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Choice of Sclerosant: An Experimental Study

W. K. BLENKINSOPP

Department of Pathology, St. Mary's Hospital Medical School, London

Abstract

The sclerosant hydroxypolyethoxydodecan (HPD) was studied in rats, and the results were compared with those from a previous study of tetradecyl sulphate of sodium (TSS). There appeared to be no significant difference between the two. The sclerosant efficiency increased with increasing concentration up to 6%, but a higher concentration than 6% is unlikely to be more effective in the rat or in man. In man, good results probably depend on exposure of the endothelium to sclerosant undiluted with blood for 1 s, and the total volume of 6% HPD or 6% TSS injected at one visit should not exceed 10 ml. 3%?

Key words

Experimental study
Sclerosants
Hydroxy-polyethoxydodecan
Tetradecylsulphate

Sclerosants are widely used in the treatment of varicose veins of the leg, haemorrhoids, and some angiomatous malformations. In previous papers the effect on rat veins of one of the newer sclerosants (tetradecyl sulphate of sodium, TSS) was described [BLENKINSOPP, 1968a], and the effectiveness of TSS was compared with that of ethanolamine oleate and phenol in almond oil [BLENKINSOPP, 1968b]. At that time the sclerosant of choice was clearly TSS, but since then hydroxypolyethoxydodecan (HPD) has come into use, and in the present paper the results obtained with HPD in rats are described and compared with those previously obtained with TSS. The sclerosant effect on the femoral vein, the mortality following intravenous injection, and the incidence of ulceration after intradermal and subcutaneous injection were studied.

Material and Methods

Male albino rats weighing 150–180 g were anaesthetised by intraperitoneal injection of chloral hydrate solution before injection of the sclerosant hydroxypolyethoxydodecan (HPD) ('Aethoxysklerol', made by Kreussler). Sixty-seven rats were given an intravenous or perivenous injection of 0.1 ml HPD into or around the distal part of the exposed femoral vein on one or both sides (table I). Six rats died within 24 h of injection (table II). The rest were killed 4 weeks after injection, and each injected vein was excised, with the adjacent nerve, artery and muscle, fixed in formol-saline, and processed for histology; paraffin sections (5 μm) were cut at 1 mm intervals through each block and stained with haematoxylin-elastic-van Gieson.

Eighteen rats were each given a single intravenous injection of HPD to study the mortality (table II).

Ten rats were given a subcutaneous injection of 0.2 ml 6% HPD into both forelegs, and an intradermal injection of 0.05 ml 6% HPD into both ears. The injection sites were examined daily for 12 days for ulceration.

These procedures were the same as those used in the earlier study of TSS [BLENKINSOPP, 1968b].

Results

Effect on vein. Examination of the sections showed that 'good' and 'poor' results could be distinguished. A 'good' result was characterised by almost complete occlusion of the vein lumen by fibrous tissue, leaving only narrow capillary channels with a total cross-sectional area of less than 5% of the original lumen; a 'poor' result consisted of a patent channel of more than 10% of the original lumen (and was usually 80% or more). The results are given in table I, where the results previously obtained with TSS are also given for comparison. Perivenous injection of sclerosant was very unsatisfactory. Intravenous injection of 1% HPD or 1% TSS was moderately effective (chi^2 tests showed no significant difference between the two). Intravenous injection of 6% HPD or 3% TSS was entirely effective if the exposure was more than 1 s, but if the exposure to 3% TSS was reduced to 1 s it was not always effective, whereas this did not occur with 6% HPD until the exposure time was reduced to 0.2 s. The difference between exposures to 6% HPD of 1 s and 0.2 s was significant (chi^2 test gave $p < 0.01$). The difference between 6% HPD and 3% TSS at the 1-second exposure level was not significant (chi^2 test gave $0.20 > p > 0.10$).

