Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2016, 5, 3:66-72

Sub-neurolytic dose of phenol for popliteal-sciatic nerve block under ultrasound guidance for the relief of ischemic leg pain

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ABSTRACT

Ischemic leg pain is often intractable. Pain relief with conventional analgesics, opioids and non-opioids is often unsatisfactory. It provides only a sub-optimal pain relief in spite of the grievous side effects it causes with the heavy dose required. Interventional procedures like surgical or chemical lumbar sympathectomy also not rewarding. Sciatic nerve can be easily visualized and blocked under ultrasound guidance in the popliteal fossa. Phenol causes temporary axonal demyelination and disruption interrupting nerve conduction. At a low concentration of less than 4% Phenol is reported to have a differential effect disrupting predominantly the pain fibers, retaining the other sensory functions and motor power. This provides sufficient analgesia for 3-6 months. To assess the analgesic efficacy of sub-neurolytic dose of phenol in chronic ischemic leg pain. 43 patients who had chronic leg pain due to ischemic etiology were included in the study after obtaining informed and written consent. Pre-procedural pain was rated using Numerical Rating Scale (NRS). Sciatic nerve in the popliteal fossa was blocked under ultrasound guidance with 3% Phenol in 0.5% Ropivacaine. Pain was rated everyday for first seven days and weekly thereafter for the next 6 months using NRS. Rescue analgesia was offered in the form of oral Paracetamol and Tramadol combination tablets on an 'as and when required' basis. Oral Pregabalin was specially planned to be prescribed to control unbearable or neuropathic pain. Post-procedural pain scores were significantly lower as compared to pre-procedural score in all patients for the entire study period ($p < 0.01$). Sub-neurolytic dose of phenol causes significant reduction in pain scores in an ischemic limb for 6 months, the period of study.

Keywords: Regional Analgesia, Phenol, Chronic pain, Popliteal- Sciatic nerve Block, Ischemic pain, differential nerve block.

INTRODUCTION

The objective of Palliative Care is considered as improvement of the quality of life of a patient suffering from an incurable disease. Pain is one of the common symptoms that have to be relieved in any chronic illnesses. In addition to the site, nature and characteristics of pain, other aspects like mechanism of pain is also helpful in managing pain[1].

Pain due to ischemia of the leg is intractable. The present medical or surgical treatment modalities to improve the perfusion in the diseased limb are very often not successful. The ischaemic pain starts as pain on exertion and deteriorates to continuous, excruciating pain even at rest[2] and disturbs the sleep. Usual treatment for such pain includes analgesics like non-steroidal anti-inflammatory drugs (NSAID), opioids and analgesic adjuvants like the anti-convulsants and anti-depressants. High doses of these drugs causing intolerable side effects may not provide adequate pain relief in these patients. Tolerance can develop to opioids demanding a dose escalation. Sedation, nausea, vomiting and constipation are other side effects. Chronic use of NSAIDs leads to renal and hepatic damage.
Nerve destruction (neurolysis) is an analgesic modality for chronic and intractable pain especially of malignant origin. Ischaemic leg pain is more severe than most of the malignant pains. Approaches to nerve destruction for chronic ischaemic leg pain relief include surgical or chemical lumbar sympathectomy. These methods have not produced consistent analgesia in all patients[2,3]. Significant pain relief with surgical lumbar sympathectomy is

obtained in only 40% of patients3. For the chemical sympathectomy under C-arm guidance it is even lesser. Surgery is an invasive procedure and chemical lumbar sympathectomy needs expertise and there is risk of radiation exposure. Generalized vasodilatation associated with sympathectomy can lead to a 'steal syndrome' and further decrease blood supply in ischemic areas with already diseased arteries[11].

Ultrasound guidance has revolutionized regional nerve blocks. Sciatic nerve can be visualized in the popliteal fossa easily using ultrasound. Unlike the X-rays, the ultrasound waves are non hazardous. Ultrasound guided Popliteal-Sciatic nerve block with a local anaesthetic is successfully performed for surgical procedures below the knee. The longest acting local anaesthetics; Bupivacaine and Ropivacaine provide analgesia for about 10-12 hours only. Patients with ischemic leg have chronic and intractable pain. If we had some drug that could provide prolonged analgesia, it would have been useful for these patients. Search for a long acting local analgesic agent, which may act for months, lead us to this study.

