Journal of Postgraduate Medicine

Volume 49, Issue 2, April-June, 2003
Print ISSN 0022-3859 CD ISSN 0972-2823

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Role of Left Cardiac Sympathetic Denervation in the Management of Congenital Long QT Syndrome

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Abstract:
Congenital long QT syndrome (LQTS) is a rare but life-threatening disorder affecting cardiac electrophysiology. It occurs due to mutation in genes encoding for the ion channels in ventricular cell membrane. Syncopal attacks and cardiac arrest are the main symptoms of the disease. Anti-adrenergic therapy with oral β-blockers has been the mainstay of treatment for LQTS. However, up to 30% of patients fail to respond to medical therapy and remain symptomatic. An alarming 10% of patients still experience cardiac arrest or sudden cardiac death during the course of therapy. Left cardiac sympathetic denervation (LCSD) has been used as an alternative therapy in patients who are resistant to β-blockers. Although LCSD appears effective in reducing the frequency of syncopal attacks and improving the survival rate in both the short and long-term, its use has not gained popularity. The recent advent of minimally invasive thoracoscopic sympathectomy may improve the acceptance of LCSD by physicians and patients in the future. The primary objective of this article was to review the current evidence of the clinical efficacy and safety of LCSD in the management of LQTS. The review was based on Medline search of articles published between 1966 and 2002. (J Postgrad Med 2003;49:179-181)

Key Words: Long QT syndrome, cardiac sympathectomy, arrhythmia, electrophysiology

Congenital long QT syndrome (LQTS) is an electrophysiological disorder of the heart. It mainly affects children, and carries a high risk of cardiac arrest and sudden cardiac death. The main clinical features of LQTS are episodic syncopal or pre-syncopal attacks. Body surface ECG demonstrates a prolongation of QT interval. The current therapeutic options for LQTS include anti-adrenergic therapy, implantable cardioverter-defibrillators (ICD) and permanent pacing. Anti-adrenergic therapy with oral beta-blockers, which reduces the frequency of cardiac events and sudden cardiac death in up to 70% of the patients, has been the mainstay of treatment. However, approximately one-third of patients on beta-blockers still experience syncopal attacks and more than 10% still have cardiac arrest or sudden cardiac death during the course of therapy. For patients who are resistant to beta-blockers, left cardiac sympathetic denervation (LCSD) has been used as an alternative. It has a high success rate in preventing cardiac events and reducing mortality in LQTS patients. Currently, LCSD is being performed in only a few centres, most of them in Europe. The recent advent of video-assisted thoracoscopic sympathectomy (VATS) has significantly reduced the complexity of LCSD and has also shortened hospital stay after the surgery. However, the long-term effects of this minimally invasive LCSD procedure remain to be seen. The primary aim of this article is to summarize the latest developments in LCSD with a view to stimulating more basic or clinical research in this area. To achieve this aim, we have searched all articles related to sympathectomy in the Medline, between 1966 and 2002.

Role of sympathetic activity in LQTS
The mechanism of arrhythmia, mainly ventricular tachycardia (torsade de pointes) or ventricular fibrillation, in LQTS patients is not well-understood. Sympathetic activity plays a crucial role in the development of arrhythmias and syncopal attacks in patients with LQTS. In animal models, stimulation of the left stellate ganglion induces T wave alternans, which is one of the characteristic changes associated with LQTS. Isoproterenol induces ventricular arrhythmias in animal models mimicking LQTS. In patients with LQTS, the pre-syncopal or syncopal attacks are often triggered by sympathetic activation with the usual stimuli being startled, frightened or physical exercise. Furthermore, anti-adrenergic therapy with beta-blockers or LCSD prevents cardiac events including torsade de pointes.

Rationale of LCSD in treating LQTS
Although β-blockers are the most commonly used anti-adrenergic therapy, implantable cardioverter-defibrillators (ICD) and permanent pacing. Anti-adrenergic therapy with oral beta-blockers, which reduces the frequency of cardiac events and sudden cardiac death in up to 70% of the patients, has been the mainstay of treatment. However, approximately one-third of patients on beta-blockers still experience syncopal attacks and more than 10% still have cardiac arrest or sudden cardiac death during the course of therapy. For patients who are resistant to beta-blockers, left cardiac sympathetic denervation (LCSD) has been used as an alternative. It has a high success rate in preventing cardiac events and reducing mortality in LQTS patients. Currently, LCSD is being performed in only a few centres, most of them in Europe. The recent advent of video-assisted thoracoscopic sympathectomy (VATS) has significantly reduced the complexity of LCSD and has also shortened hospital stay after the surgery. However, the long-term effects of this minimally invasive LCSD procedure remain to be seen. The primary aim of this article is to summarize the latest developments in LCSD with a view to stimulating more basic or clinical research in this area. To achieve this aim, we have searched all articles related to sympathectomy in the Medline, between 1966 and 2002.

