

Correspondence

Comparison of oral prednisolone and intramuscular depot triamcinolone in patients with severe chronic asthma

Sir,—I am very interested in the report of Dr RF Willey and his colleagues (May 1984;39:340–4).

Having had over 15 years experience of long term therapy with triamcinolone acetonide in asthmatic patients, I would like to contribute a few comments of my own. According to the references cited it might be assumed that so far only one paper has been published on this type of therapy. In fact, there have been a great many publications dealing with this problem.

Our group (apart from papers published in Polish medical journals) has published seven reports on this type of therapy in English and German medical journals.^{1–7}

During the third and fourth Charles Blackley symposia in Nottingham, in 1978 and 1981, we presented our experiences of this type of therapy. Since triamcinolone acetonide was rarely used in the United Kingdom, however, our communications did not arouse much interest.

The principles included in Dr Willey's report seem open to question, as does his interpretation. This would seem to derive from his assumption that the weight of triamcinolone acetonide in dosage is equivalent to that of triamcinolone. This is, however, not the case. According to information made available to investigators by ER Squibb Ltd triamcinolone acetonide (in rats) is 10 times more potent in anti-inflammatory and nine times more potent in neoglucogenetic properties than triamcinolone alcohol and prednisolone. To achieve an equivalent dosage of triamcinolone and prednisolone the weight of triamcinolone acetonide should be multiplied by 12. Therefore Dr Willey's statement to the effect that 80 mg of triamcinolone acetonide every 28 days is equivalent to 3.43 mg of prednisolone daily is incorrect. In fact, it is a very high dose, equivalent to over 35 mg of prednisolone daily.

In long term therapy we never exceed 1.7 mg of triamcinolone acetonide (80 mg every six weeks) as a calculated daily dosage, and when the need to exceed this dosage arises this means that the treatment must be changed and another type of steroidal drug applied, because 1.7 mg of triamcinolone acetonide daily is, in our opinion, equivalent to 16 mg of triamcinolone in tablet form.

In long term treatment of the majority of steroid dependent patients, we usually achieve good results with 1.0–1.2 mg of triamcinolone acetonide daily (equivalent of 2–3 tablets of triamcinolone). We never give injections of triamcinolone acetonide at regular intervals, but give them only when a patient exceeds the safe dosage of bronchodilators. This type of treatment excludes an unnecessary excess of glucocorticoid administration. When Dr Willey's therapy is analysed it is not surprising that 30% of the patients revealed signs of myopathy. We observed only two patients who developed myopathy among over 300 patients treated with triamcinolone acetonide over a period of two years. These two patients had been taking 80 mg of triamcinolone acetonide every three weeks without medical supervision. Nevertheless, our study on a group of 20 patients, treated with triamcinolone acetonide for an

average of 6.4 years and without clinical signs of myopathy, confirmed that in 15 of them an abnormal electromyographic tracing could be observed.

Four out of 12 of Dr Willey's patients showed menstrual disturbances. We do not know how many of the female patients were still menstruating (the ages of the whole group were given as 15–76 years). This side effect ought to have been discussed in terms of the percentage of females of reproductive age.

In our study menstrual disturbances were quite frequent, so we decided that women of reproductive age were not to be treated with triamcinolone acetonide.

Easy bruising was the most frequent side effect of triamcinolone acetonide treatment, particularly in the elderly (we call this "kenalog hands"). This is very often the reason for taking patients off the triamcinolone acetonide regimen. It is extraordinary that this side effect was not observed in Dr Willey's study.

The authors conclude that better results can be achieved with triamcinolone acetonide than with prednisolone. This is true, but with a much higher equivalent dosage.

I fully agree that even with a high triamcinolone acetonide dose adrenal cortex suppression was less pronounced. Our "twin studies" (4) have revealed that long term triamcinolone acetonide therapy (more than six years) causes less damage to the adrenal cortex (21% abnormal tetracosactrin tests) than an equivalent dose of oral triamcinolone or prednisolone (42% abnormal tetracosactrin tests).

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- 1 Droszcz W, Malunowicz E, Lech B, Krawczyńska H, Madalinski M. Assessment of adrenocortical function in asthmatic patients on long-term triamcinolone acetonide treatment. *Ann Allergy* 1979;42:41.
- 2 Droszcz W, Malunowicz E, Lech B, Krawczyńska H, Madalinski M. Adrenocortical function in asthmatic patients on long-term triamcinolone acetonide therapy compared with oral steroid therapy. In: *Proceedings of The Third Charles Blackley Symposium on the Clinical Aspects of Allergic Disease*. Nottingham, 1978:21.
- 3 Droszcz W, Lech B, Malunowicz E, Piotrowska B. Factors in influencing adrenocortical suppression during long-term triamcinolone acetonide therapy. *Ann Allergy* 1980;44:174.
- 4 Droszcz W, Piotrowska B. The adrenocortical function in patients on long-term oral steroid therapy in comparison with triamcinolone acetonide treated patients — twin studies. In: *Proceedings of The Fourth Charles Blackley Symposium on the Clinical Aspects of Allergic Disease*. Nottingham, 1981:80.
- 5 Droszcz W, Piotrowska B, Malunowicz E, Lech B. Funktion der Nebennierenrinde bei Asthmapatienten, die über 5 Jahre mit Triamcinolonacetonid behandelt wurden. *Atemw Lungenkrkh* 1981;4:238.
- 6 Droszcz W, Chazan R. The effect of triamcinolone acetonide on the human phagocytosis by human polymorphonuclear leukocytes. *Int J Clin Pharmacol Ther Toxicol* 1982;20:306.
- 7 Droszcz W. Vergleichende unter Sudungen bei Langfristiger Anwendung von Depot-Triamcinolon und Depot-Betamethason in Behandlung Obstructiver Ventilationsstörungen unter besonderer Berücksichtigung der Neben-

nierenrinddefunktion. *Allergologie* 1983;6:71.

