CAN LIFESTYLE MODIFICATIONS INFLUENCE VENOUS DISEASE?

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INTRODUCTION

The classical teaching is that the aetiology of varicose veins can be explained by heredity, occupation (in particular standing occupations), pregnancy (increasing with multiparity), and obesity. It is generally supposed that varicose veins run in families yet most epidemiological studies indicate that the incidence of varicose veins in a society is primarily related to the degree that society has adopted the western lifestyle. The aim of this review article is to examine the epidemiological evidence of lifestyle factors on venous disease, to explore possible cellular mechanisms to explain how these factors manifest themselves in the development of varicose veins and to make recommendations on how lifestyle factors may be modified to beneficially influence the incidence and severity of venous disease.

EPIDEMIOLOGICAL STUDIES

Geographical

All geographical studies appear to implicate environmental rather than genetic or racial factors in the prevalence of varicose veins. These studies have all defined the presence of varicose veins as “any dilated, tortuous and elongated subcutaneous vein in the leg, when examined in the standing position.”1 Subjects with dermal telangiectasias and venulectasias only are therefore excluded with this definition. The results of the epidemiological studies are summarized in Table 1. The prevalence varies from less than 1% in lowland New Guinea women2 to 53% in south Wales women3. This is consistent with the view that the incidence of varicose veins is a direct reflection of the “westernization” or industrialization of the society. The best evidence for this comes from Beaglehole’s study of Polynesian people who are genetically homogeneous, living in contrasting environments in the South Pacific4. Atoll-dwelling people (Pukapuka, Tokelau) have substantially lower age standardized rates than Cook Island Maoris on Raratonga who in turn have substantially lower rates than New Zealand Maoris. Surprisingly, New Zealand Maoris men have substantially higher rates than non-Maori New Zealand men who have a similar prevalence rate to United States men. In Israel, there is a lower prevalence rate in North African born people compared with people born in the United States, Europe or Asia5.

Table 1

Variations in the Prevalence of Varicose Veins in Adults
(Derived from Beaglehole et al1)

<table>
<thead>
<tr>
<th></th>
<th>Men % (No.)</th>
<th>Women % (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Zealand</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maori</td>
<td>33 (366)</td>
<td>44 (355)</td>
</tr>
<tr>
<td>Non-Maori</td>
<td>20 (173)</td>
<td>38 (183)</td>
</tr>
<tr>
<td>Cook Island</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raratonga</td>
<td>16 (219)</td>
<td>15 (198)</td>
</tr>
<tr>
<td>Pukapuka</td>
<td>2 (199)</td>
<td>4 (178)</td>
</tr>
<tr>
<td>Israel</td>
<td>10 (2245)</td>
<td>30 (2557)</td>
</tr>
<tr>
<td>Wales</td>
<td>37 (124)</td>
<td>53 (160)</td>
</tr>
<tr>
<td>United States</td>
<td>19 (2033)</td>
<td>36 (2434)</td>
</tr>
<tr>
<td>New Guinea</td>
<td>5 (728)</td>
<td>0.1 (729)</td>
</tr>
<tr>
<td>India</td>
<td></td>
<td></td>
</tr>
<tr>
<td>South (Madras)</td>
<td>25 (323)</td>
<td></td>
</tr>
<tr>
<td>North (Ajmer)</td>
<td>7 (354)</td>
<td></td>
</tr>
</tbody>
</table>

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This invites the conclusion that environmental factors play an important part in the development of varicose veins, and the further conclusion that the condition is potentially preventable.

The geographical distribution of venous thrombosis and pulmonary embolism follows a similar geographical distribution, being highest in industrialized societies and lowest in societies that have not adopted the western lifestyle. Therefore the highest incidence of thromboembolic disease is seen in countries such as the United Kingdom and the United States (both Negroes and white groups), and is lowest in African countries such as Uganda. Following the progressive adoption of western lifestyle features, the incidence of thromboembolic episodes found at necropsy in Uganda rose from 2.4% in the period 1951-6 to 6% in the years 1965-7. This compares with incidences ranging from 44% to 60% in Britain.

