The heart and hypothyroidism

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Summary

The association of hypothyroidism with heart disease is reviewed. The relative rarity of cardiac failure due to hypothyroidism is stressed, and structural abnormalities of the heart due to hypothyroidism are discussed. The clinical management of hypothyroid patients with heart disease is described.

S Afr Med J 1983; **63:** 564-565.

Hypothyroidism may initiate cardiac disease or worsen that which already exists. Treatment of the cardiac problem is influenced by the thyroid disorder and vice versa. We recently saw a patient with hypothyroidism who presented with cardiomyopathy and severe heart failure resistant to treatment with digitalis and diuretics. This case focused our attention on the problems of management of hypothyroidism complicated by heart disease. The clinical presentation and management of such patients are reviewed.

Myocardial function

Graettinger *et al.*[1] have found that resting cardiac output is reduced in hypothyroid patients but that cardiac output, stroke volume and pulse rate increase normally during exercise. This finding implies that cardiac function is still normal, i.e. with the reduction in oxygen requirements and metabolism there is a parallel reduction in cardiac function. It is generally accepted that cardiac function in hypothyroid patients is in keeping with their metabolic requirements. Treatment with thyroxine reduces myocardial size to normal,[2,3] a process which may take from 3 weeks to 10 months. Even when the heart is functionally normal, histological changes in the cardiac muscle have been reported. The prognostic implications of these changes are not quite clear.

The heart may be dilated and hypertrophied when the patient is first seen.[2] Hypothyroid patients often have symptoms compatible with those of heart failure such as tiredness, dyspnoea and even orthopnoea. Clinical signs of hypothyroidism which may be confused with heart failure include oedema, ascites, cardiomegaly and pleural effusions. Since hypothyroidism is a rare cause of heart failure other causes of heart failure must be excluded in such patients.[2,3] According to De Groot[3] heart failure occurs more commonly in older patients, in whom other factors causing heart disease are more common. Hypothyroidism has been listed as a cause of hypertension, but a recent study showed that hypothyroidism does not accelerate the development of hypertension.[4] In our experience cardiac failure due to hypothyroidism *per se* is rare. We have seen only 1 such a patient, a young girl in whom no other factors could have caused the heart failure. She responded poorly to conventional treatment with digitalis and diuretics. A vasodilator improved her exercise capacity, but it remained limited. Other patients with initial cardiomegaly all improved with thyroxine replacement therapy only.

Santos *et al.*[5] recently described the echocardiographic findings of asymmetrical septal hypertrophy (ASH) in patients with hypothyroidism. Septal thickening was present in 17 of 19 patients. In 10 patients who were re-investigated the thickness of the septum returned to normal after thyroxine therapy. The manner in which septal thickening is caused in hypothyroidism is still unknown. What is important is that this is one form of heart disease which can be cured when diagnosed and treated appropriately. We have seen no signs of this condition in 7 consecutive patients with hypothyroidism seen in our clinic. It is known that patients with ASH can present with symptoms of angina pectoris and that in some patients with hypothyroidism the angina improves with hormone substitution therapy. It is interesting to speculate that this group of patients might perhaps have had ASH which improved on therapy.

Pericardial effusion

Dilation of the heart and pericardial effusion are known causes of radiological cardiomegaly. Kerber and Sherman[6] found echocardiographic evidence of pericardial effusion in 10 of 33 patients with hypothyroidism. Only 7 of the 10 had cardiomegaly. No patient had cardiac tamponade, this being a rare finding in hypothyroidism. We have seen 1 patient with signs of cardiac tamponade and echocardiographic features of a large pericardial effusion. After aspiration of 2,9 litres of straw-coloured pericardial fluid the patient's condition improved dramatically. The fact that it probably takes a long time for the effusion to develop explains the rarity of tamponade in these patients. Pericardial effusions usually disappear after treatment. The fluid usually has a high cholesterol and protein content and is sometimes described as resembling 'gold paint'.

Ischaemic heart disease

The association of ischaemic heart disease and hypothyroidism is controversial.[7,8] However, hypothyroidism is mentioned as a risk factor for ischaemic heart disease. A raised serum cholesterol level and other lipid abnormalities are known to occur in patients with hypothyroidism. Agdeppa *et al.*[9] found that high-density lipoprotein cholesterol (HDL-C) levels are reduced and low-density lipoprotein cholesterol (LDL-C) levels are increased in hypothyroidism. The ratio between LDL-C and HDL-C is high in hypothyroid and normal in hyperthyroid patients. It was reduced during thyroxine therapy in patients with hypothyroidism but showed little change in patients with hyperthyroidism.