Table I. Number, procedure and result of veins injected with sclerosant (TSS data from BLENKINSOPP [1968b])

Sclerosant	Intravenous injection						Perivenous injection	
	10 s exposure		1 s exposure		0.2 s exposure			
	No. of 'good' results	Total no. of results	No. of 'good' results	Total no. of results	No. of 'good' results	Total no. of results	No. of 'good' results	Total no. of results
6% HPD	13	13	11	11	2	4	0	20
1% HPD	15	20	7	16	–	–	0	20
3% TSS	37	37[1]	17	20	–	–	1	8
1% TSS	28	35[1]	8	14	–	–	0	8

[1] Indicates exposure of 3–60 s (varying the exposure time within this range made no difference to the result).

The length of vein showing a 'good' result was estimated: the mean values were 4.6 mm (6% HPD), 4.0 mm (1% HPD), 6.2 mm (3% TSS), and 4.7 mm (1% TSS). The mean value for length of vein examined was 9.9 mm.

No nerve lesions were seen, but segmental arterial wall damage was present beside 5 of 24 veins (6% HPD), 2 of 36 veins (1% HPD), 11 of 65 veins (3% TSS), and 11 of 57 veins (1% TSS) following intravenous injection. Arterial wall damage was much less common after perivenous injection, and occurred in 1 of 16 arteries (TSS) and none of 40 arteries (HPD).

Subcutaneous and intradermal injection. Subcutaneous injection of 6% HPD was followed by ulceration at 5 of 20 sites, compared with 9 of 16 sites when 3% TSS was used. Ulceration followed intradermal injection of 6% HPD at 10 of 20 sites, whereas ulcers occurred at all of 10 sites injected with 3% TSS. HPD therefore appears to be less likely to produce ulceration than TSS.

Mortality following intravenous injection. The mortality is shown in table II, with the previous results of TSS for comparison. The lethal volume of sclerosant is clearly about 2 or 3 times as high for 3% TSS as for 6% HPD.

Table II. Mortality following intravenous injection of sclerosant (TSS data from BLENKINSOPP [1968b])

Sclerosant	Procedure	No. of deaths	No. of rats
6% HPD	Bilateral injections of 0.1 ml	6	11
6% HPD	Single injection of 0.1 ml	0	14
6% HPD	Single injection of 0.15 ml	7	8
6% HPD	Single injection of 0.2 ml	10	10
3% TSS	Bilateral injections of 0.1 ml	1	20
3% TSS	Single injection of 0.1 ml	0	46
3% TSS	Single injection of 0.2 ml	0	6
3% TSS	Single injection of 0.3 ml	0	6
3% TSS	Single injection of 0.4 ml	2	16
3% TSS	Single injection of 0.6 ml	6	6

Discussion

In a previous study of rat femoral veins [BLENKINSOPP, 1968b], TSS was found to be a much better sclerosant than 5% ethanolamine oleate or 5% phenol in almond oil when each sclerosant was given by intravenous injection. Perivenous injection of the three sclerosants gave poor results, as was found in the present work with HPD. Intravenous injection of 6% HPD appeared to give slightly better results than 3% TSS, whereas there was no difference between the two sclerosants when a 1% solution was used.

HPD appeared to be less likely than TSS to produce ulceration after intradermal or subcutaneous injection, but the lethal volume was 2 or 3 times as high for 3% TSS as for 6% HPD.

These results suggest that there is no significant difference between HPD and TSS in either sclerosant activity or toxicity, and that the differences observed between 6% HPD and 3% TSS were due to the former being twice the concentration of the latter. As the 6% was lethal at less than half the volume of the 3% solution, but gave only slightly better results than the 3% solution, it is clear that in the rat the use of a stronger solution than 6% would give little or no increase in efficiency but a considerable increase in mortality. It seems reasonable to conclude that in man good results depend on exposure

of the endothelium to sclerosant undiluted with blood for at least 1 s, and that a higher concentration than 6% of HPD or TSS is unlikely to be more effective than 6%.

The volume of sclerosant injected into any one site is immaterial [BLENKINSOPP, 1968a] provided the sclerosant is in contact with the endothelium for the necessary second, but the total volume of 6% HPD or 6% TSS injected at one visit should not exceed 10 ml.

3%?

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References

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Author's address: Dr. W. K. BLENKINSOPP, Crumpsall Hospital, *Manchester M8 6RB* (Great Britain).