Phenol was first used as a neurolytic agent in 1936 by Putnam[9]. Phenol at concentrations of 6% and above are used for neurolysis[4,5,9..] Phenol leads to demyelination and axonal disruption. Yet, the effects are not permanent. Axonal regeneration occurs and it is completed by 3-6 months. Phenol blocks used for spasticity are known to last for weeks to months[5]. It is being commonly used for spastic conditions associated with chronic neurological diseases (motor neuron disease, cerebral palsy)[7]. It has been used for Obturator nerve block for spastic conditions involving adductor muscles and for Femoral nerve block for spastic conditions involving Quadriceps muscles5. Doses of up to 1200 mg of phenol have been found to be safe in adults[5].

Differential blockade of nerve fibers by the local anaesthetic agents is well documented[10]. Phenol also is reported to have similar differential blocking effects. At a concentrations below 4%, Phenol is known to have a differential effect interrupting predominantly the pain fibers[4,6,9].

The effect of Phenol block depends not only on volume and concentration of solution but also on the precision of the injection technique and the spread of drug[4]. The effects of Phenol last for at least 3 months in most cases[5,9]. The block can be repeated at resurgence of pain. Nerve regeneration after neurolysis may lead to nerve arborization and neuroma formation. This can cause neuropathic pain which may be most disturbing or even agonizing. This dreaded squeal of neurolysis is comparatively less with sub- neurolytic doses of phenol than alcohol[1,8].

Our objective was to investigate the analgesic efficacy of sub-neurolytic dose (3%) of Phenol. We hypothesized that a sub-neurolytic dose (3% Phenol) produce selective and temporary destruction of pain carrying fibers producing lasting analgesia in these patients with chronic ischaemic leg pain.

MATERIALS AND METHODS

The study was conducted at the 'Jubilee Mission Medical College and Research Institute, Thrissur, India'.
Ethical clearance was obtained from the institutional ethics committee.
Study was designed as a prospective cohort study.
Enrollment period lasted for 12 months from July2014 - June 2015.

Adults presented to surgical OPD with lower limb ischemic pain were considered for the study. Procedural details and the probable benefits and risks were explained before obtaining an informed written consent.

Inclusion criteria- Adults who had a leg pain of ischaemic etiology for more than six months with a pain score of more than or equal to 7 on Numerical Rating Scale (NRS) even after treatment with analgesics, was included in the study.

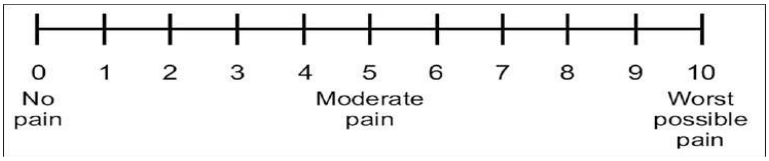
Exclusion criteria- Patients who were allergic to local anaesthetics or phenol and deranged coagulation profile.

The minimum sample size was calculated statistically and was found to be 32. We had enrolled 43 patients for the study to compensate those who were excluded from the study due to death or amputation of the leg.

A medical evaluation was done. Co-morbid conditions were optimized by concerned medical specialties.

On the day of procedure, patients were called in to the specifically designated Block Room in the OR (Operating Rooms). Pain was reassessed by the NRS (Figure 1). Prior to the procedure, all patients were trained in NRS, so that they can later report their pain in NRS verbally over the phone. NRS below 3 indicates a bearable pain.

Figure 1: Numeric Rating Scale



A good IV line was secured. ECG, Pulse Oximetry and non-invasive Blood Pressure monitoring was done. After cleaning and preparing the area with Chlorhexidine and alcohol solution, nerve visualization in popliteal fossa was attempted using ultrasound with all sterile precautions. Needling was performed with a 25G Quinke type spinal needle, connected to the syringe with a high pressure extension tube, by the in-plane approach. 3% Phenol in 0.5% Ropivacaine was injected, close to but outside the epineurium, after negative aspiration for blood. The spread of the drug was observed real-time with the ultrasound. Target was to get a spread of 2.5cm along the length of the nerve. The total volume of drug injected was noted.

Good pain relief in the first hour (due to the added Ropivacaine) indicate correct placement of the drug. For those patients who had inadequate pain relief in the first hour, a repeated injection was done to obtain the desirable effect.