Gender

It is generally accepted that the prevalence of varicose veins is higher in women than in men and this has been verified in most studies particularly in the industrialized civilizations. However there are some notable exceptions and these occur primarily in populations where there is a low prevalence rate such as New Guinea local people and small island dwelling Polynesians (Pukapuka, Tokelau). Also none of the five surveys reported from India show a female predominance.

Pregnancy and multiparity

It is often suggested that pregnancy and multiparity in particular, have a strong causative role, but this doesn’t explain why men get varicose veins and is inconsistent with the fact that third world women have more pregnancies than those in industrialized societies but have a lower prevalence rate. The relationship between increasing parity and varicose veins has not been found in studies from the United States, Rarotonga or south Wales. The Framingham study in the United States showed a positive relationship with parity that was not statistically significant. Positive relationships between parity and prevalence of varicose veins have been found in New Zealand, Israel and English cotton workers. It is likely therefore that pregnancy places an extra haemodynamic and nutritional burden on veins and in the presence (or deficiency) of some other factor, the changes that occur in pregnancy become pathological. So pregnancy becomes a precipitating factor rather than a causative factor.

Occupation

Several studies have shown a positive relationship between varicose veins and standing at work. The Framingham study reported a positive relationship between sedentary activities (standing or sitting) and the presence of varicose veins. In a Netherlands study, the severity of chronic venous insufficiency diagnosed by clinical examination and Doppler ultrasound investigation was associated with the number of years in a standing occupation. Prolonged sitting may also be a factor in increasing prevalence of varicose veins and was the factor that was implicated in the higher incidence of varicose veins in New Guinea men compared to women.

Obesity

The relationship between varicose veins and obesity varies between studies. In general, studies of communities with high prevalence have a positive relationship between body mass index and varicose veins whereas in communities with low prevalence there is no association. This would indicate that varicose veins and obesity have a common aetiological factor but that varicose veins are not caused by obesity. This is consistent with the Basle study, which found that the association of obesity with varicose veins was not statistically significant when the confounding effect of age was eliminated.

Familial

A number of studies have implicated a familial factor in the pathogenesis of varicose veins but in general these studies are flawed in that they are unable to separate environmental influences from genetic influences. One of the recent studies that demonstrated the existence of a significant familial factor agreed that this factor could be explained by inherited habits. The strongest evidence against genetic predisposition playing a primary role is the geographic differences described above. In the New Guinea study there was not one male with varicose veins who had a first degree relative with varicose veins. Also varicose veins are equally common in American Negroes and Caucasians whereas the condition is still rare in the parts of Africa from which these Negroes originated.

Cardiovascular

Several studies have looked at more detailed risk factors common in industrial societies. These factors have included systolic and diastolic blood pressure, cigarette consumption, physical activity, diabetes and serum lipids. In the French policemen study varicose veins were associated with higher values of diastolic blood pressure and cigarette consumption with a trend towards higher values with more severe varicosities. In contrast, there was no association with diabetes or lipid levels. The Framingham study found positive relationships with systolic blood pressure, lower levels of physical activities and cigarette smoking in men. Again no association was found with serum cholesterol.

These two studies also looked at the association between varicose veins and cardiovascular disease. In the French study there was no association between varicose veins and angina but there was a significant association with myocardial infarction, coronary artery disease deaths and intermittent claudication. The Framingham study found that both men and women with varicose veins tended to have a higher incidence of coronary heart disease, congestive heart failure, and intermittent claudication than those without varicose veins but the difference was statistically
significant only for coronary heart disease in women. However, this finding was not significant after allowing for the confounding factors of body mass and systolic blood pressure.

Age

As would be expected virtually all studies note that the prevalence of varicose veins increases with age, however longitudinal studies\(^5,11\) show that the incidence (i.e. the rate of new cases per year) does not increase. This means that someone at the age of 30 has the same chance of developing varicose veins in the next year as someone aged 60. So there is an increase in prevalence of varicose veins with age simply due to an accumulation of affected people as the sample ages. The increasing prevalence of varicose veins with age supports the theory that varicose veins are an acquired degenerative disorder rather than an inherited condition.

