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Varicose veins in pregnancy: Recent experience with medicinal therapy

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INTRODUCTION

The frequency of varicose veins in pregnancy was estimated by Rast (14) as 10%, and by Bach (1) as up to 50%; Sigg (18) mentioned figures as high as 30% for primigravidae and 55% for multigravidae. When one considers that 90% of pregnant women with varicose veins suffer from heaviness in their legs, 32% from oedema, and 10% from night-time cramps, (14) one appreciates the importance of treatment. The varicose state generally gets worse as pregnancy advances, and keeping the symptoms at a constant level of intensity may in itself be regarded as successful therapy.

The effects of the venotropic agents I have previously tried for leg disorders in pregnancy (varicose conditions chiefly) have been for the most part transient and slight when measured in terms of relief of symptoms (15, and unpublished observations). It was therefore with some scepticism that I undertook a clinical evaluation of Doxium (calcium dobesilate, calcium 2,5-dihydroxybenzenesulphonate).

Doxium has been shown pharmacologically to act on the capillary wall, reducing fragility and hyperpermeability, (10, 20) protecting from histamine-induced injury, (13) and diminishing experimentally induced endothelaemia (8). In human subjects, especially patients with disordered microcirculation and chronic venous insufficiency, it improves capillary resistance, reduces capillary permeability, combats swelling (9), and decreases pathologically elevated transcapillary filtration (7).

The striking improvement produced by Doxium

in the signs and symptoms of venous disorders has been demonstrated in both open trials (2, 3, 4, 11, 16, 19, 21) and double-blind controlled trials (5, 12). Of special interest in connection with the present study is a report of its success in these disorders in 57 pregnant women (19).

Good tolerance has been noted in all the published trials of Doxium (17). The very rare unwanted side effects have been mainly mild gastrointestinal troubles. Hyperthermia, sometimes accompanied by sweating, reported in 0.2% of over 3000 Doxium-treated patients in a multicentre trial (16), quickly subsided after withdrawal of the drug. Although these side effects with their very low incidence are no contraindication to the use of Doxium for chronic venous insufficiency during pregnancy, we none the less think it right to mention them. Rare as they were, they occurred with calcium dobesilate in tablet form. The recently introduced capsules (Doxium 500) are even better tolerated, with a frequency of gastrointestinal upset of less than 1% (6).

PATIENTS AND METHODS

Ninety pregnant women, mean age 29.1 years, with leg disorders were given two capsules of Doxium 500* (500 mg of calcium dobesilate) daily for periods ranging from two to 26 weeks (mean 10 weeks), beginning (with one exception) in or after the 12th week of pregnancy (Fig. 1). The effects were assessed on termination of the treatment.

* OM Laboratories, Meyrin-Geneva, Switzerland.

RESULTS

The effects of Doxium in these 90 pregnant women with varicose disorders have been compared with the effects of two other venotropic agents, 0-(β -hydroxyethyl)-rutoside (HR) (15) and a drug containing phenopyrazone, horse-chestnut and Miroton extracts (unpublished observations) in comparable groups of patients previously treated in our department (Table 1 and Fig. 2).

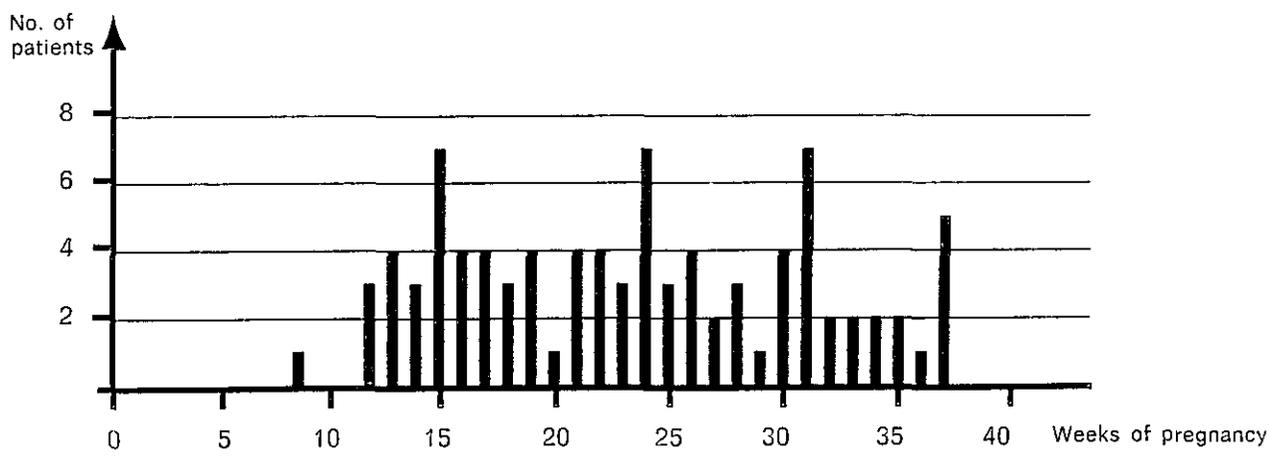
After treatment with Doxium, 53.3% of the 90 patients were symptom-free and in 25.6% the symptoms were alleviated. The corresponding figures with the two other venotropic agents mentioned above — 28.4% and 0% for freedom from symptoms and 28.8% and 68.4% for alleviation of symptoms — are a measure of the superiority of Doxium. Doxium in fact produced

