Lumbar Sympathetic Chain Neuromodulation with Implanted Electrodes for Long-Term Pain Relief in Loin Pain Haematuria Syndrome

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ABSTRACT

Introduction. Loin pain-hematuria syndrome (LPHS) is a rare clinical entity causing unilateral or bilateral intractable flank and loin pain with hematuria. The etiology is poorly understood, and the diagnosis is made by exclusion of urological and nephrological conditions. The management is mainly symptomatic aiming for pain relief with nonopioid and opioids analgesics, and interventions such as capsaicin infusion into the renal pelvis, percutaneous regional nerve blocks, and laparoscopic or open surgical procedures, none of them providing lasting pain relief.

Methods. We describe four cases of LPHS in which long-term pain relief was achieved successfully by neuromodulation of lumbar sympathetic plexus with implanted electrodes. All patients underwent an initial successful trial of neuromodulation with Stimulong monoelectrode (Pajunk, GmbH, Geisingen, Germany) inserted percutaneously to lie adjacent to L3–L4 vertebral bodies followed by permanent implantation of the stimulation system using four contact electrodes (Medtronic Inc, Minneapolis, Minnesota, USA) in two patients with excellent long-term pain relief.

Results. All our patients had significant reductions in visual analog scale scores and analgesic consumption for the duration of the monoelectrode trial and in one patient beyond six months. Of the two patients who had full implants, pain relief is excellent with minimal analgesic consumption and one has resumed employment. There were no complications.

Discussion. LPHS is very difficult to treat with some experts maintaining it is mainly psychological. Conservative treatments are often unsatisfactory and radical measures not reliable. Peripheral stimulation of nerves and plexuses has been successful as shown from case reports. All our patients preferred low-frequency stimulation although its precise mode of action is uncertain.

Conclusion. Our experience shows that lumbar sympathetic chain neuromodulation in intractable LPHS not amenable to conservative therapy is a reasonable alternative before radical interventions. More experience is needed in multiple centers before its recommendation for refractory LPHS.

KEY WORDS: Loin pain haematuria syndrome, lumbar sympathetic chain, neuromodulation, percutaneous peripheral stimulation.
is often unremarkable apart from some tenderness in the costovertebral angle. Patients have normal renal function, radiographic and endoscopic studies of the genitourinary system, and no evidence of infection, malignancy, trauma, nephrolithiasis, or renal insufficiency. The etiology is poorly understood and diagnosis is made by exclusion. Patients never develop evidence of progressive renal disease. Therapy is aimed primarily at relief of pain. There is no effective treatment for cessation of the hematuria. Pain management is a progressive combination from non-steroidal anti-inflammatory agents to narcotics and nerve blocks to surgical interventions. The analgesic requirements can be substantial with a risk of opiate dependence. Interventional procedures include intra-ureteric capsaicin, lumbar sympathetic, epidural and splanchnic blockade, Intrathecal opioids pumps, dorsal column stimulation, renal denervation, autotransplantation and nephrectomy with variable success and without lasting pain relief.

We report four cases of loin pain-hematuria syndrome (LPHS) of variable duration referred to our pain unit by renal and pain physicians after thorough evaluation. The pain had a significant impact on the life of all patients and medical management was ineffective in controlling their pain. In our opinion this is the first case series of successful pain management of LPHS with permanent electrode neuromodulation of lumbar sympathetic chain.

**Case Report 1**

A 33-year-old gentleman was referred to the Pain Management Center at Guy's and St Thomas' Hospital with a four-year history of left loin pain. He initially presented to his local urology services with pain in his left loin and hematuria. A large renal stone was identified and he underwent lithotripsy and placement of a ureteric stent which was subsequently removed. The pain in the loin and hematuria persisted. Cystoscopy and Ureteroscopy revealed no abnormalities nor was there any sign of infection. A repeat cystoscopy, abdominal CT scan, abdominal MRI, ultrasound of the genitourinary tract, and Intravenous ureterogram were performed which were all normal and a diagnosis of LPHS was made. He was otherwise fit and healthy.