Diet and Clotting Factors

Beaglehole\(^1\) made a number of observations regarding diet and geographic prevalence of varicose veins:

1. The New Zealand diet of both Maori and non-Maori is typical of industrialized countries with a high proportion of calories from meat, dairy products, refined sugars and cereal.

2. The atoll dwellers of Pukapuka and Tokelau have traditionally subsisted on coconut, starchy roots, fruit and fish.

3. The inhabitants of Raratonga had a traditional Polynesian diet with some introduced western dietary influences.

4. Daily intake per person of refined sugar in a society was directly related to varicose veins.

5. Daily intake per person of dietary fibre was inversely related to varicose veins.

The French police study\(^11\) also showed that men with varicose veins had a significantly greater average carbohydrate and caloric intake. Burkitt\(^6\) assembled evidence that varicose veins were related to deficiency of dietary fibre, but this was not supported by data from the French police study.

The study of Indian railroad workers\(^14\) concluded that diet was the most important variable in explaining the high incidence of varicose veins in south Indian railway sweepers compared to northern Indian sweepers. This conclusion was based on the finding that south Indian workers had significantly faster clotting times than their northern counterparts and that this was related to decreased fibrinolysis. This in turn was thought to be related to the relative proportions of different fatty acids in the diets. The association between cigarette smoking and varicose veins in French policemen was also attributed to decreased fibrinolysis. The authors of the French study concluded that the common factor associating cardiovascular disease with varicose veins was decreased fibrinolysis as this also explained the association with myocardial infarction or sudden death but not angina\(^11\).

Dietary factors have also been recently implicated as a factor in thromboembolic disease\(^17\). Strong epidemiological evidence has emerged implicating moderate homocysteinaemia in the development of premature and recurrent deep venous thrombosis\(^18\). Hyperhomocysteinaemia is usually associated with subclinical deficiency of folate, vitamin \(B_12\) and Vitamin \(B_6\)\(^19\). Cigarette smoking is also associated with hyperhomocysteinaemia\(^20\). In addition, platelet aggregation is inhibited by blood levels of omega-3 fatty acids\(^21\) which are related to dietary intake of fats containing these essential fatty acids. Fish oils have high concentrations of these fatty acids whilst meat from domesticated animals has small or undetectable amounts\(^22\). On the other hand, wild game eaten by hunter-gatherers has moderate amounts of omega-3 fatty acids\(^23\).

Platelet aggregation is partly dependent on the relative levels of thromboxane \(A_2\) (prothrombotic) and prostacyclin (antithrombotic). Diets high in omega-3 fatty acids reduce serum levels of thromboxane \(A_2\) and increase prostacyclin\(^24\). The formation of thromboxane \(A_2\), prostaglandin \(E_2\) and prostacyclin has also been investigated in segments of varicose and non-varicose veins. Prostacyclin was decreased whilst thromboxane \(A_2\) and prostaglandin \(E_2\) were increased in varicose vein segments regardless of whether the vein was macroscopically affected.\(^25\)

### POSSIBLE LIFESTYLE FACTORS CONTRIBUTING TO VARICOSE VEINS

The epidemiological evidence presented above suggests that varicose veins are a degenerative disorder with similar aetiological factors to other common diseases in industrialized societies such as heart disease and cancer. These diseases are the result of interaction between genetically controlled biochemical processes and biocultural influences - lifestyle factors - that include diet, exercise and exposure to environmental noxious substances\(^26\). Over the past 35000 years cultural change has outpaced genetic adaptation to such an extent that there is now discordance between our late Paleolithic pre-agricultural hunter-gatherer genotype and many features of our present lifestyle. The dietary requirements of hunter-gatherers (who have the lowest incidence of varicose disease) are made up exclusively of uncultivated vegetables and wild game. As a result the mean protein intake for 58 hunter-gather groups studied in the 20th century was 34%\(^23\). In contrast, the typical western diet derives 12 percent of its energy from protein. Because game animals are extremely lean, hunter-gatherers eat much less fat than do western cultures and generally eat more polyunsaturated than saturated fat. In addition, hunter-gatherers eat an enormous variety of wild plants whereas in modern...
societies only a small proportion of plants make up the bulk of the food supply, with the greatest percentage contributed by cereal grains. Cereal grains are high in carbohydrates and omega-6 fatty acids but low in omega-3 fatty acids and anti-oxidants.

