

From the Department of Dermatology, University Central Hospital and
Department of Hygiene, University of Helsinki, Finland.

SENSITIVITY TO TOPICAL DEQUALINE

By

O. P. SALO, V. PIRILÄ & EILA VILJANEN

A quaternary ammonium compound, dequaline chloride, decamethylene-bis-(4 aminoquinaldinium chloride), had for many years been used for the topical treatment of bacterial infections of the skin before any untoward effects were reported. In 1958, *Coles et al.* (1), reported a clinical trial using dequaline products in which they noted no toxic or irritant effects and a low rate of sensitization. In their series there were two patients who, in the patch tests, reacted to the „active cream“ containing dequaline but not to the base alone. In a later report *Coles & Wilkinson* (2) reviewed 43 patients with necrotic lesions on the penis and found that 30 of these had used dequaline-containing products before the appearance of the necrosis. *Tilsley & Wilkinson* (7) produced necrotic lesions by applying dequaline onto a scarified area which was kept under waterproof patch tests.

At the Department of Dermatology, University Central Hospital, Helsinki, no case of sensitization to dequaline chloride was observed during the two first years of its use. Irritation of the skin due to sensitization to dequaline was first observed in 1963. Thereafter dequaline chloride was included in the routine patch test series.

MATERIAL AND METHODS

Since 1964 about 6000 dermatological patients have been tested with a patch test series including two brands of dequaline chloride of different grades of purity, ten per cent in petrolatum (5). The results were read 24, 48 and 72 hours after fixation of the tests.

RESULTS

309 patients or five per cent of the cases tested gave positive reactions to one or both brands of dequaline chloride. The diagnosis and sex of these patients are presented in Table 1. Patients with leg ulcer and/or varicose eczema are dealt with separately because they represent a larger part of the series than would be expected. Leg ulcer and/or varicose eczema is seen in less than five per cent of all patients treated at the clinic whereas they represent 28.8 per cent of the patients with positive reactions to dequaline chloride. In this series of 309 dequaline sensitive patients, on the other hand, positive reactions to other topical remedies were found in 60.7 per cent of patients with leg ulcer and/or varicose eczema and in 28.3 per cent of other patients.

TABLE 1

Diagnosis and Sex of Patients Showing Positive Reactions to Dequaline Chloride.

Diagnosis	Number of		Total	
	males	females	number	%
Leg ulcer and/or varicose eczema	15	74	89	28.8
Others	78	142	220	71.2
Total	93	216	309	100.0

TABLE 2

Numbers of Patients with Positive Reactions to Pure and Impure Dequaline Chloride Preparations in the Different Years of Study.

Year	Number of patients with positive reactions	
	Total	To impure brand only
1964	77	32
1965	78	66
1966	57	25
1967	97	41
Total	309	164

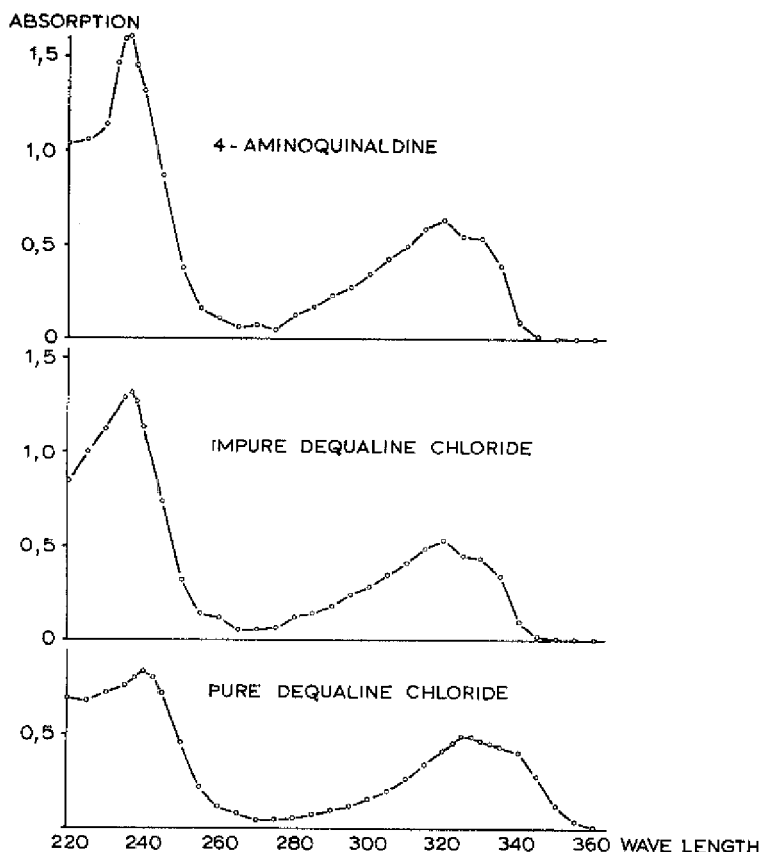


Fig. 1.

Ultraviolet spectograms of 4-aminoquinaldine and the pure and impure brands of dequaline chloride.

Table 2 presents the number of positive reactions to both the pure and impure brands of dequaline chloride in the different years of study. The number of new cases with positive reactions has been relatively stable during the study period. In 1965 a very high proportion of patients reacted to the impure brand of dequaline only.

Positive reactions to both brands developed slowly, being often observed first in the second or third reading. Irritation



Fig. 2.

Thin layer cellulose chromatography of 4-aminoquinaldine, impure dequaline chloride and pure dequaline chloride.

by topical dequaline could be clinically observed in 50 per cent of the patients with positive patch tests to dequaline, irrespective of the reactivity to the different brands.