His pain was mainly in the left loin radiating to the left groin and testis and at its worst was 10/10 on a visual analogue scale. It was constant in nature and worsened with exercise or stress and improved with rest. He stopped working because of the pain. Analgesia was Oxycodone 120 mg/day, Dihydrocodeine and Paracetamol combination up to four to eight tabs/day when needed and Gabapentin 2700 mg/day. The urologist thought he was a good candidate for renal denervation but the patient was not keen on it. He underwent neuromodulation of the left lumbar sympathetic chain in our unit. Under fluoroscopic guidance, a 22-gauge 150-mm short beveled insulated Stimuplex (B. Braun, Melsungen, Germany) needle was inserted to the left anterolateral aspect of the third lumbar vertebra in the prone position (Fig. 1). After confirming position with contrast, stimulation of the lumbar plexus was done with gradually increasing voltage at 2 Hz and 2 mA for ten minutes. He had pleasant sensation over the left loin and complete pain relief (visual analog scale [VAS] was 4 prior to stimulation and 0 during and for twenty four hours after stimulation).

A catheter trial was carried out subsequently with a Stimulong (Pajunk, GmbH, Geisingen, Germany) mono-electrode catheter inserted under fluoroscopy into left lumbar sympathetic chain plexus adjacent to the third lumbar vertebra (Fig. 2). Stimulation at 1.2 mA at a frequency of 2 Hz for five minutes reduced the VAS from 6 to 0. The trial lasted two weeks with complete pain relief.

Following successful catheter trial, he underwent a full psychological assessment. Afterwards a permanent system was implanted. Two 33-cm Pisces Quad electrodes (Medtronic Inc, Minneapolis, Minnesota, USA) were inserted percutaneously, in a manner similar to performing a lumbar sympatholysis, to lie side by side under fluoroscopy through 14-gauge Tuohy needles adjacent to the lumbar sympathetic chain at L3 level on the left side (Fig. 3). The reason for implanting two leads was an attempt to cover a larger area which we later abandoned in favor of a single lead in our subsequent case with equally good results. After confirming position with contrast and obtaining successful stimulation of the lumbar sympathetic chain which is felt as a pleasant tingle in the painful area,
a small skin incision was made where the catheters entered the skin. Two 51-cm extension leads (Medtronic Inc, Minneapolis, Minnesota, USA) were tunneled under the skin through this incision to the anterior abdominal wall where the pulse generator was to be implanted. They were attached to the quad leads and to the IPG—Synergy (Medtronic, Inc, Minneapolis, Minnesota, USA) which was implanted in a pocket over the anterior abdominal wall under the left sub costal area adjacent to the umbilicus through a skin incision. The electrodes themselves were firmly secured the fascia subcutaneously with anchors to prevent their movement. The unit was programmed and the patient was discharged. The patient was pain free for three months and had come off all opioids. Unfortunately he had a setback in the form of a renal stone and restarted opioids to combat pain till he underwent lithotripsy. At follow-up afterwards he continued to have loin pain and his unit was reprogrammed. At follow-up one year later, the patient reported complete pain relief and has stopped taking all pain medications. He has resumed full-time employment. He is using the system for two hours at a time two to three times every day. The stimulation parameters were a frequency of 5 Hz, pulse width 450 msec and current of 2–3.5 amps.

Case Report 2

A 44-year-old lady was referred to our Pain management center by renal physicians with severe bilateral loin pain and microscopic haematuria which started approximately eight years ago following a series of urinary tract infections. The infections settled but the pain persisted. She also had a long-standing history of back ache but she could clearly distinguish between the two pains. MRI scan of the lumbar spine showed narrowed L5-S1 disc space and was otherwise normal. Cystoscopy, flexible retrograde studies were normal. She was initially seen at the local pain clinic. Physiotherapy, facet joint injections and lumbar epidural for backache and also aimed at loin pain had limited success.

Her loin pain varied between 8 and 10 on VAS scale, continuous in nature without any exacerbating or relieving factors. She has also been extensively investigated by the renal teams and no cause was identified. She was initially treated for her loin pain with dihydrocodeine, Tramadol, and amitriptyline without much benefit. She was otherwise healthy.

She underwent neuromodulation of the bilateral lumbar sympathetic chains. Under fluoroscopic guidance, two 22-gauge 150-mm short beveled insulated Nanoline (Pajunk, GmbH, Geisingen, Germany) needles were inserted to the right and left anterolateral aspect of the third lumbar vertebra. After confirming position with contrast, stimulation of the lumbar plexus was done with gradually increasing voltage at 2 Hz and 2 mA for ten minutes. She had complete pain relief (VAS was 8 prior to stimulation and 0 during and for one week after stimulation).

Subsequently she underwent a catheter trial with a Stimulong (Pajunk, GmbH, Geisingen, Germany) monoelectrode catheter inserted under fluoroscopy into right lumbar sympathetic chain plexus adjacent to the third lumbar vertebra which was continued for two weeks. With
stimulation at 1.2 mA at a frequency of 2 Hz for ten minutes a day, she recorded VAS scores of 0 during that period and did not need any analgesics.

