Physician's Awareness of the Prevention of Corticosteroid Induced Osteoporosis

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Background and Objective: *Corticosteroid induced osteoporosis (CIO) is a preventable condition that is often not realized by physicians who prescribe corticosteroids. The present study was carried out to study the awareness of CIO prevention in a teaching hospital.*
Material and Method: *The medical records of patients who received corticosteroids equivalent to prednisolone of ≥ 5 mg/day for a minimum of 3 months between 1 May 2004 and 30 June 2004 were reviewed.*
Results: *Four hundred and forty nine patients of 1,540 who received corticosteroids (29.1%) were included in the present study. Rheumatologists, nephrologists, and dermatologists were the top three specialists to prescribe corticosteroids in 189 (42.1%), 103 (23.0%), and 46 (10.2%) cases, respectively. Only 146 patients (32.5%) received calcium supplement. Rheumatologists and neurologists were the top two specialists to prescribe calcium supplementation in 100 of 189 (52.9%) and 13 of 36 (36.1%) cases, respectively. Bone mineral density measurement was determined in only 26 of the 449 patients (5.8%).*
Conclusion: *Prevention of CIO is still neglected by internal medicine specialists, even in a teaching hospital. An educational campaign for physicians is warranted to improve the practice for the prevention of this treatable complication.*

Keywords: *Corticosteroid, Osteoporosis, Prevention, Awareness*

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Corticosteroids are widely used in the treatment of many chronic non-infectious diseases that are related to the immune system, particularly in rheumatic and connective tissue diseases. Use of corticosteroids in clinical practice varies in both the daily dosage and duration of the treatment, depending on the diagnosis and activity of the diseases. Prolonged use of corticosteroids is associated with a wide range of adverse reactions, including electrolyte imbalance, elevation of blood sugar and lipids, thinning of the skin, muscle weakness, hypertension, glaucoma, avascular necrosis of the bone, adrenal gland suppression, and osteoporosis[1].

Osteoporosis is a serious complication of corticosteroid therapy. It can lead to fractures, which in turn, increase both morbidity and mortality in the patients[2-4]. The skeletal side effect of corticosteroids appears to be both dose and duration dependent. A daily dosage equivalent to prednisolone of 7.5 mg for more than 3 months can result in significant bone loss and increased fracture risk[5-7]. A recent meta-analysis showed that oral corticosteroid use of more than 5 mg/day could reduce bone mineral density, and rapidly increase the risk of fracture during the treatment period and decrease it after stopping therapy[8]. Bone loss begins at 1 month and reaches maximal rate during the first 3-6 months of therapy[4]. Post menopausal women who received long term corticosteroid therapy had approximately twice as much risk of developing a fracture than those who did not receive corticosteroids[8].

Corticosteroid induced osteoporosis (CIO) is a preventable disease. However, previous studies showed that only 4.5-5.5% of the patients treated with corticosteroids received bone-active medication (e.g. estrogens, bisphosphonate, vitamin D and calcitonin) to prevent bone loss[9,10]. In 1996, the American College

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of Rheumatology (ACR) recommended that calcium supplement should be given to all patients who received corticosteroids equivalent to prednisolone ≥ 7.5 mg/day for more than 6 months[11]. In 2001, the recommendation was changed to calcium supplement given to all patients who received corticosteroids equivalent to prednisolone ≥ 5 mg/day for more than 3 months[12]. This signifies the seriousness of CIO that needed early treatment.

As corticosteroids are widely used to treat immune mediated diseases, particularly in teaching care hospital, the present study was aimed to study the awareness of osteoporosis prevention among physicians who prescribed corticosteroids in a teaching hospital.

Material and Method

A computer search for out-patients who were prescribed corticosteroids at a dosage equivalent to prednisolone of ≥ 5 mg/day between 1 May 2004 and 30 June 2004 was done at the pharmacy section of Chiang Mai University Hospital. The present study period was chosen prior to research planning (October 2004) in order to avoid bias in the prescription of calcium supplement. From hospital pharmacy records, the medical data of patients who were 14 years of age and older, and prescribed corticosteroids at a dosage that was equivalent to prednisolone of ≥ 5 mg/day for more than 3 months, were selected for analysis. The diagnosis of patients, osteoporosis prevention, and specialists, who prescribed corticosteroids was recorded. Bone mineral density measurement and drugs used to treat osteoporosis were also noted. The patients were divided into three groups according to their dosage of corticosteroids that had equivalence to prednisolone as follows: low dose = prednisolone < 15 mg/day; moderate dose = prednisolone 15-30 mg/day and high dose = prednisolone > 30 mg/day. Patients were excluded if they received corticosteroids irregularly. The present study was approved by the Ethic Committee of the Faculty of Medicine, Chiang Mai University. Data were expressed in frequency and percent.

