

Primary Sjögren's Syndrome and Cardiovascular risk

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Cardiovascular disease is an umbrella term used to refer to conditions that affect the circulation and the heart, namely angina, heart attack and stroke. Cardiovascular disease is the biggest cause of death in the UK and numerous public health campaigns focus on its prevention. The most common causes of cardiovascular disease are build-up of fatty deposits in the blood vessels (atheroma) and high blood pressure (hypertension). The likelihood of suffering from cardiovascular disease is associated with a series of risk factors (known as traditional cardiovascular risk factors) that include smoking, obesity, physical inactivity, hypertension and alteration in the amount of fat in the blood (lipid profile). These risk factors are modifiable through dieting, exercising and medication in contrast to other risk factors which are not such as family history of cardiovascular disease (father/brother that was under the age of 55 or mother/sister that was under the age of 65 when diagnosed with cardiovascular disease), male sex, and increasing age. In the UK, the British Heart Foundation and the Joint British Society guidelines recommend that all adults aged 40 or over should undergo physical examination and blood testing to determine their risk of developing cardiovascular disease. Once this has been assessed, measures can be taken to prevent disease from happening.

Why is this important in Primary Sjögren's Syndrome?

Extensive research over the last decade has shown that cardiovascular disease not only affects the general population but that patients with chronic inflammatory rheumatological conditions are at higher risk of suffering from cardiovascular disease. As an example, the life span of patients with rheumatoid arthritis (a condition that causes inflammation of the small joints of the hands and feet) can be shortened by up to 10 years mainly due to cardiovascular disease. Patients with systemic lupus erythematosus (an autoimmune disease that affects the joints, skin, lungs and muscles amongst other organs) may also be affected: patients are up to 50 times more likely to suffer from heart attacks than their healthy counterparts. It is therefore not far-fetched to suggest that cardiovascular disease may also be more common in another chronic inflammatory condition such as Primary Sjögren's Syndrome. The difficulty is that there is not enough research into this area and physicians are unable to provide a clear answer as to whether or not patients with Primary Sjögren's Syndrome are at increased risk.

What have we done to address this issue?

Thanks to data collected through the UK Primary Sjögren's Registry project, an initiative partly funded by the BSSA, we have been able to start research into this area in the UK.

What are the results of this work?

Here we present the results of an initial analysis of the prevalence of cardiovascular risk factors in two hundred patients with Primary Sjögren's Syndrome. We have compared these data with that of two hundred age matched healthy controls in an attempt to answer the question: do patients with Primary Sjögren's Syndrome have a higher prevalence of traditional cardiovascular risk factors?

The traditional cardiovascular risk factors measured included: age, gender, smoking, diabetes, family history of cardiovascular disease, hypertension (high blood pressure), altered lipid profile (fat levels in blood) and obesity. Data were collected from fifteen hospitals in the UK all of which had been granted the appropriate approvals to undertake the study.

All patients were female and the average age was 51 years. 88.4% of patients had positive anti Ro and 68.9% positive anti La antibodies. The mean duration of disease was 11.5 years.

We found that 3.8% of Primary Sjögren's Syndrome patients smoked in contrast to 10.1% of healthy controls ($p=0.026$). This is not surprising given that xerostomia (dry mouth) and xerophthalmia (dry eyes) are amongst the most prominent features in Primary Sjögren's Syndrome which we feel may play an important role in deterring patients from smoking. There was no difference in the prevalence of family history of cardiovascular disease, diabetes or obesity between patients and controls.

When we looked at the lipid profile, we observed that 21% of patients had elevated triglyceride levels (a type of fat in the blood) versus 9.5% of healthy controls ($p=0.002$). Through further statistical analysis (binary logistic regression adjusting for statin and fibrate treatment) we looked at the likelihood of having high triglyceride levels if a patient suffered from Primary Sjögren's Syndrome. We found that patients are 2.2 times more likely to suffer elevated triglyceride levels than individuals without the condition. We did not find differences in the prevalence of high cholesterol levels between patients and healthy controls. Hypertriglyceridemia (elevated triglyceride levels in blood) is associated with atheroma (build-up of fatty deposits in the blood vessels) and can predispose to cardiovascular disease even in the absence of high cholesterol levels. Some cases run in families or are caused by underlying conditions (i.e. diabetes, hypothyroidism) whilst others do not have an apparent underlying cause or are related to life style and dietary habits (i.e. excess alcohol intake, obesity). Weight loss and dietary modifications (aimed to decrease the intake of fat) can be very effective in decreasing triglyceride levels in most cases but some patients (especially those with very high triglyceride levels) may also need medication to reduce levels and prevent atheroma formation.

