.1

expected (SMR 0.98; 95% CI 0.40 - 2.03). No deaths due to cancer were found in women.

Conclusions

The census published in 2001 pointed to an underestimation of the population of San Carlos used by San Sebastian et al. to analyze the cancer cluster of San Carlos. The use of census data for the calculation resulted in no excess cancer risk in the village of San Carlos.

Background

San Carlos is a small village in the province of Orellana, in north eastern Ecuador. More than 30 oil wells surround the village, some of which have been in operation for more than 20 years. The occurrence of a series of cancer cases in San Carlos prompted an investigation presented in three documents on environmental exposure to oil and incidence and mortality of cancer[1,2,3]. Summarizing, the authors reported that ten patients were diagnosed with medically confirmed cancer while residing in the village of San Carlos between 1989 and 1998. They reported an overall excess for all types of cancers combined for males (8 observed v. 3.5 expected) yielding a risk 2.26 times higher than expected (95% confidence interval (95% CI) 0.97 to 4.46) and an overall excess of deaths due to all types of cancers combined (6 v. 1.6 expected) among the male population, 3.6 times higher than expected (95% CI 1.31 to 7.81). In the light of these results, the authors concluded that there was an excess of cancer among the villagers and that this could be linked to environmental pollutants stemming from the oil production activities.

The authors of the San Carlos study describe its purpose as an investigation of a suspected excess occurrence of cancer cases, i.e., a possible “cancer cluster”, a “potential grouping of cancers”[1]. The presence of a cluster is frequently seen as proof of a causal effect; however this is frequently not the case. For example, Schulte et al.[4] reviewed 61 investigations of reported cancer clusters, and only 16 confirmed that an excess of cancer occurred. Even from these 16 studies, little or no etiologic insight emerged. Many of the reports involved cases for which there was no identifiable exposure to carcinogenic agents on the job or insufficient time after suspected exposures for cancer to develop. Seldom was an exposure quantifiable in any meaningful way. Only four reports of the 61 involved more than 10 cases; the small numbers hindered more useful data analyses. Since clusters present many epidemiological biases and provide little information on causation, the Centers for Disease Control (CDC) issued a set of guidelines[5] in 1990 to ensure the effective use of resources for the investigation of such clusters. These guidelines call for an integrated approach that seeks to systematically screen suspected clusters and carefully evaluate the value of launching a full-scale investigation into the causes of the suspected cluster, while at the same time being responsive to community concerns. Steps outlined in the CDC guidelines include a preliminary assessment involving: a) the determination of the number of cases, the population at risk, if possible, and definition of the geographic area and time period to be examined, b) verification of cases for biological plausibility, c) verification of whether an excess has occurred, and if so, description of its epidemiologic characteristics.

The objective of this study is to perform the preliminary assessment of the possible cluster of cancer cases in the village of San Carlos following the steps described in the CDC guidelines and include more recently published census data. In the absence of census data on the village of San Carlos in 1998, San Sebastian et al. estimated its population as about 1000 inhabitants and the annual census of San Carlos during the period 1989-1998 was assumed to be constant[1,2,3]. The “Instituto

Nacional de Estadística y Censos" (National Institute of Statistics and Census) of Ecuador performed a more recent census in 2001 that includes accurate information on the population of the village of San Carlos and the population growth of the province of Orellana. According to the census, the number of inhabitants in the village of San Carlos in 1989 was almost 50% bigger than assumed by San Sebastian et al. (1471 vs. 1000) and grew at rate of 84% in 11 years[6].

Methods

DATA COLLECTION

Cancer cases from 1989 to 1998 were obtained from the original report[1]; cases were included only when pathological evidence was present. Since no cancer registry is available in the Amazon region, data on cancer occurrence was obtained using GLOBOCAN[7] from the National Cancer Registry of Ecuador, Quito (1993-1997)[8] associated to the International Agency for Research on Cancer (IARC). We also used GLOBOCAN as the source for cancer mortality. The IARC estimates cancer mortality from national mortality data (1998-2000) corrected for estimated completeness (72% for male, 68% for female) to avoid the effect of deaths not notified to health authorities. Population data for the village of San Carlos was obtained from the "Instituto Nacional de Estadística y Censos" of Ecuador census performed in 2001[6]. We considered the age distribution of the province of Orellana and its population growth as reported in the 2001 census for the calculation of the study population.

