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Epidemiological study of alendronate-related osteonecrosis of the jaw in the southeast of Scotland

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Abstract

We aimed to establish the incidence of alendronate-related osteonecrosis of the jaw (ONJ) in the southeast of Scotland, and to assess the effect of corticosteroids on it. We studied a prospective case series of patients between June 2004 and March 2012 separated into steroid and non-steroid groups. There were 34 cases of alendronate-related ONJ and 78 732 drug patient years (DPY) of alendronate, making the overall occurrence 43.1 cases/100 000 DPY. There were 12 patients in the steroid group (mean (range) age 68.2 (48-87) years) making 42.5 cases/100 000 DPY, and 22 in the non-steroid group (mean (range) age 76.2 (63-91) years) making 119.6 cases/100 000 DPY. The mean (range) age at presentation of alendronate-related ONJ was significantly lower in the steroid group (68.2 (48-87) compared with 76.2 (63-91) years, $p = 0.019$) as was the duration of exposure to alendronate before it developed (28.9 (6-120) compared with 61.3 (13-168) months, $p = 0.03$). The overall incidence seems to be higher in the southeast of Scotland than elsewhere. Concurrent use of corticosteroids is not associated with an increased incidence of alendronate-related ONJ, but it seems to reduce the duration of exposure before it develops. Age is likely to be a confounding factor.

Keywords: Bisphosphonate; Osteonecrosis; Jaw; Incidence

Introduction

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a rare but debilitating adverse effect of bisphosphonate drugs. It is defined by the American Association of Oral and Maxillofacial Surgeons (AAOMS) as the presence of exposed bone or bone that can be probed through an intraoral or extraoral fistula that has persisted for more than 8 weeks in a patient who is being, or has been, treated with a bisphosphonate, and has no history of radiation to the jaws.[1] It is usually associated with long-term use of bisphosphonates, and is thought to be dependent on both the dose and the duration of treatment.[2]

It is hard to calculate the incidence of BRONJ, as it may not always be recognised or reported.[3] The incidence among patients with cancer who are given bisphosphonates intravenously is much higher than in patients who take them for osteoporosis, either orally, intravenously, or both.[1] Reports range from fewer than 1% - 11%[4] in patients who are given them intravenously, and fewer than 1% - 4% in those who take them orally.[5–7]

Some retrospective studies have reported risk factors that may be associated with its development. They include the use of corticosteroids or chemotherapy,[8] increasing age,[9] a history of smoking,[10] poor oral hygiene, obesity,[10] and diabetes,[11] as well as the site of the operation (either the mandible or the maxilla), the dose, type of bisphosphonate,

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and duration of exposure to the drug.[9] The risk is thought to be higher in patients who take corticosteroids at the same time as a bisphosphonate.[8]

The results of a recent collaborative study suggest that in the United Kingdom there are around 620 new cases of BRONJ each year,[12] which, in a population of 62 million, equates to a risk of 1/100 000/year. The risk for postmenopausal women in the UK who take bisphosphonates orally is between 1/1000 and 1/10 000/year. This does not include the number of men who may be taking oral bisphosphonates.

We aimed to establish the incidence of alendronate-related ONJ in the southeast of Scotland and to assess the effect of concomitant treatment with corticosteroids given systemically.

Material and methods

The southeast of Scotland includes the Lothians and the Borders, and has a population of around 950 000.[13] The oral and maxillofacial unit for the region is spread across 2 sites and has a database of all patients who have presented with BRONJ (as defined by the AAOMS) after taking alendronate orally. Those who developed BRONJ after the use of any other bisphosphonate, either orally or intravenously, were excluded. Data from June 2004 to March 2012 were collected prospectively and included sex, age, date of presentation, site affected, whether prednisolone had also been used, and duration of treatment with alendronate. We then separated the patients into 2 groups, those who took steroids and those who did not.

We derived the number of drug patient years (DPY) of alendronate dispensed in this region of Scotland from 1998 (when these data were first recorded) from the National Services Scotland Information Services Division.[13] The DPY statistic takes into account the fact that the duration of exposure to the drug (in this case alendronate) is different for different subjects. We then calculated the overall number of cases of alendronate-related ONJ (as cases/100 000 DPY) together with separate figures for those who did, and did not, take steroids. To calculate this we divided the number

Table 1
Distribution of age and sex, site of osteonecrosis, and duration of alendronate.

	Age (years)	Sex	Spontaneous/ extraction	Site	Duration of bisphosphonate (months)
Non-steroid group:					
1	67	F	Extraction	Mandible	24
2	82	F	Spontaneous	Mandible	13
3	64	F	Extraction	Mandible	36
4	78	F	Extraction	Maxilla	120
5	81	F	Extraction	Mandible	43
6	85	F	Extraction	Mandible	80
7	83	F	Extraction	Mandible	84
8	91	F	Spontaneous	Mandible	48
9	63	F	Extraction	Maxilla	60
10	76	F	Extraction	Mandible	60
11	67	F	Extraction	Mandible	36
12	87	F	Spontaneous	Mandible	72
13	73	F	Spontaneous	Mandible	96
14	78	F	Spontaneous	Mandible	24
15	66	F	Extraction	Maxilla	24
16	78	F	Extraction	Mandible	144
17	83	F	Extraction	Maxilla	45
18	80	F	Extraction	Maxilla	168
19	72	F	Extraction	Mandible	81
20	72	F	Extraction	Maxilla	18
21	78	F	Extraction	Mandible	24
22	73	F	Extraction	Mandible	48
Steroid group:					
23	56	F	Extraction	Maxilla	12
24	48	M	Extraction	Mandible	6
25	62	F	Spontaneous	Mandible	10
26	80	F	Extraction	Mandible	22
27	72	F	Spontaneous	Mandible	17
28	87	M	Extraction	Mandible	24
29	68	F	Extraction	Mandible	10
30	82	F	Extraction	Mandible	120
31	60	F	Extraction	Mandible	12
32	70	M	Spontaneous	Mandible	6
33	63	F	Extraction	Maxilla	36
34	70	M	Extraction	Maxilla	72