She then underwent a full psychological assessment before undergoing a full implant. No major psychological issues were identified apart from anxiety about the implant. Following monoanode catheter trial, she underwent successful permanent implant. Two 33-cm Pisces quad electrodes (Medtronic Inc, Minneapolis, Minnesota, USA) were inserted percutaneously under fluoroscopy through 14-gauge Tuohy needles adjacent to the lumbar sympathetic chain at L4/5 level one on the either side (Fig. 4). After confirming position with contrast and obtaining successful stimulation of the lumbar sympathetic chains, small skin incisions were made where the catheters entered the skin. Two 51-cm extension leads (Medtronic Inc, Minneapolis, Minnesota, USA) were tunneled under the skin through these incisions to the anterior abdominal wall on the right side where the pulse generator was to be implanted. They were attached to the quad leads and to the IPG—Synergy (Medtronic Inc, Minneapolis, Minnesota, USA) which was implanted in a pocket over the anterior abdominal wall under the right sub costal area adjacent to the umbilicus through a skin incision. The unit was programmed and the patient was discharged. One year following the implant, she is using the system twice a day for ten minutes with complete pain relief in her loins. The stimulation parameters were a frequency of 5 Hz, pulse width 450 msec and current 2–3 amps. She continues to suffer from backache for which she had L3–L5 facet joint steroid injections on the left side.

Case Report 3
A 43-year-old gentleman was referred to our clinic with a five-year history of bilateral loin pain and left groin pain. The pain often varied in severity between right and left groins. Fifteen years prior to this, he had a left pyeloplasty and has had intermittent renal pain ever since sometimes associated with vomiting. Five years ago he started having severe episodes of bilateral loin pain without haematuria and described it as 10 out of 10 on VAS often. He was diagnosed with pyelonephritis after renal stones were excluded and underwent bilateral nephrostomies and ureteric stents which were removed a few months later. However, he continued to have severe bilateral loin pain colicky and continuous with considerable sleep disturbance. He had several hospital admissions via emergency room at a rate of ten a year requiring strong intravenous opioids for pain relief. He had been extensively investigated by urologists at two different hospitals including an MRI scan of thoracolumbar spine and no cause was identified. He was treated at two different chronic pain units. His medications at various times included a transcutaneous electrical nerve stimulation machine, fentanyl patches 50 mcg/hour, pethidine 50 mg up to ten doses per day, gabapentin 1200 mg/day, methadone and local anaesthetic patches to the pyeloroplasty scar with variable benefit. He had to give up his work as a professional for four years and was keen to go back to work. He had a full psychological assessment in one of the pain clinics prior to referral.

Four months after referral, he underwent targeted neuromodulation of the left lumbar sympathetic plexus under fluoroscopy with contrast and insertion of Stimulong (Pajunk, GmbH, Geisingen, Germany) monoanode catheter adjacent to L3 vertebra and was stimulated at 2 Hz for 5 min with increasing voltage which decreased his VAS from 4 to 0. The trial lasted one week during which time he was stimulating three or four times a day for approximately five minutes and got total pain relief. An assessment for a full system implant was withheld because he had complete pain relief for seven months following the trial stimulation.
and was weaning off his methadone at the time of writing this paper.

**Case Report 4**

A 44-year-old lady was referred to the pain management unit by the nephrologists with severe left loin pain and haematuria of five and a half years duration. The pain was of varying intensity with VAS scores ranging from 2 to 8. Ultrasound, CT, retrograde, laparoscopy, and cystoscopy were all normal. She was taking Tramadol SR 400 mg/day, Oramorph 10–20 mg as required, Amitriptyline 50 mg at night, and thyroxine. She had been treated in another pain unit including psychotherapy before being referred to us. The pain was severe enough to interfere with her job. She underwent single needle Nanoline (Pajunk, GmbH, Geisingen, Germany) neuromodulation of left sympathetic chain with complete pain relief for 24 hours with VAS scores of zero. After further assessment she underwent left sided Stimulong (Pajunk, GmbH, Geisingen, Germany) mono electrode catheter trial for three weeks which gave her complete pain relief. She is awaiting implantation of a permanent system and is scheduled to undergo a full psychological assessment.

