The prescription and side-effects of steroids

A survey by the North-east England Faculty of the Royal College of General Practitioners

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PRESCRIBING steroids can be life-saving or cause considerable hazards. The numerous complications, both major and minor, due to the use of steroids are familiar to most practitioners. It was decided to investigate the prescribing of corticosteroids by general practitioners in the North of England and record the side-effects.

Soon afterwards a study on the prevalence of corticosteroid administration in the general population by the Wessex Faculty of the Royal College of General Practitioners was published (Sleet, 1969). A high incidence (16·4 per cent) of side-effects was noted with patients on prolonged therapy. An overall incidence of 12 per cent of all patients on steroids developed at least one complication and 0·4 per cent of the population of 248,256 were prescribed steroids in a six-month period.

A retrospective controlled study of mortality and morbidity of the incidence of serious complications of corticosteroid therapy in respiratory disease was done at the Brompton Hospital (Smyllie and Connolly, 1968). This involved 550 patients who were steroid takers, and there were 499 controls. It was found that the incidence of serious side-effects was similar in those receiving corticosteroids as compared with those not receiving corticosteroids. However, gastro-intestinal bleeding, diabetes and mental disturbance occurred more frequently in the corticosteroid group. There was an increased frequency of complications with an increased dose.

Method

All general practitioners in the North of England were invited to take part. They were asked to complete one form for any patient receiving one or more prescriptions for steroids in the three months 1 October, 1970 to 31 December, 1970. Details of the patient's name, address, age, diagnosis, type of steroid, dose and whether continuous, intermittent or a short single course, was noted together with side-effects, if any, and whether a consultant or general practitioner initiated treatment.

Results

Seventy-six practices took part involving 154 doctors who were responsible for 358,910 people.

There were 1,201 patients who were steroid takers, an incidence of 0·3 per cent. The incidence per doctor varied between 0·05 per cent to 0·96 per cent of patients being prescribed steroids. The average size of practice was 2,331 patients, each doctor prescribing steroids for, on average, eight patients.

Of the 1,201 steroid takers, 455 (38 per cent) were male and 746 (62 per cent) were female.

The age distribution is shown in figure 1. In the 0–5 year age group there were four children on steroids and in the 5–10 year age group there were 11 steroid takers.

The diseases for which steroids were prescribed are shown in table I. The most

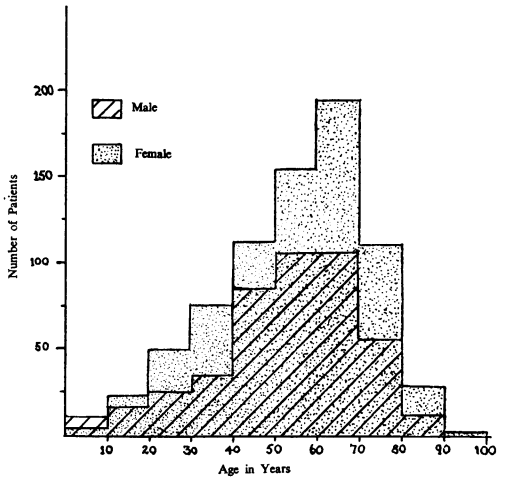

Figure 1
Age distribution

TABLE I

DISEASES FOR WHICH STEROIDS WERE PRESCRIBED. PERCENTAGES IN BRACKETS

Disease	*Male*		*Female*		*Male and female combined*	
Asthma	252	(*55·0*)	342	(*46·0*)	594	(*50·0*)
Rheumatoid arthritis	52	(*11·0*)	187	(*25·0*)	239	(*20·0*)
Other	21	(*5·0*)	58	(*8·0*)	79	(*7·0*)
Chronic bronchitis	53	(*12·0*)	21	(*3·0*)	74	(*6·0*)
Skin	17	(*4·0*)	21	(*3·0*)	38	(*3·0*)
Other collagen diseases	10	(*2·0*)	15	(*2·0*)	25	(*2·0*)
Carcinoma	4	(*0·9*)	19	(*3·0*)	23	(*2·0*)
Arteritis	8	(*2·0*)	10	(*1·0*)	18	(*1·5*)
Other blood	4	(*0·9*)	12	(*2·0*)	16	(*1·0*)
Allergic	8	(*2·0*)	8	(*1·0*)	16	(*1·0*)
Multiple sclerosis	6	(*1·0*)	9	(*1·0*)	15	(*1·0*)
Sarcoidosis	0	(*0·0*)	13	(*2·0*)	13	(*1·0*)
Other chest diseases	5	(*1·0*)	8	(*1·0*)	13	(*1·0*)
Ulcerative colitis	5	(*1·0*)	7	(*0·9*)	12	(*1·0*)
Leukaemia	4	(*0·9*)	5	(*0·7*)	9	(*0·7*)
Hypo-adrenal	2	(*0·4*)	5	(*0·7*)	7	(*0·6*)
Crohn's disease	0	(*0·0*)	5	(*0·7*)	5	(*0·4*)
Kidney	4	(*0·9*)	1	(*0·1*)	5	(*0·4*)
TOTAL	455	(*100·0*)	746	(*100·0*)	1,201	(*100·0*)