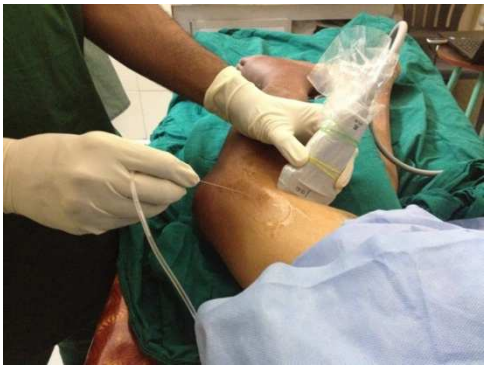


Figure 2: **Popliteal Sciatic Nerve Block being performed. Shows probe position and in-plane needling**

Post procedure, pain was rated using NRS everyday for the first week and there after weekly for 24 weeks over the telephone. While noting the pain scores, the worst pain experienced during that particular day or week was noted. The data was recorded in a pain chart.

If the patient had initial adequate pain relief which had worn off during the study period of six months, a repeat block would be suggested. A repeat sub-neurolytic block will be done only if the patient is willing and demands for it, and submits a new consent.

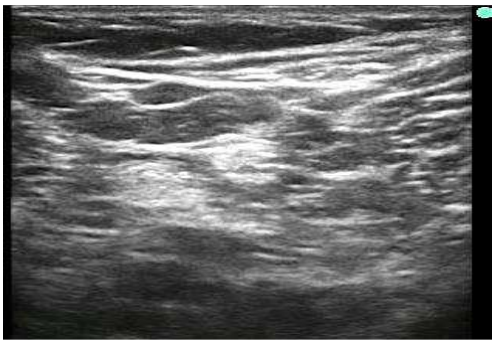
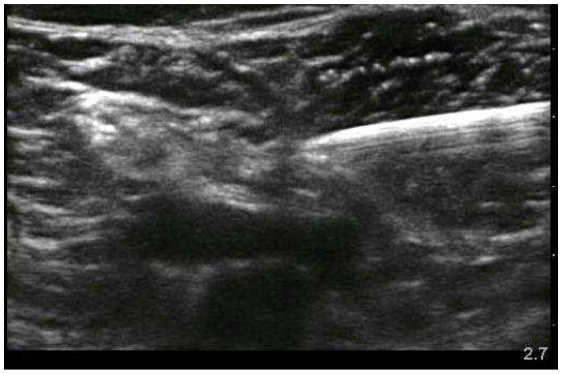


Figure 3: Ultrasound Images Sciatic nerve in the popliteal fossa divided into the Common Peroneal and Tibial nerves



In-plane needling and injection

After the procedure, all patients were prescribed oral Ultracet tablets (Paracetamol 325mg + Tramadol 37.5mg) as a rescue analgesic on an "as and when required" basis. They were allowed to consume up to 4 tablets per day. Oral Pregabalin 75mg tablets (up to 2 tablets per day) was planned to be additionally prescribed to control neuropathic pain if it occur.

Pain during surgical dressing and minor surgery was managed with a general anaesthetic or intravenous procedural sedation and analgesia. Additional doses of Ultracet tablets were used before (pre-emptive) and after such procedures. The extra pain experienced during a procedure and immediately after was not recorded onto the pain chart.

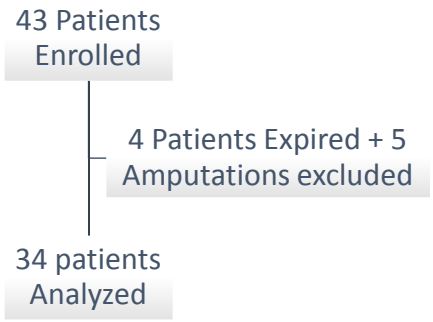
Statistics

Statistical analysis was carried out using SPSS Statistics for Windows, Version 17.0 (SPSS Inc., Chicago, Illinois, USA). Normality of data was tested using Kolmogorov-Smirnov test. Data are represented as mean (± standard deviation) and numbers. Differences in the pain score were compared non-parametrically using Wilcoxon signed rank test. p value of less than 0.05 was considered statistically significant.

RESULTS

Out of the 43 enrolled patients, 4 patients died during the study period and 5 patients underwent amputations due to gangrene (ischemic or infective). They were excluded and remaining 34 patients were analyzed (Figure 4).

Figure 4: Flow diagram of patient enrollment



General data of the patients and the total drug volume used are summarized in Table 1.

