Pharmaceutical treatment of symptomatic vertebral fractures in primary care

D J Torgerson, D Sykes, S Puffer, P Brown, C Cooper

Background: Vertebral fractures are associated with a reduction in quality of life and are an important predictor of other non-spine fractures. Previous work has shown that up to 60% of patients with a vertebral fracture identified in primary care remain untreated.

Objective: To examine the prevalence of pharmaceutical treatment and predictors of treatment in a primary care setting.

Methods: Case–control study using the general practice research database (GPRD). All women aged 50 years and over with a first diagnosis of a vertebral fracture between 1990 and 1999 were identified and matched with a control by age and practice. Appropriate use of a pharmaceutical agent was defined as a prescription occurring within 30 days of the diagnosis being recorded.

Results: We identified 2719 women with the same number of controls. Within 30 days of diagnosis, 61% of women were prescribed treatment, compared with only 3% of the controls. Bisphosphonate was the single most important treatment prescribed. Predictors of any drug treatment included: year of fracture (most recent year increased the likelihood of treatment); age (younger patients were more likely to receive treatment); history of back pain; low body weight; history of steroid use.

Conclusions: Treatment of diagnosed vertebral fractures is becoming more common. Treated patients tend to be younger but to have a higher prevalence of clinical risk factors than untreated patients. There remain significant numbers of patients who are not offered treatment.

METHODS

We identified all women aged 50 years and over who were diagnosed with an incident vertebral fracture between the years 1990 to 2001 and who were registered with a general practice that contributed data to the general practice research database (GPRD). The GPRD is a computerised database that contains the medical records of 685 general practices in the United Kingdom. This is approximately 6% of the total registered population. The GPRD contains all the routine medical data held on GP computer records (with the patients’ names and addresses deleted). Thus it includes demographic and routine clinical information (such as prescription details, clinical events, referrals, and major outcomes) and is representative of the UK primary care population. A recent validation of the database found that fracture diagnosis was confirmed by an x-ray report in more than 85% of cases.

Because there is evidence that early treatment of vertebral fractures is effective we classified women as being “treated” if they were treated within 30 days of the diagnosis being made. Treatment was defined as receiving one or more prescriptions of the following drugs: alendronate, risedronate, etidronate, calcium with or without vitamin D, HRT (including tibolone), or raloxifene. For this analysis, women treated after 30 days were classified as being untreated.

As well as identifying the number of women receiving treatment within 30 days, we wanted to determine whether there were any important variables that GPs took into account when they were prescribing treatment. We therefore undertook multivariate analyses to evaluate characteristics that predicted whether a woman was prescribed treatment or not.

To ascertain whether the diagnosis of a vertebral fracture increased the prevalence of treatment relative to no diagnosis, we sampled an equal number of age and practice matched control women.
The greatest increase for bisphosphonates. Cases showed a much greater absolute rise in drug use, with rose from 1.1% to 3.13% in the controls. Nevertheless, there was a small rise in the use of antifracture agents by the control group—for example, bisphosphonate use slightly, the same variables remained statistically significant (that is, year of fracture (OR = 1.06, p = 0.005); age (OR = 0.96, p < 0.001), back pain (OR = 1.59, p < 0.001), weight less than 58 kg (OR = 1.33, p = 0.01), and use of steroids (OR = 1.58, p < 0.001). Because women using HRT were so much younger than the rest of the sample, we examined whether excluding this group changed the results. While the odds ratios changed slightly, the same variables remained statistically significant (mean difference 2.2 kg; p < 0.001). Women who were prescribed antifracture treatment were more likely to have received oral corticosteroids (19.3% (n = 321), v 13.0% (n = 138) of women who did not receive antifracture treatment (p < 0.001)). However, there was no difference in previous history of non-vertebral fracture. In a stepwise logistic regression model the significant predictors of any treatment prescription were: year of fracture (OR = 1.06, p < 0.001), age (OR = 0.96, p < 0.001), back pain (OR = 1.59, p < 0.001), weight less than 58 kg (OR = 1.33, p = 0.01), and use of steroids (OR = 1.58, p < 0.001).

Results of antifracture drugs.

Antifracture drug treatment rose sharply among vertebral fracture cases had received a prescription for pharmaceutical treatment within one month of the diagnosis of the index fracture. Interestingly, as table 2 shows, there was a small rise in the use of antifracture agents by the control group—for example, bisphosphonate use rose from 1.1% to 3.13% in the controls. Nevertheless, the cases showed a much greater absolute rise in drug use, with the greatest increase for bisphosphonates.

Table 2  Comparison of clinical characteristics and drug use of cases and controls

<table>
<thead>
<tr>
<th>Clinical characteristic</th>
<th>Cases (n = 2719)</th>
<th>Controls (n = 2719)</th>
<th>Difference (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75 (10)</td>
<td>75 (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>61.88 (13.14)</td>
<td>64.60 (12.89)</td>
<td>2.72 (1.91 to 3.53)</td>
<td>0.122</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.43 (13.15)</td>
<td>158.25 (13.28)</td>
<td>0.82 (0.46 to 1.67)</td>
<td>0.804</td>
</tr>
<tr>
<td>Steroid users (1+ prescriptions in year before fracture)</td>
<td>459 (16.9%)</td>
<td>121 (4.5%)</td>
<td>12.43 (10.82 to 14.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Women reporting back pain in year before fracture</td>
<td>540 (19.9%)</td>
<td>71 (2.6%)</td>
<td>17.25 (15.64 to 18.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number (%) with a previous non-vertebral fracture</td>
<td>364 (31.8%)</td>
<td>516 (19.0%)</td>
<td>12.80 (10.51 to 15.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bone drug prescriptions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>213 (7.8%)</td>
<td>31 (1.1%)</td>
<td>6.70 (5.62 to 7.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HRT</td>
<td>123 (4.5%)</td>
<td>94 (3.5%)</td>
<td>1.00 (0.04 to 2.04)</td>
<td>0.045</td>
</tr>
<tr>
<td>Calcium and vitamin D</td>
<td>75 (2.8%)</td>
<td>75 (2.8%)</td>
<td>0.00 (0.00 to 0.00)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean (SD) or n (%). CI, confidence interval; HRT, hormone replacement therapy.

