

Inappropriate Sinus Tachycardia

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Clinical Presentation

Heart rate is inversely related to age and independently related to height, physical activity and intake of stimulant (such as caffeine) in healthy individuals.^{1,2}

Epidemiology

Inappropriate Sinus Tachycardia (IST) is a clinical syndrome characterized by a sinus heart rate inexplicably higher than one hundred beats per minute (bpm) at rest that is associated with symptoms like palpitations, dyspnoea or dizziness in the absence primary causes of tachycardia.^{3,4} Therefore, individuals with sinus tachycardia without associated symptoms do not qualify for the diagnosis of IST. Diagnosis can be obtained through a 24 hour holter monitor or event monitor or loop recorder or telemetry. Some publications suggest that an average heart rate of greater than ninety beats per minute at rest can qualify for diagnosis of IST.⁵

An Icelandic study of randomly sampled patients from insurance registries for hypertension estimated the prevalence of IST to be 1.16% with no difference between IST and the control group in age, gender and physical activity.⁶

Patients with IST often present with non-specific symptoms including palpitations, exercise intolerance, light headedness, dizziness, dyspnoea, syncope or weakness. Symptoms can be debilitating and vary between individuals. Symptoms are not always related to heart rate and may affect quality of life.³ Even though the symptoms can have a profound effect on the patient, IST is generally a benign condition. Studies have not demonstrated any increase in mortality or cardiomyopathy with patients with IST.⁶

Diagnosis and Differential Diagnosis

Diagnosis of IST is based on the criteria of heart rate greater than 100 beats a minute (while some publications suggest greater than 90 beats per minute) in symptomatic patients.^{3,6} The diagnosis requires exclusion of other causes of tachycardia including medications/substances (such as anti-cholinergic, beta-blockers withdrawal, caffeine, alcohol) or medical conditions (such as panic attacks, pulmonary embolism, fever, hyperthyroidism, hypovolemia, anaemia, pain).⁷ An important distinction to make is that inappropriate sinus tachycardia must be distinguished from other forms of tachycardia including supraventricular tachycardias and atrial arrhythmias.

Work up should include an EKG to differentiate other causes of tachycardia, 24-holter monitor if indicated, serum thyroid levels, haemoglobin levels and toxicology screen.

Electrophysiological studies are not routinely recommended, but should be considered in certain patients in concurrent supraventricular tachycardia is suspected.

Another condition that can mimic IST is postural tachycardia syndrome (POTS). IST and POTS can present similarly and both syndromes overlap and can affect the same individual. The key distinguishing feature is that patients with POTS have symptoms and tachycardia induced by standing and relieved by recumbence (usually along with blood pressure changes) while IST is mainly provoked by emotional or physiological distress.³

Mechanism

The underlying pathology in IST is yet to be completely understood. However, it is thought that the causes of IST can be broadly classified into two groups. It can be classified either as an intrinsic increase in sinus node automaticity or an extrinsic cause (sympatho-vagal imbalance, increased sympathetic receptor sensitivity, decreased parasympathetic tone, and impaired neurohormonal modulation). Among extrinsic causes, is evolving evidence that IgG anti- β receptor antibodies is found in IST patients that triggers positive chronotropic action by inducing long lasting increment in cAMP which mediates calcium influx and depolarization causing unopposed tachyphylaxis. This mechanism is thought to be the similar in patients with Chagas disease, in which antibodies directed against a ribosomal P protein of *Trypanosoma cruzi* cross-react with and stimulate the β adrenergic receptors causing tachycardia.^{8,9}

Recent evidence revealed a familial form of IST associated with a gain-of-function mutation in the HCN4 pacemaker channel causing increased sensitivity to the second messenger cAMP leading to increase sympathetic drive.⁹

Treatment

Inappropriate Sinus Tachycardia is a chronic medical condition and can be associated with significant loss of quality of life. The treatment is multifaceted and remains a substantial challenge; mainly because the IST is a complex syndrome and controlling heart rate doesn't always lead to elimination of symptoms. Managing patients with IST includes lifestyle modification, non-pharmacological and pharmacological interventions.

Treatment options for IST are limited. The uses of negative chronotropic agents such as β -adrenergic blockers are not usually effective and are associated with many adverse effects.^{3,10} In a study of 20 patients, Metoprolol was compared to ivabradine, and was found to be less likely to be successful in reduction of heart rate and improvement of symptoms in patients with IST.¹⁰

Ivabradine is a promising drug that was recently approved that acts by inhibiting the If current causing reduction in heart rate and improvement in symptoms and quality of life. Multiple studies including randomized trials have reported its efficacy, although long term follow up is lacking.¹¹⁻¹⁵ However, the high costs of ivabradine makes it use prohibitive.

Radiofrequency ablation to modify sinus node has been studied in small populations.¹⁶⁻¹⁸ Primary success rates were excellent acutely, however, in many patients, tachycardia may come recur from other sites of the sinus node or from the atrioventricular junction. Both patients and physician should be aware of the high risk of such intervention which includes: requirements for permanent pacing, phrenic nerve damage or superior vena cava narrowing. Given severity of the complications and no statistically significant long term efficacy in terms of symptomatic relief, radiofrequency ablation should be preserved as a last line option for patients who remain severely symptomatic despite medical treatment and life style modification.^{3,5}

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