Intermittent pneumatic compression therapy for peripheral arterial occlusive disease

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There is a long history of usage of intermittent pneumatic compression (IPC) for the prevention of deep vein thrombosis and in the treatment of lymphedema. While IPC is well accepted for these indications, it is also now being used in a different form for treating lower extremity peripheral arterial disease (PAD).

History

Increased arterial flow was observed in the mid 1960's by Henry[1], et al using a DVT type of IPC device with the pressure advanced to 100 mmHg. Henry measured flow using a tissue clearance technique of injecting an I^{131} labeled tracer into the foot. Limbs with IPC applied demonstrated a more rapid clearance of injectate than did the control limbs.

Dillon[2] developed a cardiosynchronous compression device that applied high pressure, rapid compression from the groin or calf to the toes. He observed increased pulse volumes in the calf, subcutaneous oxygen pressures in the foot and pedal artery Doppler signals in severe arteriopaths. Dillon has a large body of anecdotal evidence showing limb salvage in patients not suitable for arterial revascularization.

Banga[3] in Utrecht applied simultaneous rapid, high pressure compression to the foot and calf of patients with Fontaine stage III-IV and found increased blood flow (using a plethysmographic method) and improved transcutaneous oxygen pressure recovery time.

Mechanisms of action

Van Bemmelen[4] investigated the effect of rapid, intermittent calf compression on popliteal arterial flow using color duplex ultrasonography. He found that using pressures of about 100 mmHg applied to the dependent limb of arteriopathic patients approximately tripled popliteal artery flow. Not only was peak systolic increased but end diastolic flow was as well which suggests a significant decrease in peripheral resistance. He suggested that two physiologic mechanisms contributed to the hyperemic response: Emptying of the veins under the cuff dropped their venous pressure to almost zero while not affecting the arterial pressure. The arterial to venous pressure gradient was therefore increased and flow increased by a similar factor. Second, since the calf cuff is inflated rapidly (in 0.3 seconds to peak pressure), the high shear rate causes the endothelium to release nitric oxide (NO), a powerful vasodilator[5,6,7]

Investigations by Eze and Comerota[8] from Temple University showed that rapid, high pressure IPC not only increased popliteal artery flow (using duplex imaging) but also significantly increased foot skin perfusion using laser Doppler fluximetry. They later showed that the 86% to 93% of the cutaneous blood flow increases were due to augmentation from the arterial side and only a small part of the cutaneous flow increases were due to reverse venous flow[9]. Van Bemmelen[10] also showed significant increases in cutaneous laser Doppler flux in patients with severe of the crural outflow arteries while using IPC with combined foot/ankle and calf compression.

Labropoulos[11] demonstrated the acceptable variability of duplex ultrasound derived blood flow measurements and that the application of rapid, high pressure IPC of the foot/ankle and calf greatly enhances popliteal artery flow; that the increase is due to a dramatic drop in peripheral resistance as the peak systolic and end diastolic flow velocities increase while the reverse-flow component diminishes.

Optimization

Nicolaides' group in London[12] determined the optimum IPC stimulus for IPC. Since a primary mechanism is the reduction in venous pressure and likely abolition of the veno-arteriolar reflex, they directly measured venous pressure by cannulating a dorsal vein in the foot. They then comprehensively evaluated compression variables effect on reducing venous pressure. Those variables included frequency, pressures, air bladder location combinations and delay between bladders. They used an IPC device (ArtAssist model AA-1000, ACI Medical, Inc., San Marcos, CA, USA) that was modified to set timing and pressures over a wide range. The resulting optimized variables are: Frequesncy- 3 to 4 compressions per minute; Pressure- rapid (0.33 Sec) increase to 120 to 140 mmHg, held for 3 seconds; Bladder locations- foot/ankle and calf regions; Delay between bladders- one second. These settings have since been incorporated into the commercial device. The study concluded that calf compression is superior to foot only compression and that combined foot/ankle and calf compression with a delay between them is the most favorable mode of compression for improving the primary physiological parameter.