noticeable difference between male and female is the larger proportion of men on steroids for asthma and chronic bronchitis and the greater proportion of women on steroids for rheumatoid arthritis. The bulk of steroids are prescribed for rheumatoid arthritis and asthma (69 per cent).

Steroid treatment was initiated with consultant advice in 57 per cent of the patients, general practitioners started treatment in 40 per cent and in three per cent this fact was not known. General practitioners were more inclined to initiate treatment in patients with asthma than in other diseases. Forty-nine per cent of asthmatics had treatment initiated by the general practitioner, 48 per cent with consultant advice and three per cent unknown. On the other hand, general practitioners were less inclined to initiate treat-

ment in patients with rheumatoid arthritis (36 per cent); consultant advice was sought in 59 per cent of cases of rheumatoid arthritis, with five per cent unknown. Consultant advice was nearly always sought in carcinoma, leukaemia, blood dyscrasias, ulcerative colitis, Crohn's disease, multiple sclerosis and hypo-adrenal and kidney disorders. General practitioners usually initiated treatment in allergies.

Prednisone or prednisolone were prescribed for 76 per cent of patients, seven per cent were given one of the ACTH preparations, three per cent were given cortisone or hydrocortisone and the remainder received either triamcinolone, betamethasone, methylprednisolone, enteric-coated prednisolone or dexamethasone.

Duration of treatment

Treatment is being given continuously to 75 per cent of patients, intermittently to 14 per cent, as a short single course to eight per cent and in three per cent it may have been given as a short course leading to intermittent or continuous treatment. A smaller proportion than average of asthmatics (68 per cent) were given steroids continuously; 91 per cent of patients with rheumatoid arthritis were on continuous treatment. Duration of treatment is shown in figure 2.

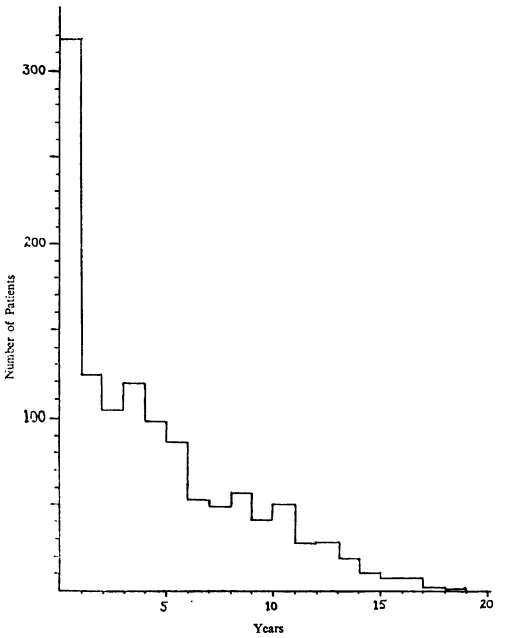

Figure 2
Duration of treatment

Side-effects

Of the 1,201 steroid takers, 305 patients (25 per cent) were noted to have one or more side-effects. In all, 441 side-effects were noted. Most were minor complaints such as moon face, but 199 (45 per cent) could be classified as major side-effects. Table II lists the side-effects. Statistical analysis shows that males are less likely to develop side-effects than females.

There were 898 patients on continuous treatment with various types of cortico-steroids. Of these 266 (30 per cent) developed side-effects. Male patients on continuous treatment numbered 335 and in 80 (24 per cent) of these, 112 side-effects were noted. There were 563 females and in 186 (33 per cent), 278 side-effects were noted.