The theory that best explains the pathophysiology of chronic degenerative diseases at the cellular level is the theory of free radical damage that results from oxidative metabolism and environmental toxins. This free radical damage is countered by the anti-oxidant system of the body, which is dependent primarily on a wide range of vitamins, and other phytochemicals found in fruit and vegetables. A number of these plant-derived substances are well known and include ascorbic acid, tocopherol and bioflavonoids.

In relation to venous diseases, bioflavonoids have been the substances attracting most attention. Flavonoids are a diverse group of compounds and are responsible for the colours of fruits and vegetables. Over 4000 flavonoids have been classified according to chemical structure. Flavonoids in the form of venotonic herbs and O-(8-hydroxyethyl)-rutaside have been used empirically in the management of chronic venous disorders for many years. There is growing evidence that free radicals damage the microvasculature, leading to an increased permeability. It has been shown that flavonoids are able to suppress the formation of free radicals, either by the scavenging of radicals such as lipid peroxides, or by the binding of heavy metal ions - in particular Fe - which catalyze many reactions resulting in the formation of free radicals. It is thought that this powerful antioxidant effect is responsible for the improvement in vascular endothelial permeability observed by the use of bioflavonoids.

A decrease in tocopherol levels has been observed in the walls of varicose veins. This is independent of serum tocopherol levels. It is postulated that this decrease in tocopherol levels is the result of consumption of tocopherol in blocking lipid peroxidation damage in the vascular wall. In this respect tocopherol is acting in a similar way to the bioflavonoids.

CONCLUSION

It is likely that the western diet is deficient in a number of micronutrients essential for the integrity of the vein wall. Compared with a hunter-gather society, industrialized societies are characterized by (1) an increase in energy intake and decrease in energy expenditure; (2) an increase in saturated fat, omega-6 fatty acids and trans fatty acids, and a decrease in omega-3 fatty acid intake; (3) a decrease in complex carbohydrates and fibre; (4) an increase in cereal grains and a decrease in fruits and vegetables; and (5) a decrease in protein, antioxidants and calcium intakes. Owing to the virtual absence of research into dietary nutrients and venous disease it is difficult to pinpoint the essential nutrients for healthy venous systems. However, from epidemiological evidence it would appear that the balance of essential fatty acids and relative deficiency of a range of antioxidants is important. This nutritional hypothesis can also be applied to explain the development of varicose veins in pregnancy (in Western cultures) and the subsequent spontaneous resolution of the veins following pregnancy. Possibly, pregnancy unmasks the relative deficiency of these nutrients by greatly increasing the demand for the nutrients. This nutritional effect would compound with the hormonal and haemodynamic influences of pregnancy.

Comprehensive lifestyle changes (low-fat vegetarian diet, stopping smoking, stress management training, and moderate exercise) have been demonstrated to bring about regression of severe coronary atherosclerosis after only 1 year, without the use of lipid-lowering drugs. These changes also address some of the common aetiopathological factors of varicose veins. It cannot be expected that similar lifestyle changes will reverse the structural changes of advanced venous disease. However, the concept that radical changes in our lifestyle to match our Paleolithic genetic make-up (especially if instituted at an early age) will prevent venous disease or reverse early disease, should not be dismissed without serious consideration. At the very least, it is our duty as phlebologists to inform patients of the known risk factors and advise them appropriately of the lifestyle changes needed to reduce the impact of venous disease on their future health.

REFERENCES

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