complete relief in at least twice as many cases as the other two preparations. The symptoms did not become worse in any patient treated with Doxium, whereas they did become worse in 6.3% and 2.7% of the patients treated with the 2 other drugs respectively.

The individual symptom that responded best to Doxium (Table 2) was leg pain, with complete relief in 54.2% of the patients. Leg cramps disappeared in 42.8%, were alleviated in 28.6%, and became worse in none. Oedema disappeared in 33.3%, improved in 16.7%, and became worse in 8.3%. Side effects occurred in only one (1.1%) of the Doxium-treated patients; they consisted in gastric pain and vomiting, common occurrences in any pregnancy.

The state of the infants born of these pregnan-

Fig. 1 — Ninety women treated with DOXIUM for leg disorders during pregnancy: histogram showing stage of pregnancy at which DOXIUM (2 x 500 mg daily) was begun. Duration of DOXIUM therapy ranged from two to 26 weeks (mean 10 weeks).

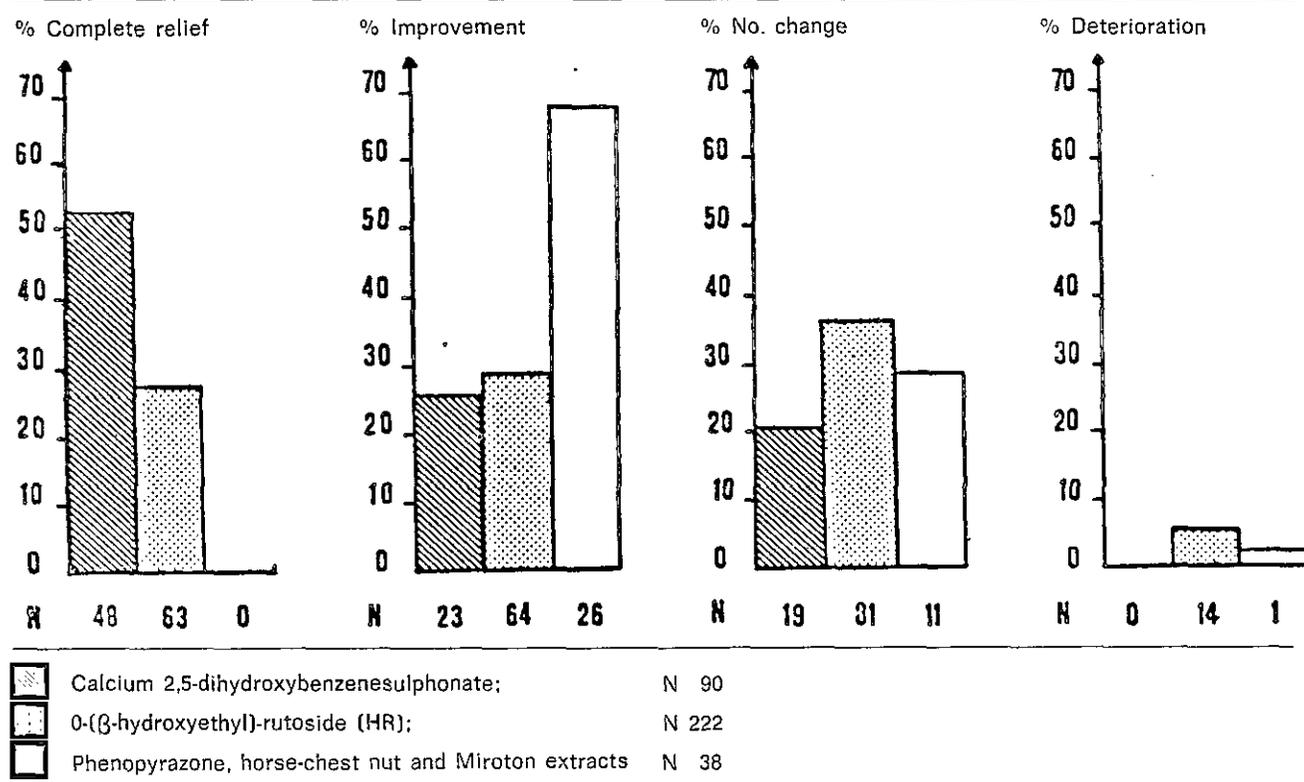


Tab. 1 — GENERAL EFFECTS OF TREATMENT WITH THREE VENOTROPIC DRUGS IN PREGNANT WOMEN WITH LEG DISORDERS

General effect	Calcium 2,5-dihydroxybenzenesulphonate (Doxium) (2 x 500 mg)		0-(β -hydroxyethyl)-rutoside (HR) (2 x 300 mg)		Phenopyrazone with horse-chest nut and Miroton extracts (3 x 2 tab.)	
	No. patients	%	No. patients	%	No. patients	%
Complete relief	48	53.3	63	28.4	—	—
Improvement	23	25.6	64	28.8	26	68.4
No change	19	21.1	81	36.5	11	28.9
Deterioration	0	—	14	6.3	1	2.7
Total	90	100.0	222	100.0	38	100.0

This table is illustrated in Fig. 2

Fig. 2 — General effects of treatment with three venotropic drugs in pregnant women with leg disorders. Graphic illustration of the data presented in Table 1.



Tab. 2 — EFFECTS OF TREATMENT WITH DOXIUM ON INDIVIDUAL SYMPTOMS IN 90 PREGNANT WOMEN WITH LEG DISORDERS

Effect on symptom	Leg pains		Leg cramps		Oedema	
	No. patients	%	No. patients	%	No. patients	%
Complete relief	39	54.2	3	42.8	4	33.3
Improvement	20	27.8	2	28.6	2	16.7
No change	11	15.2	2	28.6	5	41.7
Deterioration	2	2.8	—	—	1	8.3
Positive result	59	82.0	5	71.4	6	50.0

cies is considered in Table 3. Out of the births in the 90 women treated with Doxium, 86 could be reviewed. Taking this figure as 100%, we found the followings: postmaturity, six (6.9%); prematurity, five (5.8%); underweight at birth, four (of which three were twins) (4.6%); deformity, two (2.3%); still birth, two (2.3%); and death on the first postnatal day, one (1.1%). Comparison of these figures with those of the published study (15) in 222 pregnant women treated with HR (Table 3), and with the mean