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Surgical techniques of LCSD

LCSD was first performed in the late 1960s to treat patients with LQTS who were refractory to pharmacological therapy. The initial procedure was known as left stellactomy, where the left stellate ganglion was removed. This procedure was often associated with Horner’s syndrome due to the interruption of the nerve fibers directed to the ocular region via the upper portion of the stellate ganglion. Left stellactomy provided only limited cardiac denervation in humans.

Another technique, the left cervico-thoracic sympathectomy, was later introduced to remove the left stellate ganglion and the first 4 or 5 left thoracic ganglia. This procedure produced an adequate cardiac sympathetic denervation but was also associated with Horner’s syndrome.

The recent advent of cardiac sympathectomy in the form of high thoracic left sympathectomy (HTLS) has widened the interest in the possibility of surgical intervention in the treatment of congenital LQTS. With HTLS, the lower part of the left stellate ganglion and the first 4 or 5 left thoracic ganglia are removed. This procedure produces an adequate cardiac sympathetic denervation and is associated with a very low incidence of Horner’s syndrome. The latter is attributable to sparing of the ocular sympathetic fibers during resection. For these reasons, HTLS has become a popular option for the surgical treatment of LCSD. In a recent analysis of 123 patients who underwent this procedure, approximately one-third experienced some degree of left ptosis that was barely noticeable to the naked eye. A full-blown Horner’s syndrome was not reported in these patients. The major disadvantage of these surgical techniques is that the surgery is often extensive, and patients are usually hospitalized for several days. Recently, left thoracoscopic cervico-thoracic sympathectomy was performed in a 6-year-old female LQTS patient who failed to respond to the medical treatment. The procedure took 85 minutes to complete and blood loss was minimal. There were no intra-operative or post-operative complications. The patient’s QT interval decreased and she was discharged on the 4th post-operative day. After 9 months of follow-up, the patient remains asymptomatic.

We have also developed a video-assisted thoracoscopic sympathectomy (VATS) technique for the treatment of LQTS. Under general anaesthesia, the pleural cavity is entered via two small incisions in the left 3rd and 5th intercostal spaces at the midaxillary line. The left thoracic sympathetic chain is identified and resected from T1-T5. The lower one third of the left stellate ganglion is also removed. This minimally invasive procedure only takes about 15 min to complete and is associated with no major complications. Patients can be discharged 2-3 days after the surgery. This procedure was initially performed in four patients with LQTS, who failed to demonstrate any response to beta-blocker therapy. Shortening in QTc was observed immediately after the LCSD in 3 of the 4 patients. All patients remained symptom-free after a 7-month follow-up.

Effects of LCSD in the management of LQTS

There has been no randomized, controlled clinical trial to systematically evaluate the therapeutic effect of LCSD. The current data on LCSD are mainly from clinical observations from a small number of cardiology groups. The clinical effect of LCSD appears to be dependent on the thoroughness of sympathetic denervation and the experience of the operators. The greatest reduction in cardiac events and mortality after LCSD is reported from an Italian group who has performed more than half of the reported LCSD procedures around the world.

A recent review of left cardiac sympathectomy in 123 patients, who had failed to respond to beta-blocker therapy prior to the surgery, shows that the cardiac events, mainly syncopal attacks and cardiac arrests, are halved by LCSD. The five-year survival of these patients is 94%, and 10-year survival is above 80% after the surgical treatment.

Apart from improvement in symptoms and survival, QTc interval on body surface ECG is also shortened by LCSD, whereas the heart rate and left ventricular function remain unaffected. In some patients, however, QTc does not return to normal even after LCSD, although the clinical symptoms are markedly improved. The reduction in QTc interval is achieved immediately following LCSD or within 24 hours of the surgery. Once normalised, it remains so in most patients in the long-term.

Summary

LCSD is an effective anti-adrenergic therapy for congenital LQTS. It is indicated in patients resistant to beta-blocker therapy.
Wang: Left Cardiac Sympathetic Denervation for Long QT Syndrome

or in those in whom such a therapy is contra-indicated. Currently, only a limited number of centers are performing LCSD in LQTS patients. Video-assisted thoracoscopic sympathectomy has simplified the LCSD procedure but its long-term effects and the wider acceptance by physicians and patients remain to be seen.

References


Editorial Comments

Interest in the long QT syndrome has been kindled in the 'lay'-press after the acquittal of an Indian mother in UK who was accused of murdering three of her children. She was acquitted following the testimony other grandmother who stated that a number of her own children had died suddenly with no obvious underlying cause.