Results

During the present study period, 449 cases of 1,540 (29.1%) who had received corticosteroids met the study criteria. There were 83 males (18.5%) and 366 females (81.5%), with a ratio of male to female of 4.4:1. The age group distribution of patients who received corticosteroids is shown in Table 1. Eighty-six female

Table 1. Age distribution of patients receiving corticosteroids

Age (years)*	Number (%)
14-19	24 (5.4)
20-29	77 (17.1)
30-39	88 (19.6)
40-49	137 (30.5)
50-59	80 (17.8)
60-69	18 (4.0)
70-79	25 (5.6)
80 and more	0 (0.0)
Total	499 (100.0%)

* Mean ± SD 37.7±18.6
* Median (range) 43.2 (14-79)

Table 2. Details of disease specialties that required corticosteroid treatment

Specialty/disease	N	(%)
1. Rheumatology	189	42.1
Systemic lupus erythematosus (n = 115)		
Rheumatoid arthritis (n = 27)		
Others (n = 47)		
2. Nephrology	103	23.0
Systemic lupus erythematosus (n = 55)		
Nephritic syndrome (n = 33)		
Others (n = 15)		
3. Dermatology	46	10.2
Systemic lupus erythematosus (n = 11)		
Pemphigus (n = 10)		
Cutaneous vasculitis (n = 4)		
Others (n = 21)		
4. Hematology	41	9.1
Idiopathic thrombocytopenic purpura (n = 19)		
Autoimmune hemolytic anemia (n = 16)		
Others (n = 6)		
5. Neurology	36	8.0
Myasthenia gravis (n = 30)		
Others (n = 6)		
6. Endocrinology	22	4.9
Panhypopituitarism (n = 13)		
Others (n = 9)		
7. Ophthalmology	8	1.8
Ocular myasthenia gravis (n = 3)		
Others (n = 5)		
8. Pulmonology	4	0.9
Chronic obstructive lung disease (n = 4)		
Total	449	100.0

patients were older than 50 years old. Patients aged between 40-49 years were most commonly prescribed corticosteroids. Details of the specialists who prescribed corticosteroids and the diseases requiring that therapy are shown in Table 2. Rheumatologists, nephrologists and dermatologists were the top three specialties to prescribe corticosteroids in 189 (42.1%), 103 (23.0%), and 46 (10.2%) cases, respectively. Systemic lupus erythematosus was the most common disease of which corticosteroids were prescribed in 184 cases (40.9%).

Details of calcium supplementation in accordance to the specialist and dosage of corticosteroids received are shown in Table 3. Overall, only 146 of 449 patients (32.5%) received a calcium supplement for the prevention of CIO. The percentage of patients receiving calcium supplementation was similar with regard to the dosage of corticosteroids received. However, when looking at the specialists who prescribed corticosteroids, rheumatologists and neurologists were the top two specialists to prescribe calcium supplementation. In addition, there tended to be more prescriptions of calcium for patients who received higher doses of corticosteroids. Interestingly, none of the patients who were prescribed corticosteroids from ophthalmologists received calcium supplement.

Calcium gluconate was most commonly used for calcium supplementation (139 patients ; 95.2%). The dosage of calcium gluconate supplementation was 500, 1,000, and 1,500 mg/day in 68, 58, and 11 cases, respectively. Two patients received calcium supplementation at the dose of 3,000 mg/day. Of seven patients receiving calcium carbonate, four cases received 835mg/day and three cases received 1,670 mg/day. Vitamin D supplementation (calcitriol 0.25 ugm/day) was also prescribed by rheumatologists in 10 patients. All of these patients were older than 50 years, and had osteoporosis documented by bone mineral density (BMD) measurement. Hormonal therapy was given in four out of 86 female patients who were older than 50 years of age (3 by rheumatologists and 1 by endocrinologists). The patient who was prescribed hormonal therapy by endocrinologists had pan-hypopituitarism. Bisphosphonate was prescribed by rheumatologists in 12 patients who had osteoporosis. Ten of these 12 patients were also received vitamin D.

BMD measurement was done in only 26 of 449 patients (5.8%), with 24 of them ordered by rheumatologists. The other two patients were under the care of an endocrinologist and a neurologist. Osteoporosis and osteopenia were found in 15 (57.7%) and 10 cases (38.5%), respectively. The other patient had normal BMD. Four patients, younger than 50 years of age, were found to have osteoporosis. One was a 26-year-old patient who had been taking corticosteroids for 6 years. The other three patients were 36-38 years old, one was female with premature menopause.