The accelerated atherosclerosis in patients with hypothyroidism is therefore related not only to the elevated total cholesterol level but also to the low level of HDL-C. According to Steinberg[10] ischaemic heart disease is more prevalent among hypothyroid patients when hypertension is present. It is interesting to note that angina improves in some patients when thyroxine therapy is started even though oxygen requirements

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Date received: 6 July 1982.

are increased by thyroid hormone.[7] However, most patients develop angina pectoris when treatment with thyroxine is started. This form of angina is also dependent on the amount of thyroid hormone the patient is receiving. In this group of patients an anatomical narrowing of the coronary vessels seems to be the logical explanation.

Schoolmeester and Jackman[11] described a case in which they thought coronary artery spasm caused angina. A hypothyroid patient developed electrocardiographic features of coronary artery spasm (ST elevation) during pain after treatment with propranolol (a non-cardioselective ß-blocker). Their explanation is that both hypothyroidism and propranolol increase α-adrenergic tone. This is accompanied by raised levels of noradrenaline (primarily an α-adrenergic stimulant) in hypothyroidism. This raised α-adrenergic tone potentiated by the use of a non-cardioselective ß-blocker may cause spasm. Although this is a single case, one should bear it in mind when prescribing ß-blockers to patients with hypothyroidism.

Electrocardiographic features

The typical ECG of a patient with hypothyroidism exhibits sinus bradycardia, small complexes and inverted or flattened T waves. The small complexes have been attributed to an accompanying pericardial effusion, but in the study of Kerber and Sherman[6] small complexes were seen in only 5 of the 10 patients with and even in some of the patients without pericardial effusion. It has been stated that changes occur in patients after aspiration of the pericardial fluid. We have only seen this phenomonen in the patient who had tamponade. Conduction abnormalities such as first-degree heart block may be present but are uncommon.

Pharmacokinetics of drugs

The kinetics of most drugs are affected by hypothyroidism. An excellent review on this subject has been provided by Shenfield.[12] The metabolism of thyroxine changes, with an increase in half-life from 6 - 7 to 9 - 10 days. The half-life of free tri-iodothyronine (T_3) is also prolonged, as is that of propranolol, the dosage of which must therefore be reduced. Reduced hepatic blood flow (part of the low-output syndrome) produces this effect. Digitalis is often prescribed (whether correctly or not) for hypothyroid patients because of their symptoms. These patients are sensitive to the effects of digitalis and toxicity develops more readily. There is a reduction in the $Na^+ K^+$-ATPase and thus less digitalis is needed to inhibit this enzyme. The dosage of oral anticoagulants must be increased in hypothyroidism owing to an increase in the half-life of clotting factors II, VII, IX and X.

These are the more common drugs used in patients with hypothyroidism. It is obvious that most drugs can be influenced by this condition.

Treatment

Treatment of the hypothyroid patient with heart disease must be individually tailored. Even though signs and symptoms may lead to suspicion of heart failure, it must be kept in mind that heart failure is an uncommon complication of hypothyroidism *per se*. When digitalis is prescribed, the patient must be carefully monitored for toxic side-effects. We have seen 1 patient who developed total atrioventricular heart block after commencement of digitalis therapy and in whom blood digitalis levels were in the therapeutic range. Reduction of the digitalis dosage overcame this problem. This patient focused our attention on the doubtful value of 'therapeutic' blood levels of drugs in such patients. L-thyroxine is generally recommended instead of T_3 for substitution therapy.[13] Patients must be started on a low dosage (25 μg/d), which can be increased every 2 weeks up to an appropriate dosage (0,1-0,15 mg/d). Heart failure may be precipitated in some patients by commencing with too high a dosage.[8] Thyroid status should be evaluated by determination of serum thyroid-stimulating hormone levels, which normalize when replacement is adequate.

Some patients will develop angina pectoris when substitution therapy is started.[13] Propranolol has been used with varying degrees of success in this group.[14] Keeping the problem of spasm in mind, it might be wise to consider using a selective $ß_1$-blocker such as metoprolol or atenolol. Even when ß-blocking agents are used it will be impossible to achieve normal thyroid hormone values in certain patients because of their angina. Nitrates may be of value and coronary bypass surgery has been successfully performed in such patients.[14,15] Hay *et al.*[16] point out the dangers of trying to render a hypothyroid patient with incapacitating angina euthyroid. They recommend that determination of the need for and time of operation is more important than attaining normal thyroid hormone values pre-operatively. Patients can be operated on safely whether or not they have received previous thyroid hormone replacement therapy.

Pericardial effusion is rarely the cause of any haemodynamic impairment and aspiration is usually unnecessary. Any other cause contributing to the heart disease, such as anaemia or hypertension, must be treated as required.

Conclusion

Newer methods of evaluation such as echocardiography and coronary angiography aid in the evaluation and treatment of hypothyroid patients. The alterations in drug pharmacokinetics in hypothyroid patients must be kept in mind when prescribing drugs for them. Most patients can be treated effectively with relief of their cardiac symptoms as well as those caused by abnormal thyroid hormone levels.

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