British Journal of Cancer (2003) 89, 951–953

www.bjcancer.com

Letters to the Editor

Glucocorticoid use and skin cancers

MP Purdue[*,1]

[1]*Division of Preventive Oncology, Cancer Care Ontario, Toronto, Canada M5G 2L7*

British Journal of Cancer (2003) **89,** 951–952. doi:10.1038/sj.bjc.6601221 www.bjcancer.com

Sir,

Karagas *et al* (2001) reported modest elevations in risk of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) accompanying oral steroid use but not for use of inhaled steroids. The absence of effect from inhalants was attributed to their limited systemic effects of glucocorticoids. Another possible explanation, however, is the presence of bias owing to the confounding effects of asthma, a condition for which inhaled glucocorticoids are often used.

Asthma and other atopic conditions such as eczema and hay fever are often treated with corticosteroids and have been found by some epidemiologic studies to be associated with a reduced risk of many types of cancers, although these findings are not consistent l (Vena *et al*, 1985; McWhorter, 1988; Mills *et al*, 1992; Kallen *et al*, 1993; Vesterinen *et al*, 1993). It has been postulated that the hypersensitivity to allergens associated with these conditions protects against cancer by providing superior recognition of, and immune response to, tumour antigens (Volkers, 1999). Consequently, if atopic conditions do confer protection from cancer, the failure to adjust for atopic disease in the original analysis would bias the estimated relative risks of both oral and inhaled glucocorticoids towards the null.

A reanalysis of data pertaining to oral glucocorticoid use presented in the paper by Karagas *et al* suggests the possibility of such confounding. Table 1 provides the distribution among cases and controls of oral glucocorticoid use (use for 1 month or longer) subcategorised by reason for possible steroid use. The data for steroid users were pooled into two groups: one group representing subjects treating possibly atopic conditions (specifically, those using steroids for 'respiratory conditions and asthma' and 'allergy') and the other group representing subjects with other conditions (those categorised under other reasons).

Table 1 Distribution of oral glucocorticoid use and skin cancer (based on data presented in Table 1 of Karagas *et al*, 2001)

Steroid use[a]	Reason	Controls *N* (%)	BCC *N* (%)	SCC *N* (%)
No		491 (88.8)	534 (85.9)	245 (81.9)
Yes	Any	31 (5.6)	44 (7.1)	27 (9.0)
	Treat possible atopic conditions[b]	16 (2.9)	14 (2.3)	10 (3.3)
	Treat possible non-atopic conditions[c]	15 (2.7)	30 (4.8)	17 (5.7)

BCC = basal cell carcinoma; SCC = squamous cell carcinoma. [a]Use of oral glucocorticoid use for 1 month or longer. [b]Includes 'respiratory conditions and asthma' and 'allergies'. [c]Includes 'musculoskeletal and connective tissue disease', 'neoplasm', 'gastrointestinal disease', 'other'.

Table 2 Association between oral glucocorticoid use to treat possible atopic/non-atopic conditions and skin cancer risk

Steroid use[a]	Reason	BCC OR (95% CI)	SCC OR (95% CI)
No		—	—
Yes	Any	1.31 (0.81–2.10)	1.75 (1.02–2.99)
	Treat possible atopic conditions[b]	0.80 (0.39–1.67)	1.25 (0.56–2.80)
	Treat possible non-atopic conditions[c]	1.84 (0.98–3.46)	2.27 (1.12–4.62)

BCC = basal cell carcinoma; SCC = squamous cell carcinoma; OR = odds ratio; CI = confidence interval. [a]Use of oral glucocorticoid use for one month or longer. [b]Includes 'respiratory conditions and asthma' and 'allergies'. [c]Includes 'musculoskeletal and connective tissue disease', neoplasm, gastrointestinal disease, other.

*Correspondence: MP Purdue; E-mail: mark.purdue@cancercare.on.ca

Crude odds ratios with accompanying 95% confidence intervals were calculated to measure the association between risk of BCC and SCC and oral steroid use (Table 2). Stronger increases in risk of each skin cancer were found for steroid use to treat (supposedly) non-atopic conditions, compared to nonusers. Steroid use to possibly treat atopic conditions was not found to be associated with either type of cancer. These findings suggest that the effects of atopic conditions may confound the association between glucocorticoids and skin cancer risk. The analysis is limited in that the odds ratios have not been adjusted for other confounding factors, although the adjusted odds ratios in the original analysis were very similar in magnitude to the unadjusted odds ratios. Another limitation involves the fact that four cases (two BCC, two SCC) that received steroid treatment for conditions in more than one category were not identified as such in the original table, and so could not be adjusted for in this analysis. However, other analyses involving different assumptions about the possible joint conditions suggested that the findings would not be greatly influenced by this problem. Both of these issues could be addressed by the authors through reanalysis of the original study data. It would also be interesting to know whether a similar reanalysis of inhaled steroid use resulted in comparable findings.

