Sandostene and Sandostene in Combination with Calcium: Clinical Effect in Various Dermatoses

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Although the usual initial enthusiasm associated with new therapeutic agents has levelled off, the antihistamines continue to be popular and useful medications. The large number of different antihistaminic agents now available together with their large-sales volume seemingly attest to their clinical value. Most clinicians have repeatedly observed variation in the clinical effect among different antihistamine drugs and the variation in the incidence of the type and degree of side effects with different antihistamines among individual patients is well known. The availability of various kinds of antihistaminic drugs and the investigation of additional ones, therefore, would appear to be justifiable.

Recently, a new antihistaminic agent, 1-methyl-4-amino-N'-phenyl-N'-(2'-thenyl)-piperidine tartrate has come to our attention. This substance ("Sandostene") has been the subject of considerable clinical (2, 3, 4) and laboratory (1, 5) investigation in Europe in the past several years. In common with some other antihistaminics, the following laboratory effects of Sandostene have been established: (1) antihistaminic action, (2) inhibition of acetylcholine, (3) adrenalin antagonism and (4) local anesthetic effect. Sandostene has been found to exhibit low toxicity (LD 50, intravenously, for the mouse 58 ± 3.5 mg./kg., for the guinea pig, 56 ± 5.6 mg./kg. and for the rabbit, 31 ± 3.4 mg./kg.) which values are greater than those of many other antihistaminics.

In addition to the above data, it has been demonstrated that in the presence of calcium, the toxicity of Sandostene is significantly decreased. (At the same time, this combination of drugs appears to lessen some of the untoward effects of intravenously administered calcium (e.g.) cardiac irregularities following rapid intravenous injection of large doses of calcium).

Finally, the ability to decrease tissue permeability has been demonstrated by various means for both calcium and Sandostene. Appropriate animal experiments have further established that combinations of cal-

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eium and Sandostene exhibit a remarkable synergistic effect in this direction (reduction of permeability of blood-aqueous-humour barrier as demonstrated by the fluorescein test, protection from edema observed in rats following intraperitoneal injection of "Dextran", protection from massive pulmonary edema and hemorrhage and death in rabbits following intravenous chloropicrin 1, 2, 5). The phenomenon of increased tissue permeability in certain allergic states

can be demonstrated in laboratory animals so that the clinical implications of this antipermcability effect are self evident.

Clinically, Sandostene and combinations of Sandostene with calcium in the form of Calcium-Gluconogalactogluconate (Neocalglucon) have been found to be effective in some patients with bronchial asthma, idio-pathic pruritus, some drug eruptions, urticaria, Quincke's edema, insect bite reactions, certain types of eczema ("exudative"), and rhinitis due to pollen allergy. Poor or indifferent results have been experienced in chronic urticaria, erythema nodosum, neurodermatitis, pruritus associated with diabetes or liver damage and asthma secondary to other conditions (3,4).

In view of the above, the application of Sandostene and combinations of Sandostene and calcium to some problems in clinical dermatology was undertaken. Various allergic and quasi-allergic dermatological diseases were of course selected. In addition, certain idiopathic dermatoses and pruritic states as well as pruritic phases or complications of what are generally regarded as non-allergic disturbances were included.

The following preparations and dosages were employed in this investigation: Sandostene Tablets each containing 25 mg. of 1-methyl-4-amino-N'-(2'-thcnyl)-piperidine tartrate. The usual dose was 25 mg. three to four times daily or 25 mg. two to three times daily with 50 mg. at bedtime. In some instances larger doses were necessary and in children approximately half the above amounts were administered.

Sandostene Calcium syrup (containing 50 mg. of 1-methyl-4-amino-N'-(2'-thenyl)-piperidine tartrate (Sandostene) together with calcium ion content of four grams of calcium gluconate per 16 c.cm). The average dose was one table spoonful three to four times daily but larger amounts were well tolerated. One third to one half the above dose was administered in children.

