Managing corticosteroid induced osteoporosis in medical outpatients

ABSTRACT – As a preliminary step to developing a protocol for the management of corticosteroid induced osteoporosis we examined the case notes of patients attending medical clinics and studied the first 100 consecutive patients estimated to have taken 1 gram or more of prednisolone, or equivalent, in the previous six months. The patients who satisfied the inclusion criteria represented 2% of all medical outpatients. Inflammatory arthritis and obstructive airways disease together accounted for 50% of cases. The average daily dose of corticosteroids was highest in the respiratory patients (12 mg) and lowest in the rheumatology patients (7.5 mg). The question of osteoporosis had been considered in 47% of cases: of these, 27 (57%) were diagnosed as having osteoporosis by bone mineral density measurement or x-ray appearances, and 93% of the latter patients were receiving treatment for osteoporosis. The results indicate that while most physicians were aware of the problem of corticosteroid induced osteoporosis and treated most patients when diagnosed, more than 50% of patients on significant doses of corticosteroids were not investigated. We have therefore devised a management protocol and implemented it within the medical directorate.

Corticosteroids produce a net loss of bone through a number of mechanisms which result in a greater rate of bone resorption than formation1. The consequent long-term risk for fracture is approximately three times greater than of equivalent patients not treated with corticosteroids2. The risk of fracture is related to the dose and duration of treatment as well as to other factors such as patient’s age, sex, disease, race, etc. While there is uncertainty about primary prevention of bone loss in patients requiring corticosteroids, there is now evidence that treatment of established corticosteroid induced osteoporosis with agents such as hormone replacement therapy (HRT)3, bisphosphonates4,5, calcitriol and calcitonin6 is effective in increasing bone mass and likely to reduce the risk of fractures.

The aims of this study were to establish the proportion of outpatients who were receiving long-term corticosteroids; whether the occurrence of osteoporosis was being considered in those patients; whether and how the diagnosis was confirmed or refuted and what proportion of patients diagnosed were subsequently treated. The results would be used to aid in the production of a management protocol.

Methods

Case notes for all patients attending medical clinics for rheumatology, respiratory medicine, gastroenterology, elderly medicine and dermatology at Poole Hospital NHS Trust were examined daily by a single observer. The case notes of the first 100 consecutive patients estimated, from the written records of the managing physicians, to have taken 1 gram or more of prednisolone, or equivalent, in the previous six months were examined for written or typed statements that answered the following questions:

1. Had a diagnosis of osteoporosis been considered?
2. Had a diagnosis of osteoporosis been substantiated or refuted and by which method?
3. If the diagnosis had been confirmed, had appropriate treatment been started?
4. If the diagnosis had been excluded, had the patient and/or GP been advised on preventive measures and had a repeat bone mineral density (BMD) measurement been arranged?

At Poole Hospital BMD measurement by dual energy x-ray absorptiometry (DEXA-Lunar DPX) or quantitative computed tomography (QCT) has been available since 1991. BMD measurements are reported in terms of standard deviations above/below the mean for normal young adults (T score). According to the definition of the World Health Organization (WHO)7 osteoporosis is diagnosed if the BMD is more than 2.5 standard deviations (SD) below the mean for young adults. In some cases osteoporosis was considered likely if spinal radiographs showed osteopenia and at least one vertebral fracture, other causes of pathological fracture having been excluded.

The information collected on data sheets was transferred to a Statistical Package for Social Services (SPSS) database for analysis. With reference to the results of the survey and published guidelines8,9 a management protocol has been adopted by members of the medical directorate.

Results

A total of 4,816 case notes was examined in order to identify the 100 patients; thus approximately 2% of medical outpatients attending specialist clinics were receiving the equivalent of 5 mg of prednisolone or
more per day. The total number of case notes examined, age and sex of patients, percentage of patients on 5 mg of prednisolone or more and mean and standard deviation of the daily prednisolone dose during the previous six months are shown in Table 1 for each specialty. The most common diagnoses are shown in Table 2. Inflammatory arthritis and obstructive airways disease together accounted for half of the cases.

Overall, a diagnosis of osteoporosis had been considered in 47% of patients (rheumatology 68%, respiratory medicine 48%, elderly medicine 42%, gastroenterology 25% and dermatology 21%). In the 47 cases where a diagnosis of osteoporosis was considered, it was confirmed in 27 (57%), 16 by DEXA, 3 by QCT and 8 by x-rays. In 13 cases (28%) the diagnosis of osteoporosis was excluded, all by DEXA, and in 7 cases (15%) the diagnosis was neither confirmed nor excluded.

At least 25 (93%) patients who had a diagnosis of osteoporosis confirmed were receiving treatment (16 cyclical etidronate, 6 calcitomin, 1 calcium, 2 vitamin D and calcium, 0 HRT). One of the two patients not prescribed treatment according to the hospital notes was involved in a clinical drug trial and the other had been diagnosed by the general practitioner but no treatment details were available. Of the 13 patients on corticosteroids in whom a diagnosis of osteoporosis had been excluded, only two had documented evidence of counselling, three had had their corticosteroid dose reduced, one had been referred to the physiotherapy department for exercises, one had been advised about the importance of calcium and four were booked for repeat BMD measurements within the next two years.