The sources of medical care coverage were identifiable in 260 patients (57.9%). Of these patients, the universal coverage system covered 146 patients (56.2%), social security insurance covered 60 (23.1%), and the government service health welfare covered 39

Table 3. Calcium supplementation, according to the dosage of corticosteroids received and specialists

Specialists	Number of patients who received calcium supplement/corticosteroids			
	Whole group n/N (%)	Corticosteroids equivalent to prednisolone		
		< 15 mg/day n/N (%)	15-30 mg/day n/N (%)	> 30 mg/day n/N (%)
Rheumatologists	100/189 (52.9)	70/147 (46.9)	28/38 (73.7)	2/2 (100.0)
Nephrologists	19/103 (18.4)	13/77 (16.9)	5/22 (22.7)	1/4 (25.0)
Dermatologists	3/46 (6.5)	2/26 (7.7)	1/17 (5.9)	0/3 (0.0)
Hematologists	5/41 (12.2)	5/33 (15.2)	0/6 (0.0)	0/2 (0.0)
Neurologists	13/36 (36.1)	5/18 (27.8)	5/13 (38.5)	3/50 (6.0)
Endocrinologists	5/22 (22.7)	5/22 (22.7)	-	-
Ophthalmologists	0/8 (0.0)	0/3 (0.0)	0/4 (0.0)	0/1 (0.0)
Pulmonologists	1/4 (25.0)	1/2 (50.0)	0/2 (0.0)	-
Total	146/449 (32.5)	101/330 (30.6)	39/102 (38.2)	6/17 (35.3)

(15.0%). The other 15 patients (5.8%) paid for themselves. BMD measurement was carried out in seven patients (4.8%) in the universal coverage system group, 3 (5.0%) in the social security insurance group, and nine (23.1%) in the government service health welfare group. The medical care coverage was not known in seven patients who had BMD measurement.

Diseases associated with the prolonged use of corticosteroids were common among the studied patients. They included hypertension in 89 patients (33.8%), infection in 66 (25.1%), dyslipidemia in 60 (22.8%), diabetes mellitus in 22 (8.4%), avascular necrosis of the bone in six (2.3%), osteoporotic fracture in five (1.9%), myopathy in four (1.5%), and glaucoma in two (0.8%).

Discussion

In the present study, it was found that the majority of patients (70%) were prescribed corticosteroids for a short period of time, i.e. less than 3 months. Long-term corticosteroids prescription was prescribed mostly by rheumatologists (42.1%), followed by nephrologists (23.0%). Systemic lupus erythematosus was the most common disease being treated with long term corticosteroids (40.9%).

Overall, only 32.5% of the studied patients received calcium supplement to prevent CIO, and the dosage of corticosteroids did not affect the prescription of calcium supplementation. The prescription of calcium supplementation was mostly done by rheumatologists and neurologists at the percentage of 52.9% and 36.1% of their patients, respectively. The reason why rheumatologists prescribed calcium supplement to prevent CIO more than other specialties might be because they were more aware of the adverse effects of corticosteroids on the bone. It should also be noted that only 10 patients were given vitamin D in addition to calcium. They were all older than 50 years old and had osteoporosis. The reason for the low prescription of vitamin D supplementation in the present study might be because the majority of the studied patients were aged 30-59 years of age. Thus, the physicians might believe that the patients were not deficient in vitamin D. The data from a study in the urban area of Khon Kaen province showed that at least 34.9% of elderly women (mean age 69.4 years) had vitamin D deficiency[13].

In Thailand, the average age of menopause is approximately 50 years[14]. In the present study, only four of 86 female patients (4.6%) who were older than 50 years old received hormonal therapy. The explanations for the very low rate of hormonal therapy were the following: First, it might be because the majority of the patients were followed up at the Internal Medicine department. Most internists were unfamiliar with hormonal therapy and rarely prescribed hormones. Secondly, these women might be given hormonal therapy by their gynecologists, but the data were not evident in the medical records. Lastly, the Women's Health Initiative (WHI) study showed an increase in incidence of thrombo-embolism in women who took hormonal therapy[15]. This information made the physicians reluctant to prescribe hormones as shown by a significant decrease in the rate of hormonal replacement therapy after the WHI study was published[16].

The low prevalence of calcium supplementation to prevent CIO in the present study corroborated with previous reports from Western countries. Gudbjornsson et al studied 191 patients (mean age 66 years, 55% women) who were given corticosteroids for a minimum of 3 months in Northern Ireland[17]. They received vitamin D from fish oil, calcium, and milk products in 52%, 37%, and 91% respectively. Only 9% of the patients received bisphosphonate. Hormonal therapy was given in 22% of the post-menopausal women. In a review by van Staa et al, 683 patients in England and Wales received corticosteroids for a minimum period of 6 months[10]. The majority of the patients were 70-79 years of age, and their mean dosage of corticosteroids was equivalent to prednisolone at 8.1 mg/day. Only 4.5-5.5% of the patients received osteoporosis prevention medications (estrogens, bisphonates, vitamin D, or calcitonin). Walsh et al studied 303 patients (55 years or older, 65% women) who received corticosteroids at an average dose equivalent to 8.0 mg/day of prednisolone for more than 3 months. They found that only 14% of the patients received osteoporosis prevention. Only 19% of the women, who were older than 45 years, received hormonal therapy[18]. It should be noted that in all these three studies, corticosteroids were prescribed mainly by rheumatologists and pulmonologists. Therefore, the rate of CIO prevention in the present study was quite similar to those in Western countries.