TABLE II

SIDE-EFFECTS NOTED (PERCENTAGES IN BRACKETS)

	Side-effect	*Male 455 patients* number	per cent	*Female 746 patients* number	per cent	*All 1,201 patients* number	per cent
MINOR	Facial mooning	38	(8·4)	100	(13·4)	138	(11·5)
	Excessive weight gain	22	(5·0)	61	(8·2)	83	(6·9)
	Purpura	2	(0·4)	4	(0·5)	6	(0·5)
	Hirsutism	0		4	(0·5)	4	(0·3)
	Thinning of hair	0		4	(0·5)	4	(0·3)
	Acne	3	(0·7)	1	(0·1)	4	(0·3)
	Cramp	1	(0·2)	2	(0·3)	3	(0·25)
	Total number of minor side-effects	65	(15·0)	176	(24·0)	242	(20·0)
MAJOR	Peptic ulcer or severe dyspepsia	13	(2·9)	25	(3·6)	38	(3·2)
	Sodium retention, oedema	5	(1·1)	31	(4·2)	36	(3·0)
	Osteoporosis; spont. fracture	9	(2·0)	23	(3·0)	32	(2·7)
	Hypertension	6	(1·3)	13	(1·7)	19	(1·6)
	Severe laceration or bruising after minor trauma	4	(0·9)	15	(2·0)	19	(1·6)
	Cataract	3	(0·7)	8	(1·1)	11	(0·9)
	Diabetes mellitus	6	(1·3)	4	(0·5)	10	(0·8)
	Depression	3	(0·7)	7	(0·9)	10	(0·8)
	Other	4	(0·9)	4	(0·5)	8	(0·7)
	Recurrent sepsis	3	(0·7)	1	(0·1)	4	(0·3)
	Pulmonary tuberculosis	3	(0·7)	0		3	(0·25)
	Steroid myopathy	0		3	(0·4)	3	(0·25)
	Shock due to withdrawal of steroids	0		2	(0·3)	2	(0·2)
	Death	0		2	(0·3)	2	(0·2)
	Stunted growth	0		2	(0·3)	2	(0·2)
	Total number of major side-effects	59	(13·0)	140	(19·0)	199	(17·0)

Proportion of males with minor side-effects is significantly different from that of females at the 0·1 per cent level ($x^2=14·50$ $P<0·001$).

Proportion of males with major side-effects is significantly different from that of females at the 1 per cent level ($x^2=6·88$ $P<0·01$).

In all patients on continuous treatment with prednisone or prednisolone an increased incidence of side-effects was noted with an increased dose and also an increased incidence of side-effects the longer the duration of treatment. Females seem more prone than males in this group.

Table III records male and female patients on continuous treatment with prednisone or prednisolone so that doses can be compared more easily. Slight differences in total numbers are due to incomplete data. Statistical analysis shows that with increasing dose there is a highly significant increased incidence of side-effects in males but not a statistically significant difference in females. With an increased duration of treatment there is a highly significant increase in side-effects with females but not with males.

There was no significant difference in the type of steroid given to males and females on continuous treatment. Most patients (77 per cent of males and 74 per cent of females) on continuous treatment were on prednisone or prednisolone.

Two deaths occurred during this period. One was due to pyelonephritis and the other to acute or chronic suprarenal failure.

TABLE III

PATIENTS ON CONTINUOUS TREATMENT WITH PREDNISONE OR PREDNISOLONE

Number of patients with side-effects			
Dosage	*Male*	*Female*	*Total*
0– 5 mgm ..	4 out of 12 (*33·0*)	11 out of 57 (*19·0*)	15 out of 69 (*22·0*)
5–10 mgm ..	18 out of 103 (*18·0*)	52 out of 174 (*30·0*)	70 out of 277 (*25·0*)
10–15 mgm ..	25 out of 107 (*23·0*)	45 out of 145 (*31·0*)	70 out of 252 (*28·0*)
15–20 mgm ..	8 out of 25 (*32·0*)	13 out of 31 (*42·0*)	21 out of 56 (*38·0*)
20–25 mgm ..	1 out of 5 (*20·0*)	0 out of 5 (*0·0*)	1 out of 10 (*10·0*)
	$x^2=13·85$ $P<0·01$	$x^2=3·79$ $P>0·05$	
Duration	*Male*	*Female*	*Total*
0– 5	34 out of 170 (*20·0*)	50 out of 236 (*21·0*)	84 out of 406 (*21·0*)
5–10	18 out of 59 (*31·0*)	43 out of 116 (*37·0*)	61 out of 175 (*35·0*)
10–15	6 out of 24 (*25·0*)	30 out of 62 (*48·0*)	36 out of 86 (*42·0*)
15–20	1 out of 5 (*20·0*)	2 out of 5 (*40·0*)	3 out of 10 (*30·0*)
	$x^2=2·78$ $P>0·05$	$x^2=21·62$ $P<0·001$	

Because of the small numbers in 20–25 mgm and 15–20 year groups these have been combined with the group below. With this adjustment, the significance is stated.