Table 3 shows that the most commonly prescribed treatments were bisphosphonates, followed by calcium. Of the bisphosphonates, etidronate was the most prescribed product. Similar numbers of women were prescribed the other bisphosphonates and HRT. Women using HRT were substantially younger than the cohort as a whole (mean age, 63.7 years). In contrast, women using calcium tended to form the oldest portion of the cohort (mean age, 77.2 years). There was a tendency overall for more younger women to receive treatment than older women. For women aged less than 70 years and for those aged 70 to 75, similar proportions were treated within 30 days (302 women (68.6%) aged less than 70 years, and 464 women (68.2%) aged 70 to 75 years). In contrast, significantly fewer women aged over 75 years received treatment (393 (57.9%) and 302 (48.1%) for women aged 76 to 82 and 83+ years, respectively).

The proportion of untreated women tended to fall with time. In fig 1 we show the main treatment categories by year of vertebral fracture diagnosis. The number of untreated women fell throughout the 1990s. The addition of new pharmaceutical treatments, such as alendronate, in the mid-1990s did not appear to decrease the use of existing drugs; rather there was an increase in the proportion of treated women.

Discussion

In contrast to a previous study looking at prescription of drugs after vertebral fracture diagnosis, we found the majority of women were prescribed a drug within 30 days of fracture diagnosis. The most common treatments prescribed were etidronate, followed by calcium with vitamin D.
Relatively few women were prescribed raloxifene treatment. This may be because raloxifene was licensed relatively recently compared with the other drugs. We also noted relatively few women using risendronate, probably for the same reason. Drug treatment following vertebral fracture would usually be initiated in primary care and therefore would be identified from the GPRD.

The proportion of women who were offered treatment has increased in the last decade. Thus the proportion of women receiving a bone active agent has increased from less than 20% in the early 1990s to over 50% at the end of the decade. The most significant clinical characteristic associated with a vertebral fracture that appeared to trigger a prescription was the use of corticosteroids. Other common risk factors, such as a previous non-vertebral fracture, were not associated with treatment. We had intended to examine whether the use of bone densitometry had any effect on prescription rates; however, we identified only 10 women (0.37%) who had had densitometry measurements recorded.

Clearly we could only examine the prevalence of treatment among women for whom the fracture diagnosis had been made. Most vertebral fractures remain undiagnosed with only about 30% coming to clinical attention\(^1\) and probably, therefore, the vast majority of such patients will remain untreated.

Although there has been a welcome increase in the proportion of women receiving treatment for the prevention of fractures, there is still a significant minority with a diagnosed vertebral fracture that remains untreated. Furthermore, while the use of calcium with vitamin D supplementation has been shown to reduce the incidence of non-vertebral fractures within a nursing home environment, other treatments in conjunction with calcium supplementation are more effective. For example, the bisphosphonates (such as risendronate) and raloxifene have been shown in large randomised trials to be more effective at fracture prevention than calcium supplementation alone.\(^9\)\(^-\)\(^1\)\(^1\) Furthermore, bisphosphonate supplementation has been found to be a relatively cost-effective treatment option among women with a previous vertebral fracture.\(^1\)\(^2\) HRT use was relatively low, probably because of the age of the population. We could not tell whether the use of HRT among women with a vertebral fracture diagnosis fell after the women's health initiative (WHI) study\(^1\)\(^3\)—which showed increases in breast cancer and cardiovascular events—as our data were obtained before that study was published.

In addition to these findings, we also showed that diagnosed vertebral fracture rates were lower than expected; it is therefore likely that many vertebral fractures remain undiagnosed and hence untreated.

### Table 3 Use of drugs 12 months after diagnosis of vertebral fracture

<table>
<thead>
<tr>
<th>Bone drug prescriptions</th>
<th>Cases (n = 2719)</th>
<th>Controls (n = 2719)</th>
<th>Difference (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonates</td>
<td>1347 (49.5%)</td>
<td>85 (3.1%)</td>
<td>46.41 (44.40 to 48.38)</td>
<td>(p &lt; 0.001)</td>
</tr>
<tr>
<td>HRT</td>
<td>327 (12.0%)</td>
<td>122 (4.5%)</td>
<td>7.54 (6.10 to 9.00)</td>
<td>(p &lt; 0.001)</td>
</tr>
<tr>
<td>Calcium and vitamin D</td>
<td>433 (15.9%)</td>
<td>70 (2.6%)</td>
<td>13.35 (11.87 to 14.87)</td>
<td>(p &lt; 0.001)</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>20 (0.7%)</td>
<td>0 (0)</td>
<td>0.74 (1.13 to 0.44)</td>
<td>(p &lt; 0.001)</td>
</tr>
</tbody>
</table>

Value are n (%). CI, confidence interval; HRT, hormone replacement therapy.

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**Figure 1** Main treatment categories by year of vertebral fracture diagnosis.
In conclusion, the use of pharmaceutical treatments has increased with time, but many women remain undertreated.

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