8 Pomorska R, Lech B, Droszcz W, Purska-Rowińska E. The effect of long-term triamcinolone acetonide therapy on the function of the neuromuscular system. *Pneum Pol* 1981;49:627.

. This letter was sent to the authors, who reply below.

Sir,—Professor Droszcz and Dr Piotrowska make some extremely important points in their letter. They are correct in the belief that our study was performed on the assumption that there was no difference between the potencies of triamcinolone and triamcinolone acetonide. The investigation was stimulated by the publication of the report in the *British Journal of Disease of the Chest* in 1979 entitled "Triamcinolone in corticosteroid-resistant asthma."¹ The authors of that study, like ourselves, used doses of Kenalog (triamcinolone acetonide) within the range recommended by the manufacturer in the *ABPI Data Sheet Compendium*² which does not indicate that there is any difference in potency between triamcinolone and triamcinolone acetonide. In experimental animal models it is apparent that triamcinolone acetonide is very much more potent than triamcinolone, but no data from studies in man appear to be available. We therefore have to concede that Professor Droszcz and Dr Piotrowska are perhaps correct in their criticism of the way in which we discussed our data. We think it possible, however, that the information provided by ER Squibb and Sons Ltd about their product Kenalog may have misled the majority, if not all, of the physicians who use this corticosteroid preparation. Although we accept that it is very difficult to assess the relative potencies of corticosteroids, especially when they are administered by different routes, this controversy about the potency of triamcinolone and triamcinolone acetonide highlights the great need for companies to be obliged to state the potency of their products. Perhaps hydrocortisone could be the standard drug with an assumed potency of 1 and the activity of all other corticosteroid preparations for oral, intramuscular, or intravenous compared with it.

If the argument put forward by Professor Droszcz and his colleague about the potency of triamcinolone acetonide is accepted, and so far as we are aware there are no data to

refute it, it remains difficult to explain why it causes less suppression of the hypothalamopituitary axis (HPA) than daily oral prednisolone in a dose of at least 10 mg. One explanation could be that a large dose of corticosteroid is available very soon after injection of Kenalog, but is not maintained for a full period of four weeks, towards the end of which serum and tissue levels may fall below physiological requirements, with consequent stimulation of the HPA axis. If this is the case treatment with Kenalog could be dangerous when given to patients who have HPA suppression, such as those patients in our study who had been taking large doses of oral prednisolone for a considerable time.

We concluded that we would not normally recommend triamcinolone (meaning triamcinolone acetonide) in preference to prednisolone because of side effects. If triamcinolone acetonide is indeed 10 times more potent than triamcinolone it could never be justified in preference to oral prednisolone in the long term management of bronchial asthma in the doses recommended by the manufacturers. Unfortunately, the data about the relative potencies of triamcinolone acetonide, prednisolone, and hydrocortisone are not published and are only available from ER Squibb and Sons Ltd as confidential information for clinical investigators.

Since publication of our paper we have learned from the manufacturers of Kenalog that it is not an intramuscular depot preparation and the reason for its prolonged but unpredictable duration of action is unknown. We have therefore to admit that even the title of our paper is incorrect.

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1 Peake MD, Cayton RM, Howard P. Triamcinolone in corticosteroid-resistant asthma. *Br J Dis Chest* 1979;73:39–44.

2 Squibb ER and Sons Ltd. In: *ABPI data Sheet compendium 1983–84*. London: Datapharm Publications, 1983.

Corrections

Peak flow rate records in surveys: reproducibility of observers' reports

In the paper by Dr KM Venables and colleagues (November 1984;39:828–32) we regret that there are errors in the first paragraph of the methods section, in which it is stated that recordings from 61 men were studied. Of the 23 persons employed in the electronics factory, 18 were in fact women. The beginning of the last paragraph of page 828 should read: "Recordings from 61 subjects formed the basis of the study. Thirty eight subjects (all male) were currently employed in a steel coating plant. . . and 23 (18 female) were employed in an electronics factory. . ." Elsewhere in the paragraph the word men should be taken to indicate subjects.

Bronchial reactivity to inhaled histamine and annual rate of decline in FEV₁ in male smokers and ex-smokers

Smoking, allergy, and the differential white blood cell count

In the two papers by Dr RG Taylor and others (January 1985) we regret that page numbers are missing from two of the references. In ref 10 on p 16 the pages are 17–22 and in ref 24 on p 21 they are 9–16.