**Discussion**

Since its first description by Little *et al* in 1967 (1) the medical fraternity has been divided over whether LPHS is a somatoform disorder or a real entity. In spite of the fact that the presentation is fairly uniform, there is no demonstrable pathology. Laboratory and radiographic investigations are generally unrevealing and abnormal findings in individual cases have not been associated on a consistent basis (2–4). Standard renal, haematologic, and rheumatologic investigations are all normal apart from some low grade proteinuria. Renal angiography has demonstrated variable findings from normal studies to changes in small vessels and focal avascular areas and microaneurysms (6). Renal biopsies have demonstrated a number of findings including glomerular hematuria, IgA nephropathy, and thin glomerular basement membrane with normal findings in many cases (7). Various theories have been proposed to explain the pain in LPHS. Based on histological and angiographic evidence of ischemia and vascular abnormalities, many investigators proposed that vaso-occlusive episodes were the cause of symptoms (6,8–11). Theories about a possible autoimmune etiology have been stimulated by the frequent finding of complement deposition in renal specimens (12). Others have proposed that the pain may be secondary to vascular stretching caused by parenchymal swelling due to some underlying cause such as vascular injury. Some authors have suggested symptomatic nephrectomy (SN) as a cause (13). A mechanism where by the Intermittent renal pedicle stretch of SN due to the effects of gravity inducing ischaemia and sympathetic over-activity in the affected kidney have been proposed as a cause.

There have been many reports of association between LPHS and depression, somatization and drug seeking behavior with suggestions that LPHS may represent a type of somatoform pain disorder (14–19). In contrast others have suggested that psychological disability improves as the pain symptoms improve (20).

Management of LPHS is challenging and a multidisciplinary approach with close liaison between pain specialists, renal physicians and psychiatrists should be adapted from the outset (19). It has been reported that approximately 30% of patients will experience a spontaneous resolution of their symptoms after a mean of 3.5 years with conservative medical management (5). Even though the pain can be managed with simple analgesics in the initial episodes, patients often require high dose opioids and sometimes frequent hospitalizations and intravenous opioids as the duration of illness progresses. Regional techniques include intercostal, interpleural, paravertebral, and epidural blocks with temporary relief of variable duration. Lumbar sympathetic and splanchic plexus blocks with or without radiofrequency denervation have also been described (21). More invasive techniques include Intrathecal pumps delivering opioids (22) and spinal column stimulators (23,24). Instillation of capsaicin into renal calyx and ureter has been tried with temporary pain relief but questions have arisen about its safety and efficacy (25,26). Surgical interventions aimed at renal denervation were developed after temporary relief seen in some patients following nerve blockade. The procedures include laparoscopic renal denervation (27), surgical sympathectomy (28), removal of renal capsule (29), nephrectomy (30), and renal auto-transplantation (31–34). Renal denervation had only a 25% success rate and reduced analgesic requirement in a further third in one study (35). In 14% of cases pain returned in the contralateral kidney. In another study, renal auto-transplantation was found to be more effective with 76% of patients remaining pain free on long-term follow-up. Other studies reported lesser results (36). Complications included return of pain in the graft following reinervation (37), graft failure requiring nephrectomy, and onset of pain in the contra lateral kidney (23). Due to the varying long-term success rate and the associated risks and complications, surgical options are considered at a late stage and as a last resort or not at all (19).

All four patients in our series presented with typical features of loin pain hematuria syndrome of variable duration. They were comprehensively investigated by renal physicians and managed by pain specialists before being referred to our unit. Three of them were on regular opioids without much benefit and one patient was reluctant to use them. Two patients had undergone a variety of procedures including lumbar sympathetic plexus blocks with limited benefit. None considered surgical options. Two of our patients had given up employment because of disabling
pain. All our patients had significant pain relief from percutaneous catheter stimulation varying from 24 hours to a few months before the pain returned. The two patients who proceeded to full implant had a full psychological assessment.