Discussion

Any survey of British hospital case notes suffers from the difficulty of extracting uniform data. Nevertheless, the case notes that record the day-to-day management of the individual patient in a prospective fashion are likely to be an unbiased source of information to answer a research question asked some time later. We therefore contend that this method of data retrieval is valid. The utilisation of specific simple questions and a single observer trained in case-note analysis was designed to minimise attainment error.

While there is some debate about the safety of low dose corticosteroid therapy, there is little doubt that prolonged use of prednisolone in doses over 7.5 mg per day is associated with increased risk of osteoporosis10 and postmenopausal women and men lose bone on even lower doses11. Wolfe and colleagues have recently presented some worrying data concerning side effects on average daily doses of 5.5 mg prednisolone12. While the risk/benefit ratio remains uncertain we took a pragmatic view that a cumulative dose of corticosteroids of more than 1 gram of prednisolone in the last six months (5 mg per day) had potentially significant effects on bone and would be worthy of clinical consideration.

It is clear from the numbers of case notes surveyed in the different specialties (Table 1) that more patients were seen per week in rheumatology and dermatology than in other specialties. This represents hospital practice and may be different in different hospitals. This selection bias may have influenced the frequencies of diagnoses shown in Table 2. Nevertheless, our findings of a high prevalence of obstructive airways disease and inflammatory arthritis are in keeping with those of an inpatient study by Peat et al3 and suggest that these conditions account for the majority of corticosteroid treated patients in hospital populations. Of interest is the apparent low frequency of corticosteroid use in dermatology patients (2.5%). In reality the frequency of current corticosteroid use in our population of approximately 600 patients with inflammatory arthritis is 23% but most patients take less than 5 mg of prednisolone per day. These figures are in general agreement with the community based study of Walsh and colleagues14 who found 0.5% of the general population were taking 'continuous' (for at least three months) treatment, the most common diagnoses being rheumatoid arthritis, polymyalgia rheumatica and asthma. They found only 14% had received any treatment to prevent osteoporosis.

Table 1. Patient characteristics by specialty

| Specialties      | Patients (SD) | Percentage on corticosteroids | Mean (SD) dose |
|------------------|---------------|-------------------------------|---------------|
| Rheumatology     | 1,227 (15)    | 39                            | 7.7 (2.8)     |
| Respiratory      | 601 (14)      | 36                            | 11.9 (3.2)    |
| Medicine        | 690 (17)      | 8                             | 1.7 (5.4)     |
| Gastroenterology| 539 (25)      | 49                            | 9.0 (4.0)     |
| Dermatology      | 1,690 (19)    | 31                            | 8.8 (4.0)     |
| All specialties  | 4,816 (19)    | 32                            | 9.8 (6.1)     |

Table 2. Diagnoses of patients taking steroids

| Diagnosis             | Percentage of patients |
|-----------------------|------------------------|
| Inflammatory arthritis| 28                     |
| Obstructive airways disease | 22                 |
| Bullous skin diseases | 10                     |
| PMR/TA                | 12                     |
| Inflammatory bowel disease | 9                    |
| Connective tissue diseases | 4                    |
| Others                | 15                     |
The WHO has defined osteoporosis as a BMD measurement more than 2.5 standard deviations below the mean for young adults. However, the diagnosis can also be made with reasonable certainty in other situations; for example, where spinal x-rays show vertebral fractures in the absence of other pathological causes. In this study, 8 of 27 cases were diagnosed on radiological evidence alone. However, x-rays are insensitive measures of osteoporosis and reliance on them to exclude the diagnosis is likely to result in many missed cases where intervention might reduce the risk of fracture. This apparent reliance on x-rays may have resulted in underdiagnosis in the corticosteroid-treated sample studied.

The diagnosis of osteoporosis was confirmed in 57% of patients in whom the possibility had been raised. This may be an overestimate because of the lack of BMD measurement in 53 cases, but even if all the latter were in the normal range the incidence of osteoporosis in the study group would still be 27%.

The majority of patients with diagnosed osteoporosis were receiving treatment with cyclical etidronate or calcitonin. While this may be appropriate on published evidence, it is surprising that none of the patients was receiving HRT. This point has been taken into account in the treatment options subsequently recommended. It should also be noted that the cost of treatment with subcutaneous calcitonin is high and treatment with calcitriol requires regular monitoring of serum calcium because of the risks of hypercalcaemia.

A published protocol has been adopted by the members of the medical directorate (Fig 1). Patients who have received 1 gram of prednisolone over the previous six months are recommended to follow the protocol but patients taking lower doses may also be included. All patients are advised to have a DEXA scan of hip and spine and a lateral x-ray of the lumbar spine. Patients diagnosed as having osteoporosis according to the WHO criteria will be prescribed treatment with one of the agents shown in the protocol, according to the preference of the managing physician (as none of the treatments are currently licensed for the treatment of corticosteroid-induced osteoporosis). Patients with significant radiological abnormalities may need further investigation to help clarify the diagnosis, for example lateral x-ray of the thoracic spine to look for vertebral fractures or QCT of the lumbar spine to measure BMD in the presence of osteophytes. An annual repeat scan is recommended for patients...
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remaining on corticosteroids but whose DEXA results are above the osteoporosis threshold. Patients who are losing bone rapidly (> 4% per year) are at risk and treatment is recommended. It is planned to repeat the audit cycle in two years.

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