STATISTICAL METHODS

Statistical analyses were based on the comparison of observed and expected numbers of cancer cases and deaths due to cancer. The expected number of cases was estimated as follows: First, we determined the annual population growth by dividing 84% by 11 years to yield an average annual growth of 7.63%. We estimated the population in 1989 by dividing the population of San Carlos in 2001 by 1.92 to account for the 92% (i.e., 7.63%/yr X 12 yrs) increase in the regional population between 1989 and 2001. Likewise, we estimated the size of the population of San Carlos in 1998 by dividing that reported in 2001 by 1.23 (23% growth in 3 years). We calculated the average population size between that estimated for 1989 and the estimated population in 1998 and assumed that this was the average population size during the 10-year period of the study. We calculated the age group population by multiplying the total size of the population by the age specific proportion of the province of Orellana as described in the 2001 census (Percentage over total population/100).

We calculated the expected number of cancer cases, based on standard cancer incidence rates reported for Quito by the International Agency for Research on Cancer (IARC[7]). First, we grouped the population of San Carlos into the same age-groups reported for Quito. Second, we calculated the number of person-years in the study by multiplying the number of people per age-group by the duration of the study in years (10 years). We calculated the expected number of cases per age-group by multiplying the number of person-years in a specific age-group by the annual age-specific incidence of cancer of the specific age group (number of person years X rate per 100,000 / 100,000). Finally, we calculated the expected number of cancer cases by adding up all the age specific expected number of cases.

We report observed and expected values, observed/expected ratios, and their 95% confidence intervals (95% CI) based on the Poisson distribution exact method.

Results

San Sebastian et al reported ten confirmed cases; six (all males) had died; most of these deaths took place a short time after the diagnoses. The population of the village of San Carlos in 2001 was 2,823 people (1,545 male and 1,278 female). Population growth in the province of Orellana was 84% during the period 1990 to 2001 (46,781 to 86,493 people).

Cancer Incidence

Eight of the ten confirmed cancer cases were diagnosed in males with more than one type of cancer occurring only for stomach cancer. Six cases were diagnosed in the three years prior to the end of the study. Age at diagnosis ranged from 5 to 86 years.

The nature of the cases of cancer found and the corresponding expected numbers adjusted for age is shown in table 1. We did not find an excess for overall cancers. In the male population there were 8 cases observed and 8.8 expected; the standardized incidence ratio was 0.91 (95% CI 0.42-1.72). In the female population, the number of cases observed (2) was actually lower than the expected (8.9; O/E ratio 0.22; 95% CI 0.04 to 0.42).

Cancer mortality

Table 2 shows mortality due to cancer in the village of San Carlos in the 10 years of the study. We found no excess of deaths for all cancers (6 observed vs. 6.1 expected) in males. The Standardized Mortality Ratio (SMR) was 0.98 (95% CI 0.40 to 2.03). No deaths due to cancer were found in women (0 observed v 5.40 expected; 95% CI 0 to 0.46).

Discussion

We performed the preliminary assessment suggested by CDC guidelines[5] to the cluster of cancer cases of the village of San Carlos[1] in the light of the new published census data. Investigations of disease clusters may be useful when the disease of interest is rare and occurs primarily by a single disease process or mechanism. This is not the case in San Carlos where the disease of interest is not a single disease but several different types of cancer, some of which are quite common and known to develop through different pathological mechanisms. For example, among the types of cancer observed, cancer of the trachea/bronchus/lung, stomach cancer, colorectal cancer and liver cancer are each among the 20 leading causes of mortality in the world and therefore cannot be considered rare[9].

Population data are essential for defining and measuring public health problems and the groups of people associated with them. Census and vital registration statistics are the most fundamental sources of population data[10]. The Instituto Nacional de Estadística y Censos of Ecuador published a recent census in 2001[11]. It provides the population of the different villages of the canton La Joya de los Sachas[12], including the population of San Carlos (2,823 people). This census also indicates that the population in the province of Orellana grew 84% during the period 1990 to 2001[13]. This information modified considerably the number of expected incident cancers and deaths due to cancer and an excess number of cases in the village of San Carlos were not evident. According to the census, the number of inhabitants in the village of San Carlos in 1989 was almost 50% bigger than assumed by San Sebastian et al. (1471 vs. 1000) and grew at rate of 84% in 11 years. These two factors led to an estimation of the expected number that doubled the original one.

Differences in the estimation of the population of the village of San Carlos also determined the differences in the estimate of the SMR for cancer. It decreased from a mortality rate 3.6 times higher than expected in males to no excess of deaths for all types of cancer combined, SMR: 0.98 (95% CI 0.40 to 2.03). No deaths due to cancer were found in women. The source of mortality data can also explain part of this difference, GLOBOCAN estimates cancer mortality from National mortality data (1998-2000)[Error! Bookmark not defined.] corrected for estimated completeness (72% for male, 68% for female) [7]. This was not the case in the original San Sebastian analysis, in which no correction for estimated completeness was reported. In the original analyses mortality data was derived from the Quito reference population from 1989 to 1998. Quito is the only place in the country with an adequate cancer registry or publishing deaths by specific cause[14].