Sandostene and Neo-Calglucon in combination for intravenous administration. Ampoules containing 50 mg. Sandostene in 10 c.cm of a 10% solution of calcium gluconogalactogluconate (Neocalglucon). The usual dose of this intravenous preparation was 5-10 c.cm administered daily in hospitalized patients and two to three times per week in ambulatory patients.

Each of the above medications was administered alone in approximately half of the patients in this study and in various combinations in the remaining patients.

The purpose of this investigation was to determine the clinical effect of these Sandostene medications in various human pruritic dermatoses

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and to determine their effective dosage and the incidence and significance of side effects and toxicity. No attempt to provide a control series of patients was made and no placebos were given. The virtual impossibility of establishing adequate control on an investigation of this type was recognized and it was our opinion that the interpretation of results where placebo medications are provided would be both hazardous and inaccurate. In addition to this realistic attitude regarding controls, bland topical therapy, elimination of causative allergens and irritants when possible and in occasional instances, X-ray irradiation was employed concomitantly with the administration of the Sandostene preparations. In other words, the patients were treated in the more or less customary fashion usually employed by us for the particular dermatosis at hand but with the addition of the antihistaminic adjunct. No attempt to compare Sandostene with other antihistamines or other agents such as steroid substances, hormones, sedative medications, vaccines, etc., was made.

Approximately 200 patients were treated in this series. Of these, follow-up observation was adequate in only 168 individuals and the remaining patients were not included. The Sandostene medications were administered for only a few days or weeks in acute dermatoses but were given for periods of several weeks to many months in the more chronic dermatoses. The longest single continuous administration of Sandostene in this series was approximately nine months. In this individual patient, neurodermatitis lesions appeared to be favorably influenced with syrup Sandostene with calcium, three tablespoonfuls daily and intravenous injections one to three times per week in the beginning of therapy with more widely spaced injections later on.

The effect of Sandostene preparations in various dermatoses is set forth in Table I.

From the above, Sandostene and combinations of Sandostene with calcium appeared to be useful adjuncts in the management of patients with contact dermatitis, acute urticaria, penicillin and other drug eruptions, some patients with neurodermatitis, severe local reactions to insect bites and perhaps in some patients with forms of essential pruritus. The Sandostene medications were of no appreciable value or results were equivocal in atopic dermatitis, most of the patients with neurodermatitis, chronic urticaria and dermatographia, exfoliative dermatitis, infectious eczematoid dermatitis and nummular eczema and in isolated instances of a miscellaneous group of dermatoses.

With reference to the oral medications, the combination of Sandostene with calcium did not appear to be more effective than Sandostene alone except in isolated instances. Additional investigation and experience, however, will be required before definite opinions can be given in this matter. Where response to antihistamine therapy was favorable, the intravenous combination of these agents was particularly impressive. This was especially noteworthy in several patients hospitalized with severe generalized and pruritic dermatosis. In many instances the intravenous injection

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Response to Sandostene Therapy

totals 168

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was also very useful in ambulatory patients although less effective than with hospitalized patients because it could not be given as frequently.

Our experience indicates that Sandostene is well tolerated in both adults and children. Less than one per cent of the patients experienced drowsiness or other side effects. One patient complained of "heartburn" and an elderly man experienced transient dysuria (relationship to medication?) following ingestion of Sandostene tablets. In both instances

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these complaints cleared when the medication was discontinued. The intravenous preparation must be administered very slowly (approximately at the rate of one to two minutes per 2 c.cm in our experience) if the "flushing" reaction of calcium (which is of course transient and harmless but unpleasant to the patient) is to be obviated or minimized. A few of our ambulatory patients

experienced transient drowsiness or “grogg-iness” with the administration of 10 c.cm but this did not occur with smaller (5 c.cm) dosages.

Summary

Sandostene, a new antihistaminic alone and in combination with Neo-Calglucon was employed in the management of 168 patients with various dermatoses. In general, Sandostene was found to be a safe, useful and effective antihistaminic medication. The clinical effect of the intravenous combination of Sandostene and calcium was particularly impressive, especially in patients with severe generalized eruptions. The various Sandostene preparations employed in this investigation were well tolerated. The incidence of untoward side effects with the doses employed was less than one per cent.

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