general incidence of abnormalities in our department, shows that there is no reason to fear danger to the offspring of mothers treated with Doxium.

CONCLUSION

Doxium proved to be at least twice as efficacious in the treatment of varicose leg disorders in a group of 90 pregnant women as had two

Tab. 3 — STATE OF SOME INFANTS BORN FROM MOTHERS TREATED WITH TWO VENOTROPIC DRUGS FOR LEG DISORDERS DURING PREGNANCY

State	Calcium 2,5-dihydroxybenzenesulphonate (Doxium) (86 children; 90 mothers)		0-(β -hydroxyethyl)-rutoside (HR) (191 children; 222 mothers) (15)	
	No. children	%	Not children	%
Postmaturity	6	6.9	Not reviewed	
Prematurity	5	5.8	3	1.5
Underweight at birth	4*	4.6	10	5.2
Deformity	2	2.3	5**	2.6
Still birth	2	2.3	1	0.5
Death 1st day	1	1.1	—	0.5
? Slight brain damage	—	—	1	0.5
Skin disease	—	—	1	0.5

* Three twins.

** Includes two dead infants.

other venotropic agents in comparable groups of patients. It relieved the symptoms completely in 53.3% of the patients and alleviated them in 25.6%. The infants born from these pregnancies did not differ from infants from comparable populations. As venous troubles in pregnancy tend to be progressive, these results obtained with Doxium represent an important therapeutic success.

SUMMARY

Ninety pregnant women with leg disorders have been treated with two capsules of Doxium 500 (calcium dobesilate) daily for an average of 10 weeks beginning in the eighth week of pregnancy. Complete relief of symptoms resulted in 53.3% of the patients and improvement in 25.6%. Among individual symptoms, leg pains reacted the most favourably to Doxium (they disappeared in 54.2% of the patients and improved in 27.8%); next in order of good response came leg cramps (disappearance in 42.8% and improvement in 28.6%). Side effects, in the form of gastric pains and vomiting, occurred in one patient (1.1%). There was nothing specially noteworthy about the infants born of the Doxium-treated mothers. These results, when compared with those obtained with other venotropic drugs, indicate that the Doxium therapy is a very real therapeutic advance.

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