SULPHADIMETHOXINE IN SOME PYOGENIC DERMATOLOGICAL DISORDERS

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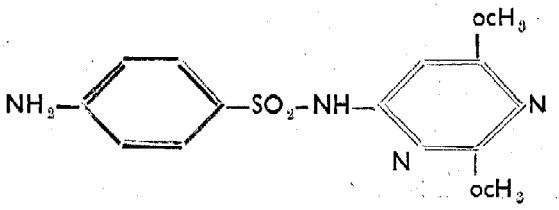
Introduction: In the year 1933, G. Domagk first administered prontosil to his four years old daughter who had developed septicaemia after a needle prick. Although, the then renowned surgeons as well as physicians had advised amputation, Domagk depended solely upon prontosil to save his daughter as well as her arm. For this bold and epoch making discovery, he was honoured with Nobel Prize in 1939.

Prontosil was synthesized by Mietzsch and Klarer at Eberfield Research Centre in West Germany. It has been reckoned as the starting point not only for the series of sulpha drugs but also for antibiotics. Fleming, a discoverer of penicillin, has aptly said that there could not have been penicillins without sulfonamides.

At present although various sulfonamides have crept into the physician's therapeutic armamentarium, the introduction of sulfa-methoxy-pyridazine in the year 1957 has ushered a new era of long-acting and single dose sulfonamides. The various long-acting sulfonamides at present available are-sulphamethoxypridazine (Lederkyn) and (Midikel), sulphaphenazole (Orisul) and sulphadimethoxine (Madribon). Long- acting sulfonamides form an easier, less troublesome as well as an economical form of treatment and are particularly suited for chronic pyogenic dermatological disorders.

Drug: Unlike othr sulfonamides, sulphadimethoxine (2, 4-dimethoxy-6-sulphanilamido-1,3-diazine) (Madribon) is metabolized chiefly to the highly soluble glucuronide form rather than relatively insoluble acetylated form. The excretion pattern of Madribon is : 7% free, 14% acetylated and 79% glucuronide form. This unique excretion pattern swings the balance of safety in favour of Madribon. According to Wollach[1], Madribon appears to be safer as well as more effective than sulphamethoxy pyridazine. It produces peak blood concentration 4-6 hours after a single oral dose and therapeutic level is maintained for more than 24 hours. Its chemical formula is as follows:



Madribon has been found to be effective against gram positive as well as gram negative organisms while Enterococci, Staphylo albus and Proteus Vulgaris have been reported to be particularly sensitive to it. According to Dave[2], Staphylococcal sensitivity to Madribon might vary from case to case. Leming et al.[3] have obtained striking results in five members of one family suffering from repeated attacks of furunculosis, which proved refractory to other forms of theraples. Reports of Kunzle[4], Wexler[5], Schuppli[6], Levy[7], Leming[8] etc. reveal the excellent results rendered by this drug in various dermatological disorders. Moreover, according to Kunzle[4], the possibility has not been excluded that this drug has a special affinity for the skin. Considering the encouraging results obtained by various leading dermatologists all over the world, we thought of evaluating this drug clinically in the skin department of our G. T. Hospital.

Clinical Material: A random sample of 95 ambulant patients with common pyogenic skin disorders were treated with Madribon during the period from 11.11. 1961 to 12.7.1962. This study included 31 females, 64 males (6 infants, 53 children and 36 adults). The disease-wise grouping was: scabies with secondary bacterial infection 29, impetigo contagiosa 26, infectious eczematoid dermatitis 17, furunculosis 13, acnevulgaris of pustular type 6 and cellulitis 4.