Side-effects classified under 'other' included thinning of the skin, slow wound healing, vasculitis, skin pigmentation, confusional state and two patients had renal colic. These latter two were included as it seems possible that this may result from the effects of excess calcium excretion.

Discussion

It is interesting that general practitioners are still very cautious about prescribing steroids and usually seek consultant advice before starting treatment. The exceptions are allergies which represent a small proportion and asthma where an acute attack may demand urgent treatment with corticosteroids.

The larger proportion of men on steroids for asthma and chronic bronchitis could be because men, being the wage earners, require more vigorous treatment to keep them at work. More women (70 per cent) suffer from rheumatoid arthritis and presumably are more likely to get severe attacks, accounting for the slightly higher proportion of women on steroids for rheumatoid arthritis.

The results indicate a high incidence of side-effects due to steroids and demonstrate again that the higher the dose the more side-effects there are likely to be and also that the longer the course of treatment the greater the number of side-effects. Women taking steroids seem to run a greater risk than men.

The prescribing rate is similar to that in the Wessex Faculty survey, but the number of side-effects noted is higher here. This emphasises the difficulty in noting side-effects; many patients develop more than one. People on steroids constitute a closely observed group, and it may be that many of these patients would have developed some of the illnesses reported as side-effects if they had not been on steroids. The Brompton Hospital survey of chest patients suggested this. A prospective controlled study would be long and difficult to arrange and probably subject to bias.

Osteoporosis is one of the most difficult side-effects to assess. Lindholm (1960) showed an incidence of 20 per cent in 144 patients on long-term steroids or ACTH for asthma. A control group had an incidence of 11 per cent. Nordin (1964) studied the calcium metabolism in 36 patients on steroids for six months to seven years. He found

that osteoporosis was present in all patients given more than 20 mg of cortisone or its equivalent per day. In this group of patients only three per cent were noted as suffering from osteoporosis, indicating how difficult it is to diagnose. Occasionally patients complain of nerve root pain in the thoracic region and no abnormality is reported on x-ray of the spine but repeat x-ray later may show a compression fracture.

Despite all the side-effects there is no doubt that corticosteroids are life-saving and improve the quality of life in many patients with a variety of diseases. They should never be withheld when indicated.

Most general practitioners maintain a simple regime of prescribing steroids and intermittent treatment (giving steroids on a few days each week) is not often used. It was thought at one time that continuous treatment given intermittently had a lower risk of side-effects (Walsh and Grant, 1966). Recently it has been shown by Grant *et al.* (1970) to be no more effective than continuous daily treatment in preserving the response to stress of the hypothalamo-pituitary-adrenal axis. The intermittent group (14 per cent) of steroid takers in this survey included patients on recurrent short courses having perhaps a ten day course of steroids three or four times a year.

Maunsell *et al.* (1968) found that side-effects were not significantly related to length of treatment but to the average dose of steroid used. In this survey longer duration of treatment in females caused a significantly higher incidence of side-effects but not in males. There was no evidence of a higher dosage the longer the duration of treatment. Indeed most practitioners try to reduce the dose as time goes on. The finding that increase in side-effects is related to dosage in males and duration in females is not accounted for by a predominance of dosage-related side-effects in males with asthma or duration-related side-effects in females with rheumatoid arthritis, these being the single diseases most prevalent in each sex of the patients on continuous prednisone therapy. It may be that these rather unusual observations are because of the small numbers involved in high dosage and long-term takers.

From the practical point of view it is often difficult to be precise as to the exact total dose of steroids. Some patients are notoriously liable to alter the dose themselves—even intelligent people who have been warned about the danger of sudden reduction and who have been given a steroid card. Some patients will even give tablets to their friends to try. However, there is a consistent tendency for woman to have more side-effects than men.

Summary

The incidence of prescribing corticosteroids in general practice in the North of England is discussed with a description of diseases for which they are prescribed and a discussion of side-effects. It is suggested that women may be more prone to side-effects than men.

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