Table 1: General Data

Demographics		Mean ± SD / Number
Age (Years)		66.58 ± 9.4
Sex	**Male**	25 (73.5%)
	Female	9 (26.5%)
Weight (Kg)		58.32 ± 6.6
Volume of Drug (ml)		6 ± 0.8

Figure 5: Numerical Rating Scale Pain Scores

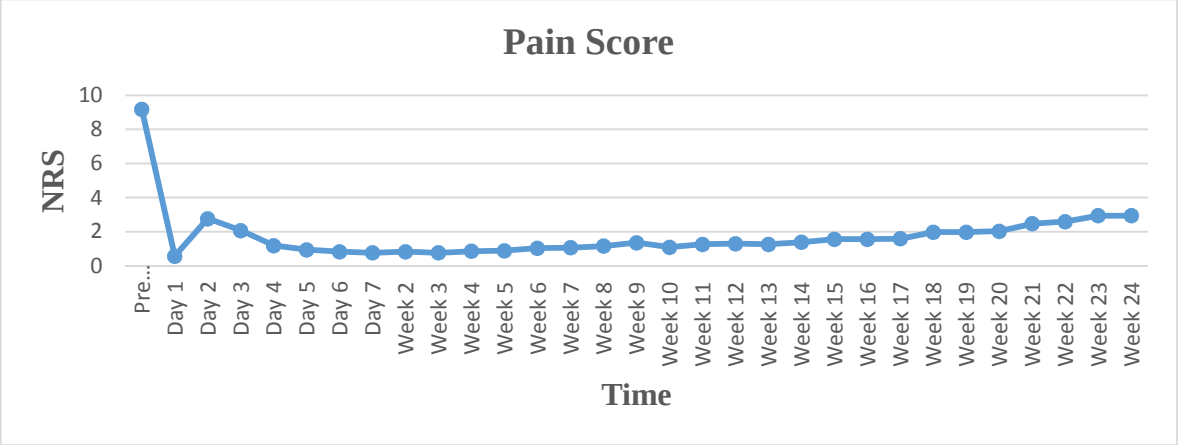


Table 2: NRS Pain Scores. (Pre procedure Pain Score:NRS - 9.18)

Time	NRS Pain Score (Mean)	Mean Difference with Pre procedure NRS	p Value
Day 1	0.56	8.6	0.002
Day 2	2.76	6.4	0.007
Day 3	2.06	7.1	0.006
Day 4	1.18	8	0.004
Day 5	0.94	8.2	0.003
Day 6	0.82	8.3	0.003
Day 7	0.76	8.4	0.002
Week 2	0.82	8.3	0.003
Week 3	0.76	8.4	0.002
Week 4	0.85	8.3	0.002
Week 5	0.88	8.3	0.003
Week 6	1.03	8.1	0.003
Week 7	1.06	8.1	0.003
Week 8	1.15	8	0.003
Week 9	1.35	7.8	0.004
Week 10	1.09	8	0.003
Week 11	1.26	7.9	0.004
Week 12	1.29	7.9	0.004
Week 13	1.26	7.9	0.004
Week 14	1.38	7.8	0.004
Week 15	1.56	7.6	0.005
Week 16	1.56	7.6	0.005
Week 17	1.59	7.6	0.005
Week 18	1.97	7.2	0.006
Week 19	1.97	7.2	0.006
Week 20	2.03	7.1	0.006
Week 21	2.47	6.7	0.008
Week 22	2.59	6.6	0.008
Week 23	2.94	6.2	0.003
Week 24	2.94	6.2	0.009

NRS pain scores were below 3 indicating a bearable pain (Figure 5). All the NRS pain scores after the procedure when compared to pre-procedural scores were significantly lower with a p value less than 0.01.

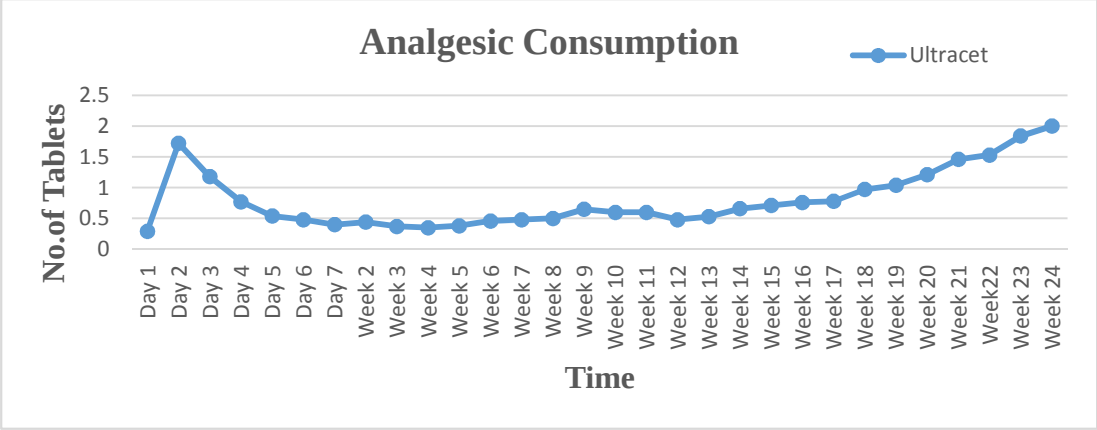
P value below 0.05 is statistically significant (Table 2).