Methods and Dosages: Depending upon the severity of the condition, adults received 1 gm. orally daily for first 1-5 days, to be followed by the maintenance dose of 0.5 gm. orally daily. Children and infants received 15 mg./kg. daily orally as on initial dose and 7-10 mg./kg. as the maintenance dose. The duration of the treatment varied from one week to one month and depended upon the intensity of the condition. Drug was used in 0.5 gm. tablet form only. During the Madribon therapy no other systemic antibacterial agents were advised. Adjunctive therapy consisted of customary topical measures suited for individual patient. Not a single patient received either X-ray or Ultra-violet ray exposures. All patients were cautioned to take adequate fluid intake and were called for check-up every fourth day. Careful watch was kept on likely side-effects. Clinical cure was the criterion of successful treatment. Clinical improvement was labelled as satisfactory or unsatisfactory. In cases labelled as unsatisfactory, drug proved failure and other antibacterial remedies had to be advised to effect the cure. Cases in which clinical improvement was found to be gratifying, were labelled as 'Satisfactory'.

Results: Out of the total number of 95 cases treated with Madribon, 26 failed to give satisfactory results and recourse had, therefore, to be taken to higher and broadspectrum antibiotics to effect cure in such resistant cases. It is our impression that severe pyogenic skin infections do not respond satisfactorily to Madribon alone. In our opinion, cases with bacterial infections of severe intensity should initially be treated with broad-specturm antibiotics and latter on with Madribon alone. In this series 69 cases showed gratifying clinical response to this drug. The obtained results have been summarised in the below table No. 1.

Results of Treatment with Madribon (Sulphadimethoxine)

TABLE-I

Diagnosis	No. of patients	Satis-factory	Unsatis-factory	% of cure	% of failure
Scabies with sacondary bact. infection	29	20	9	69%	31%
Impetigo Contagiosa	26	21	5	80.8%	19.2%
Infectious eczematoid dermatitis	17	11	6	64.7%	36.3%
Furunculosis	13	9	4	69%	31%
Acnepustularis	6	5	1	83.4%	16.6%
Cellulitis	4	3	1	75%	25%
Total	95	69	26	72.7%	27.3%

Indicating the percentages of cures and failures obtained in this study as well as by previous authors.—Table 2.

TABLE-2

Authors	Total No. of cases	% of cures	% of failures
Levy	44	97.75%	2.25%
Wexler	85	91.6%	9.4%
Wittels	71	84.6%	15.4%
Kunzle	100	78%	22%
Yawalkar et al	95	72.7%	27.3%

Relatively higher percentage of failures in our series can be attributed to the lack of proper topical care of the skin lesions which in turn can be due to our inadequate facilities to carry out local therapy efficiently and lack of awareness on the part of the majority oi our ambulant patients.

Side-Effects: Due to the peculiar excretion pattern, Madribon is relatively a safer preparation among sulfonamides. Crystalluria is unlikely with it. According to Rentsch[8], Madribon tolerance was excellent even on continuous administration for a period of ten months. Madribon was used by Leff[9] in 36 paraplegic patients for over twelve months and no toxic or side-effects were encountered. Except transient urticaria rubra in one case and giddiness in another, inspite of close watch no side effects were encountered in our series of 95 patients. Madribon did not reveal any adverse effect on digestive, urinary, nervous, hepatic and haemopoetic functions.

SUMMARY AND CONCLUSIONS

Although the domain of broad spectrum antibiotics is expanding with tremendous rapidity, there still remains a remarkably wide field for the use of a safe as well as an effective long acting sulfonamide like Madribon. Its excellent tolerance is of special value in making prolonged treatment of chronic and persistent pyogenic skin disorders possible and that too without hospitalization. In our series of 98 patients, it has given a cure rate of 72.7% while the failure rate was 27.3%

only. On the grounds of our limited experience, Madribon can be recommended as an effective, safe and economical drug in the treatment of scabies with secondary bacterial infections, Impetigo contagiosa, cellulitis, furunculosis, infectious eczematoid dermatitis and acne vulgaris of pustular type. It may also be used with success in erysipelas, hydradenitis suppurativa, ezematous and mycotic dermatoses with secondary pyogenic infections, dyshidrosis and rosacea. Excellent results obtained by Kunzle[4] in cases of dyshidrosis lead us to think that this disorder might be a bacterid. Lately Prof. Schuppli[6] of Basle has reported encouraging results with this drug in rosacea cases. It can safely be used for the prophylactic purpose, during prolonged corticosteroid therapy. Madribon can well be reckoned as a welcome addition to the today's therapeutic armamentarium.

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