The results of the test reactions led us to compare chemically the pure and impure brands of dequaline chloride. The starting point in the manufacture of dequaline is 4-aminoquinaldine which is readily soluble in water. So was also the impure brand of dequaline chloride. Pure dequaline chloride has only a slight solubility in water.

Ten milligrams of the pure and impure dequaline chloride and 4-aminoquinaldine hydrochloride were dissolved in one liter of water. The ultraviolet spectrograms of the solutions are presented in Fig. 1. Dequaline chloride has two absorption

maxima at wave lengths 240 and 326 nm. As is seen in Fig. 1 the pure brand of dequaline chloride corresponds well with this spectrum. On the other hand, the impure dequaline chloride and 4-aminoquinaldine hydrochloride have identical absorption maxima.

For thin layer cellulose chromatography, 4-aminoquinaldine hydrochloride and both brands of dequaline chloride were dissolved in methanol and run with solvent system n-butanol/ethanol/water/0.880 ammonia, 60:18:50:2.5. In this system the Rf values of 4-aminoquinaldine hydrochloride and dequaline chloride are 0.99 and 0.75, respectively. In Fig. 2 it is seen that the Rf values of 4-aminoquinaldine hydrochloride and the impure dequaline chloride are of the same magnitude thus differing from that of the pure dequaline chloride.

In highly sensitive patients, positive patch test reactions were obtained with the impure dequaline chloride even when only 0.001 per cent concentration in petrolatum was used. In general the reactions to the pure brand were weaker than those to the impure one. Because it was evident that the impure dequaline chloride was almost identical to 4-aminoquinaldine hydrochloride, patch tests were performed with 4-aminoquinaldine, both as a base and as hydrochloride. Positive reactions were obtained with both 4-aminoquinaldine base and hydrochloride. However, in some patients no reactions to 4-aminoquinaldine even in a concentration of ten per cent in petrolatum, were observed.

DISCUSSION

On the basis of the available literature the sensitizing properties of dequaline chloride seem to be small. The first to report sensitization to this antibacterial agent were *Coles et al.* in 1958 (1). During the four years, 1964-1967, altogether 309 patients sensitive to dequaline were seen at the Department of Dermatology, University Central Hospital, Helsinki.

It has been reported by *Magnusson* (4) and *Laubstein* (3) that sensitization to agents used for topical treatment of skin

disorders is more frequent among patients with leg ulcers and/or varicose eczema than among other dermatological patients. This was also shown in the present study. Of the 309 patients sensitive to dequaline 28.8 per cent had leg ulcer and/or varicose eczema. The relative number of patients with these disorders in the clinic is less than five per cent. Analogously, hypersensitivity to other topical remedies was, in the present series, found in 60.7 per cent of patients with leg ulcer and/or varicose eczema and sensitive to dequaline, whereas the corresponding figure among other dequaline sensitive patients was 28.3 per cent.

In the present series the patients were tested with pure and impure brands of dequaline chloride. In 1965 a greater proportion of the patients reacted to the impure brand only than during the other years. This may be explained by the fact that impure Italian dequaline was introduced in Finland in 1963 and its use increased during the following two years, until it was withdrawn from the market. Chemical analysis of the Italian product revealed that it was mainly 4-aminoquinaldine which is the starting point in the manufacture of dequaline, and contained only about five per cent of dequaline chloride. This finding has been corroborated by the chemical analysis performed by the English dequaline patentee (6).

Quantitative patch tests with different brands of dequaline revealed a very high degree of sensitivity to the impure dequaline in some patients. In general, the reactions to the pure dequaline were weaker than those to the impure one. Patch tests have shown that some patients sensitive to dequaline are also sensitive to 4-aminoquinaldine. On the other hand, there are patients who do not react to 4-aminoquinaldine. Thus the findings indicate that a certain proportion of the sensitizations are due to 4-aminoquinaldine but some are due either to dequaline chloride itself or to chemical impurities in the commercial products which have as yet not been identified.

SUMMARY

During the four years, 1964–1967, about 6000 patients were patch tested with two different brands of dequaline chloride. Positive reactions were obtained in 309 patients. Fifty per cent of the patients reacted to an Italian impure brand of dequaline only and the rest to a purer brand as well.

Sensitivity to dequaline chloride was more frequent among patients with leg ulcer and/or varicose eczema than among other dermatological patients.

Chemical analysis of the pure and impure brands of dequaline chloride revealed that the impure brand was mainly composed of 4-aminoquinaldine hydrochloride. This substance, from which dequaline chloride is prepared, seemed to be the main allergen in some cases, in others it was the dequaline itself or some unidentified chemical impurity.

REFERENCES

1. Coles, R. B., Grubb, C., Mathuranayagam, D. & Wilkinson, D. S.: Trial of dequalinium for skin infections. *Brit. med. J.* 2, 1014, 1958.
2. Coles, R. B. & Wilkinson, D. S.: Necrosis and dequalinium. *Trans. St. John's Hosp. Soc.* 51, 46, 1965.
3. Laubstein, H.: Therapiebedingte Sensibilisierungen bei der Behandlung des Ulcus Cruris. *Z. Arzt. Fortbild.* 60, 1107, 1966.
4. Magnusson, B.: Bensär. Dermatologiska synpunkter. *Nord. Med.* 74, 1267, 1965.
5. Pirilä, V., Rouhunkoski, S. & Salo, O. P.: Ihon herkistyminen ulkoisesti käytettyjä lääkkeitä kohtaan. *Duod.* 79, 875, 1963.
6. Smart, R. D.: Personal communication, 1967.
7. Tilsley, D. A. & Wilkinson, D. S.: Necrosis and dequalinium II. Vulval and extra-genital ulceration. *Trans. St. John's Hosp. Soc.* 52, 49, 1965.

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