In the present study, only 26 patients (5.8%) received BMD measurement, and all but one was found to have osteopenia or osteoporosis. To date, BMD is the best laboratory measurement for detecting osteoporosis. The low rate of BMD measurement in the present study might be related to several factors. BMD measurement is an expensive test. Only 15% of the presented patients could receive reimbursement

of the expense from the government service health welfare coverage. However, patients with the universal coverage system and/or the social security health insurance were able to get the test only after they were approved by authorized personnel. Recently, the Osteoporosis Self-Assessment Tool for Asians (OSTA) index, an equation using only the body weight and age to assess the possibility of osteoporosis, has been developed[19]. This could help minimize unnecessary BMD measurement screening. However, this tool was developed for post-menopausal osteoporosis. Whether it could be applied to patients receiving long term corticosteroids is not known.

Conclusion

In the present study, it was found that even in a teaching hospital many physicians, who prescribed corticosteroids, were not aware of CIO and did not prescribe calcium to prevent it. An educational campaign for physicians who prescribe corticosteroids is warranted to prevent this treatable complication, especially with fracture, which is the serious complication of osteoporosis.

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การศึกษาความตระหนักของแพทย์ในการให้การป้องกันภาวะกระดูกพรุนจากยาคอร์ติโคสเตียรอยด์

ศุภรัตน์ อึ้งประเสริฐ, ศุภราภรณ์ วังแก้ว, วรวิทย์ เลาห์เรณู

ความเป็นมาและวัตถุประสงค์: *ภาวะกระดูกพรุนที่เกิดจากยาคอร์ติโคสเตียรอยด์เป็นภาวะที่ป้องกันได้ แต่มักจะไม่ได้รับการสนใจโดยแพทย์ผู้สั่งยา การศึกษามีวัตถุประสงค์เพื่อประเมินความตระหนักของแพทย์ในการป้องกันภาวะกระดูกพรุนจากการสั่งจ่ายยาคอร์ติโคสเตียรอยด์*

วัสดุและวิธีการ: *เป็นการศึกษาเวชระเบียนผู้ป่วยนอกที่ได้รับยาคอร์ติโคสเตียรอยด์ในขนาดที่เทียบเท่ายาเพรดนิโซโลนขนาด ≥ 5 มก./วัน เป็นเวลานาน 2 เดือน ในช่วงระหว่างวันที่ 1 พฤษภาคม พ.ศ. 2547 ถึงวันที่ 30 มิถุนายน พ.ศ. 2547*

ผลการศึกษา: *ช่วงเวลาดังกล่าวมีผู้ป่วย 1,540 รายที่ได้รับยาคอร์ติโคสตียรอยด์ จากจำนวนนี้มี 449 รายที่เข้าเกณฑ์การศึกษา พบว่าอายุรแพทย์โรคข้อและรูมาติสซั่ม แพทย์โรคไต และแพทย์โรคผิวหนัง เป็นกลุ่มแพทย์ที่สั่งจ่ายยาคอร์ติโคสเตียรอยด์มากที่สุด และสั่งจ่ายเป็นจำนวน 189 ราย (ร้อยละ 42.1), 103 ราย (ร้อยละ 23.0) และ 46 ราย (ร้อยละ 10.2) ตามลำดับ มีผู้ป่วยเพียง 146 ราย (ร้อยละ 32.5) ที่ได้แคลเซียมเสริมโดยอายุรแพทย์โรคข้อและรูมาติสซั่ม และแพทย์ระบบประสาท เป็น 2 กลุ่มแพทย์ที่ให้แคลเซียมเสริมมากที่สุด โดยมีการสั่งจ่ายในผู้ป่วย 100 ราย (ร้อยละ 52.9) และ 13 ราย (ร้อยละ 36.1) ตามลำดับ มีผู้ป่วยเพียง 26 ราย (ร้อยละ 5.8) ที่ได้รับการตรวจวัดความหนาแน่นมวลกระดูก*

สรุป: *แพทย์ส่วนใหญ่ยังไม่ได้ให้ความสนใจในการป้องกันภาวะกระดูกพรุนจากการสั่งยาคอร์ติโคสเตียรอยด์ การรณรงค์ให้ความรู้แก่แพทย์จึงมีความสำคัญเพื่อป้องกันภาวะแทรกซ้อนดังกล่าว*