Our technique is based on the assumption that the visceral pain of LPHS responds to neuromodulation of the autonomic nerve supply to the kidney. The kidney is innervated by the renal plexus that is situated behind the origin of each renal artery at the level of T12 to L2. There is an autonomic contribution from celiac ganglia, aorticorenal ganglion, the aortic plexus, and the first lumbar splanchnic nerve. These fibers follow the renal artery into the kidney hilus supplying the vessels, glomerular structures, and tubules. Afferent fibers arising in the region of the renal capsule and cortex follow the same pathway and most fibers terminate in the sympathetic system with some following the vagus nerve. The response to blockade or radiofrequency denervation of celiac, splanchnic and lumbar autonomic supply to the kidney is variable in efficacy and duration (38). In our opinion, a technique where by lumbar sympathetic chain could be continuously stimulated would offer patients a reasonable long-term alternative. Although the position of our leads was at levels L3 and lower, pain relief on stimulation was still successful. In case number two, our aim during the permanent implantation was to target the sympathetic chain at L2 to L3; however, the lead position at L4–L5 produced the desirable effect therefore the position of the lead was not corrected further. Our patients preferred low-frequency stimulation both during the trial and after full implant. The direct application of a low-frequency current via a stimulating needle targeted at the sympathetic chain is a very simple procedure, but it can provide valuable information regarding effectiveness of neuromodulatory techniques. This was shown in case studies previously done by these authors to stimulate coeliac plexus and lumbar sympathetic chain using temporary Stimulong (Pajunk GmbH, Geisingen, Germany) catheters (39,40). In accordance with the Algorithm developed in our centre (41), we first carried out a trial stimulation of the lumbar sympathetic chain unilaterally or bilaterally depending on the location of pain with stimulating needles (B.Braun, Melsungen, Germany), followed by stimulating catheter trial (Stimulong, Pajunk GmbH, Geisingen, Germany). The use of monoelectrodes for a trial purpose, instead of standard multicontact leads can be very effective as well as offering an inexpensive alternative to standard trial leads (42,43). The initial stimulating trial provides an excellent assessment of usefulness of neurostimulatory approach in the management of LPHS. A varying duration of pain relief following the short duration slow frequency stimulation targeted at sympathetic chain as it showed in our cases, has been expected as previously reported (39,40,42,44).

A precise mode of action of the low-frequency stimulation on the autonomic system has not been fully understood; however, a beneficial effect of the low-frequency stimulation has been documented in basic sciences and clinical applications. Shimoji et al showed that low-frequency low-voltage electrical stimulation of spinal cord in epidural space produced spinal hypalgesia and analgesia (45,46). The development of non-invasive external stimulation in our Centre, where a similar concept of low-frequency stimulation has been applied, has further supported the use of low-frequency stimulation in control of pain (41).

Application of a low-frequency stimulation to single nerves, plexuses and targeted at a site of pain, mainly in neuropathic pain, has resulted in a substantial resolution of symptoms of varying duration (39,40,43,44). Permanent implantation in the case of targeted Stimulation, single nerves, and plexuses has confirmed these findings (39,42). The percutaneous neurostimulating approach is simpler, less traumatic for patients with potentially reduced side effects. The stability of the implanted leads has not been reported as a problem in the literature. None of the patients reported any complications. Contrary to our concerns, the leads remained firmly in place even when the patients were functioning normally. The successful stimulation of sympathetic chain in LPHS providing an excellent pain control in all our patients, we believe, is offering a new treatment possibility also for other pain syndromes where sympathetic mediated pain is suspected.

**Conclusion**

Our experience shows that patients with LPHS with intractable pain not amenable to conservative therapy can be managed successfully long term, with permanent electrode neuromodulation of the lumbar sympathetic chain. There is less drug dependency with restoration of normal life and possible return to employment. We believe that more experience is needed with this technique in multiple centers before it can be recommended for management of refractory cases of LPHS.

**Conflict of Interest**

None.

**References**


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Comments
This clinical paper reports upon a new application of neurostimulation in a recognized pain syndrome known as loin pain hematuria syndrome. Since it is a new exploratory application it deserves to be published as a report. In addition the authors give a fairly good summary from the literature of the various therapeutic strategies that have been used in the treatment of these distressed patients.

However, there must be caution by the reader. In essence it is a series of selected case reports with variable follow-up. As such there is limited scientific validity. As one reads it through there are many questions that come to mind that are not fully addressed by the text.

However, all journeys start with the first step. We really do not understand the etiology of this visceral pain syndrome. As such it makes absolute sense to find a balance between the possibility of efficacy and the possibility of significant harm. Much further investigation will be required and it is hoped that the authors and other potential collaborators will be encouraged to design further clinical studies so that the reader can be more confident of its benefits.

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This is a very interesting application of neuromodulation for a new indication. I believe that this information is valuable and should be disseminated in the medical community. In view of the varied opinions on loin pain-hematuria syndrome (LPHS) it might be more reasonable to perform the psychological assessment prior to moving forward, even with the trial.

More importantly, I believe the involved discussion of peripheral nerve stimulation and also surface stimulation is confusing and inappropriate in this paper. I would like it eliminated and for a more concise discussion of sympathetic stimulation only. There is no relevance of the others to your case series and it is a distraction.

The review of LPHS for the readers and its treatment also is a valuable review.

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