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Perhaps the most interesting finding of the study was encountered when we looked at hypertension. Normal blood pressure measurements vary between individuals. It is generally accepted that a maximum (systolic) blood pressure equal or less than 120-130 mm Hg and a minimum (diastolic) blood pressure of 60-80 mmHg are adequate and not associated with risk of developing cardiovascular disease. Persistently raised blood pressure above these figures carries an increased cardiovascular risk (which is higher, the higher the blood pressure reading). As blood pressure is a continuum and varies between individuals, it is not easy to determine precise cut offs to define hypertension. As a consequence, different health care organisations have produced different definitions of hypertension (some of which are more stringent than others). In our study, we used two of such definitions: the World Health Organisation (WHO) definition that describes hypertension as a reading equal or more than 140/90 mmHg (where the first figure denotes the systolic and the second the diastolic blood pressure value) and the National Cholesterol Education Programme (NCEP) definition that considers hypertension as a reading of more or equal to 135/85 mm Hg. Using these values as cut offs, we found that 28% of patients and 15.5% of controls had hypertension ($p < 0.001$) according to the WHO definition, whilst 50% of patients and 25.6% controls had hypertension when the NCEP definition was applied ($p < 0.0001$). Using further statistical analysis as before we found that patients with Primary Sjögren's syndrome were 2 times more likely to suffer WHO hypertension than healthy controls and 2.9 times more likely to suffer NCEP hypertension. High blood pressure puts strain on the arteries and heart and makes patients with hypertension more likely to suffer from heart attacks and strokes. In the general population, most cases of hypertension (90-95%) are defined as 'primary' or 'essential' denoting that there no underlying cause can be found to account for the raise in blood pressure. A small proportion of patients suffer from 'secondary' hypertension in which underlying conditions (i.e. kidney or endocrine diseases) are responsible for this increase in blood pressure. Regardless of the underlying cause, all patients with hypertension are strongly recommended to undertake life style modifications that include maintaining normal body weight, reducing salt intake in diet, increasing consumption of fruit and vegetables, undertaking regular exercise and limiting alcohol consumption to no more than two units per day. For some patients in which these measures are insufficient, medication is recommended.

How should these results be interpreted?

This study has strengths namely, a very well characterised cohort of patients from different geographical areas. This is important as it means these data are a good representation of the characteristics and the prevalence of cardiovascular risk factors in patients with Primary Sjögren's Syndrome in the UK. Additionally, data collection took place in routine NHS clinics and there were no restrictions to inclusion into the study other than a diagnosis of Primary Sjögren's Syndrome. This is in contrast to other studies in which the groups studied are made out of highly selected patients which makes generalisation of findings difficult. In our study, the multicentre nature of data collection and the lack of stringent selection criteria make these results easily applicable to the majority of patients.

However, there are also some important weaknesses that we need to recognise. The number of patients analysed is large but similar analyses in larger populations are required to confirm these findings. Additionally, one of the main limitations with regards to our finding of higher prevalence of hypertension is the way in which hypertension data was collected. In the study, blood pressure readings were taken on one occasion, however in order to diagnose hypertension, a physician has to be satisfied that the increase in blood pressure is persistent. Consequently to diagnose hypertension, a number of blood pressure readings are

taken on different occasions over a number of weeks, something that was not done in this study. Nevertheless, the finding of at least one high blood pressure reading is still significant and is usually regarded as an indication that further readings are required to investigate the possibility of hypertension.

Summary

In this study we have found higher prevalence of hypertension and high triglyceride levels in patients with Primary Sjögren's Syndrome compared to healthy controls. We also found lower prevalence of smoking. There was no difference in the prevalence of family history of cardiovascular disease, diabetes or obesity between patients and controls.

We must, nevertheless, emphasise that these are preliminary results and we need to undertake further work before we can draw firm conclusions. For example, we need to investigate whether those patients that have higher prevalence of cardiovascular risk factors do also have a higher prevalence of cardiovascular disease (i.e. heart attacks and strokes). We also need to look at the characteristics of the patients with higher prevalence of cardiovascular risk factors to assess whether we can easily identify patients at risk using those characteristics.

Conclusions

Although our results should be taken with caution and should be reproduced in a larger cohort, these data suggest that patients with Primary Sjögren's Syndrome may be at higher risk of suffering hypertension and hypertriglyceridaemia than healthy controls. If these results are confirmed, we may find ourselves in a position to recommend routine and regular screening for cardiovascular risk factors and assessment of cardiovascular risk in patients with Primary Sjögren's Syndrome.