Cancer is not a single disease but a group of many different diseases each having its own set of risk factors and causal mechanisms. Indeed, environmentally caused cancer cases are generally thought to result from a single exposure source and to comprise one or two specific types of cancer. In the San Carlos study, eight different types of cancer were observed in ten people and only stomach cancer had more than one case reported. A review of epidemiologic studies shows that petroleum materials have not been associated with stomach cancer or the other seven reported cancers[15]. Stomach cancer is the second leading cause of cancer death worldwide, with high rates in Japan, China, Central and South America, including Ecuador. Several studies have indicated that diet is a major risk factor for stomach cancer. Reasons commonly cited for a decline of gastric cancer in developed countries include better refrigeration, reduced consumption of salted, smoked, and chemically preserved foods, and increased intake of fruit and vegetables[16,17]. A second factor, the bacterium Helicobacter pylori (H. pylori), is causally associated with peptic ulcer disease and is considered a primary risk factor in the development of stomach cancer[18] . Huang and Hunt[19] have noted that gastric carcinogenesis is a multi-step process which begins with H. pylori associated gastritis in most cases. San Sebastian et al did not adjust for the presence of these factors[1].

Given that all cancers except stomach were present only as single cases, it is impossible to determine whether an excess risk is present. The small numbers of cases are responsible for some seemingly artificial increases (eg. SMR for melanoma in males) or decreases (eg. SIR for all cases in females).

In summary, the census published in 2001 pointed to an underestimation of the population of San Carlos used by San Sebastian et al.[1,2,3] to analyze the cancer cluster of San Carlos. The use of census data for the calculation resulted in no excess cancer risk in the village of San Carlos. In addition, the small number of cases, the different types of cancer observed, and the absence of corroborating scientific research to support a causal link between crude oil and the types of cancer observed indicate a lack of biological plausibility for the hypothesis that oil production activities have caused the cancers observed in San Carlos.

While this revision of the cancer cluster observed near oil fields in the Amazon basin of Ecuador showed no increase in cancer in the village of San Carlos, it should also encourage the pursue of further studies on cancer in the region. These studies should accrue sufficient number of cases to allow the study of individual types of cancer and ensure that exposure to oil derivatives is determined at an individual level and the presence of confounders can be ascertained and adjusted for. Maximum resources and scientific know-how should be placed in the accomplishment of such goal.

Table 1. Cancer Incidence in the village of San Carlos, 1999 (ICD= International Classification of Diseases; O= number of observed cancer cases).

CANCER		Male			Female		
	ICD-9	O	E	SIR (95%CI)	O	E	SIR (95%CI)
All Cancers[a]	140-208	8	8.79	0.91 (0.42-1.72)	2	8.90	0.22 (0.04-0.42)
Stomach	151	3	1.84	1.63 (0.45–4.35)			
Liver [b]	155-156	2	0.29	6.90 (1.37-22.1)			
Larynx	161	1	0.12	8.33 (0.75-35.8)			
Melanoma	172	1	0.10	10 (0.9-46.6)			
Leukaemia [c]	204	1	0.56	1.79 (0.16-8.33)			
Lymphoma [d]	202				1	0.33	3.03 (0.27-14.13)
Cervix	180				1	1.84	0.54 (0.04-2.53)
Others [e]		0	5.89	0 (0 – 0.42)	0	6.73	0 (0 – 0.37)

[a] All cancers excluding non-melanoma skin cancer..
[b] Includes 1 case of cancer of the ampulla of Vater=others and non-specific from the biliary tract.
[c] Acute lymphoblastic leukaemia.
[d] Non-Hodgkin's lymphoma.
[e] Other cancers are, in each gender category, those not observed in the village of San Carlos study.

Table 2. Cancer mortality in the village of San Carlos, 1999 (ICD= International Classification of Diseases; O= number of observed cancer cases).

CANCER		Male		
	ICD-9	O	E	SMR (95%CI)
All Cancers [a]	140-208	6	6.10	0.98 (0.40 – 2.03)
Stomach	151	3	1.53	1.96 (0.54 -5.23)
Liver [b]	155-156	2	0.48	4.16 (0.83 – 13.35)
Melanoma	172	1	0.03	33.3 (3.02 – 155)
Others [c]		0	4.05	0 (0 – 0.61)

[a] All cancers excluding non-melanoma skin cancer..
[b] includes 1 case of cancer of the Ampulla of Vater=others and non-specific from the biliary tract.
[c] Other cancers are those not observed in the village of San Carlos study.

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