Post procedure requirements of Ultracet (Tramadol & Paracetamol) was also correlating with the pain scores. (Figure 6).None of the patients developed neuropathic pain and oral Pregabalin was not prescribed.

Oral Pregabalin tablets were included in the study to control neuropathic pain if it occurs during the course of the study as this was one of the dreaded complications of a neurolytic block. But none of the patients developed a neuropathic pain to require this drug.

The pain in all the patients was in the tolerable limit of NRS < 3, and none of them requested for a repeated block.

Figure 6: Post procedure analgesic requirement



DISCUSSION

Our study proves that a sub neurolytic dose of phenol (3%), when administered in popliteal-sciatic nerve block in patients with chronic leg pain of ischemic etiology provides excellent analgesia.

Pain scores after the procedure were significantly lower in all the study subjects. The post-procedure rescue analgesic doses of Ultracet tablets were determined by the patient depending on his subjective assessment of pain. Satisfactory pain relief could be achieved with these tablets within the limited dose. Many patients had a bearable pain and consumed no rescue analgesics for varying periods.

The pain score reported by the patient indicate the combined effect of the sub-neurolytic block and the rescue analgesics. The amount of rescue oral analgesic required to control the pain to the bearable levels (NRS <3) is inversely proportional to the pain experienced after the block. It may be noted that all the patients under the study was experiencing excruciating pain rated above NRS 7 in spite of the heavy dose of strong opioids and NSAIDs. After the sub-neurolytic block, adequate pain relief could be achieved with a small dose of mild analgesics.

The pain scores were very low below 1 on the first day due to the profound analgesic effect of the local anaesthetic Ropivacaine 0.5% in the analgesic mixture. There is a surge of pain on the second and third day before the pain scores come down again. The reason for this phenomenon is the slow onset of action of Phenol which takes about three days to establish[9].

Patients who had an escalating pain after the block had a secondary cause like infection or worsening ischemia. Most of the time, they were subjected to amputation or disarticulation later and hence excluded from our study.

The leg remained sensitive to touch and painful to pin prick in all patients who had received the block. The ‘first pain’ or the nociceptive pain largely conducted through the A delta fibers appeared to be retained. Unmyelinated C fibers which cause the poorly localized ‘second pain’ which leads to the pain at rest and suffering, appears to be differentially blocked.

Minor surgical procedures like surgical dressing and slough excision caused pain in these patients and were carried out under General Anaesthesia or procedural analgesia and sedation. They had low pain scores following the procedure and continued in the study. The high pain scores during the surgical procedure were not recorded in the Pain chart.

This retention of nociceptive pain and touch is protective and helps in the early detection of any secondary events of ischemia or sepsis.

Motor power of the below knee muscles were retained and patients could walk with the injected leg.

The differential blockade of the thin and unmyelinated C fibers and sparing of other thick A and B fibers might be the probable cause of this beneficial effect. The sharp nociceptive pain conducted by A-delta fibers was retained. Touch (A beta) and motor power (A alpha) were also retained.

None of these patients developed neuropathic pain during the study period and required oral Pregabalin.

None of the patients under the study developed unbearable pain or requested a repeat block.

We have observed no trophic changes in these patients. This needs to be verified by further studies.

There is a slow rise in the pain scores after the 14th week with a steady rise up to the end of the study in the 24th week. There is a corresponding increase in the consumption of Ultracet tablets. This may indicate the slow wearing off of the sub-neurolytic effect.

CONCLUSION

Popliteal-Sciatic nerve block with a sub-neurolytic dose of Phenol (3%) produced significant reduction in the rest pain scores in an ischemic leg for a period of six months, the duration of this study. Touch sensation, nociceptive pain and motor power were retained. This is protective and beneficial to the patient. A rapidly escalating pain score always indicated an advancing disease process.

Acknowledgment
We are thankful the JMMC&RI for the funding and permission for the study. We would like to thank our colleagues in the Anaesthesia Department who helped us during this study. Thanks are due to the Anaesthesia technicians who appraised the pain, collected the data and put up the pain charts. We would like to thank the patients who accepted to be part of this study.

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