REFERENCES

Kallen B, Gunnarskog J, Conradson TB (1993) Cancer risk in asthmatic subjects selected from hospital discharge registry. *Eur Respir J* **6**(5)**:** 694 – 697

Karagas MR, Cushing Jr GL, Greenberg ER, Mott LA, Spencer SK, Nierenberg DW (2001) Non-melanoma skin cancers and glucocorticoid therapy. *Br J Cancer* **85**(5)**:** 683 – 686

McWhorter WP (1988) Allergy and risk of cancer A prospective study using NHANESI followup data. *Cancer* **62**(2)**:** 451 – 455

Mills PK, Beeson WL, Fraser GE, Phillips RL (1992) Allergy and cancer: organ site-specific results from the Adventist Health Study. *Am J Epidemiol* **136**(3)**:** 287 – 295

Vena JE, Bona JR, Byers TE, Middleton Jr E, Swanson MK, Graham S (1985) Allergy-related diseases and cancer: an inverse association. *Am J Epidemiol* **122**(1)**:** 66 – 74

Vesterinen E, Pukkala E, Timonen T, Aromaa A (1993) Cancer incidence among 78,000 asthmatic patients. *Int J Epidemiol* **22**(6)**:** 976 – 982

Volkers N (1999) Wheezing, sneezing, and cancer risk – still an open door. *J Natl Cancer Inst* **91**(22)**:** 1916 – 1918

Reply: Glucocorticoid use and skin cancers

MR Karagas*,[1] and DW Nierenberg[1]

[1]*Departments of Community and Family Medicine, Medicine, Pharmacology and Toxicology, and the Norris Cotton Cancer Center, Dartmouth Medical School, Lebanon, NH 03756, USA*

British Journal of Cancer (2003) **89,** 952–953. doi:10.1038/sj.bjc.6601222 www.bjcancer.com

Sir,

We appreciate Dr Purdue's interest in our report on use of glucocorticoids and skin cancers. As suggested in his letter, we reclassified indication for steroid use into two categories: (1) atopic conditions (i.e. 'respiratory conditions and asthma' and 'allergies') and (2) non-atopic conditions (i.e. 'musculoskeletal and connective tissue disease', 'neoplasm', 'gastrointestinal disease', and 'other condition') (Table 1). In the reanalysis of the data, we noted an error in Table 1 of the original report. There were only two controls that used glucocorticoids for allergies (the seven controls in the original report included users of inhaled steroids). The correct numbers appear in Table 1 below and are restricted to oral users. The odds ratios associated with oral glucocorticoid use, stratified by Dr Purdue's classification, are shown in Tables 2 and 3. The results for 'any use' differ very slightly from the original report because we removed individuals with more than one indication or with missing data on the indication for use for this reanalysis.

Table 1 Oral glucocorticoid use according to indication among skin cancer cases and controls

Steroid use[a]	Indication	Controls *N* (%)	BCC *N* (%)	SCC *N* (%)
No		491 (95.0)	534 (93.0)	245 (91.1)
Yes	Any use[b]	26 (5.0)	40 (7.0)	24 (8.9)
	Treat possible atopic conditions[c]	11 (2.1)	12 (2.1)	9 (3.4)
	Treat possible non-atopic conditions[d]	15 (2.9)	28 (4.9)	15 (5.6)

BCC = basal cell carcinoma; SCC = squamous cell carcinoma. [a]Use of oral glucocorticoid use for 1 month or longer. [b]Excludes three individuals with more than one indication (two BCC, one SCC) and two individuals with missing data on indication for use (one BCC, one SCC). [c]Includes 'respiratory conditions and asthma' and 'allergies'. [d]Includes 'musculoskeletal and connective tissue disease', 'neoplasm', 'gastrointestinal disease', 'other condition'.

*Correspondence: MR Karagas;
E-mail: Margaret.R.Karagas@Dartmouth.EDU