Clinical efficacy

Once the optimal stimulus was determined, a number of investigators have dealt with determining efficacy in treating patients with intermittent claudication and critical limb ischemia. Delis[13] of Nicolaides' team in London randomized patients with stable intermittent claudication in a controlled study of the optimized ArtAssist IPC device used at home for 2.5 hours a day. Assessment measurements included treadmill testing for initial and absolute claudication distances (ICD and ACD), resting and post exercise Ankle/Brachial Indices (ABI's), and quality of life assessment (SF-36). After 5 months, ICD and ACD increased in the experimental group by 197% and 212%. Resting and post exercise ABI's improved by 17% and 64%. The experimental group enjoyed a better quality of life than the control group. Changes in the control group were all non-significant. One year after the end of the application of IPC, the experimental group maintained their ABI's and walking benefits. This suggests that there are permanent benefits with continued use of the IPC device. It is postulated that collateralization may be responsible for the improved ABI's and long term improvement in walking distances. Similar results of increased pain free walking distances were obtained in a separate study by Ramaswami[14] at Mt. Sanai in New York.

Kakkos[15] et al presented their results of an intermittent claudication trial comparing the optimized IPC with supervised exercise and unsupervised exercise. After 6 weeks of treatment, absolute claudication distances were increased by 86%, 43% and 13% respectively.

Perhaps the most clinically important indication for IPC is in limb salvage for patients that are poor candidates for reconstructive surgery. Often, native vein for distal bypass is unavailable or unusable or target vessels are insufficient outflow vessels. Once a graft has failed, it may not be revisable and amputation may soon follow. Louridas[16] in Winnipeg, Canada applied the ArtAssist IPC device to 33 critically ischemic limbs that were expected to result in amputation. After three months on the pump, 40% of patients with rest pain were improved and became claudicants, 26% of foot ulcers healed, toe pressures showed a significant improvement and there was a 14% amputation rate (not including the higher risk chronic renal failure patients). The amputation rate was 29% for patients eligible for the study but not entered into it because their referring physician was unaware of the project.

Collateralization

Van Bemmelen[17] studied critically ischemic limbs experiencing rest pain or tissue loss that were not amenable to revascularization due to lack of outflow arteries, lack of vein or in poor general medical condition. Patients were instructed to use the optimized IPC device for four hours a day for three months. Nine of the fourteen limbs showed significant increases in pulse volume recordings. These limbs were salvaged while limbs that showed no PVR improvement went on to amputation. Further, there was a direct correlation between patient compliance and limb salvage. Those that used the pump for an average of 2.38 hours per day all had their limbs saved while those that used the pump for an average of 1.14 hours a day all required amputation. Since it is highly unlikely that compression treatment opens stenotic vessels, it is suggested that arteriogenesis or collateralization is responsible for improved distal pulses.

Moses[18] in Ashkelon, Israel published the case of a 75-year-old man with bilateral critical limb ischemia with rest pain and ulceration. He was given the optimized IPC pump and experience relief for his rest pain after 3 days along with a reduction in leg edema. After three weeks of pump treatment the ulcers had healed. After three months, the Doppler examinations demonstrated significantly improved ABI's in both legs and there were favorable changes in the PVR's.

The improvements in ABI's, PVR's and sustained improvements in claudication distances prompted Van Bemmelen[19] to look for angiographic evidence. He reasoned that the acute vasodilatation observed in duplex ultrasonographic imaging studies was attributable to the release of endothelial NO caused by the rapid, high pressure compression of the optimized IPC device. Since NO has also been shown (Unthank) to be a mediator in collateral artery development, it was likely that the physiological and clinical improvements from IPC may be associated with the development of collateral circulation. A critically ischemic patient with autogenous vein graft to the dorsalis pedis artery occluded shortly after surgery. The contralateral limb underwent a popliteal artery-to-peroneal artery bypass with saphenous vein but this too occluded despite anticoagulation and antiplatelet therapy. After lumbar sympathectomy, the patient still experienced severe rest pain requiring high doses of narcotics. The optimized IPC device was applied 1 hr. q.i.d. at home and after four months and a transmetatarsal amputation, pain resolved and an arteriogram showed extensive collateral filling of the proximal and mid-calf level posterial tibial artery. At the ankle, there was an increased caliber of the posterior tibial artery. Additional plantar branches were seen near the calcaneous.

An IPC device similar to the optimized pump but without foot compression was used on critical limb ischemics for six hours per day by the Mayo Clinic[20]. Their reported experience of 107 patients with active ulcers was, after six months of IPC treatment: Complete wound healing with limb preservation in 40% of patients with TcPO2 levels below 20 mmHg; by 48% with osteomyelitis or active wound infection; by 46% with diabetes treated with insulin; and by 28% with a previous amputation. Seven patients stopped using the device due to pain experienced with its use.

Conclusion

A review by Labropoulos[21] examined 26 studies performed using IPC on arteriopathic patients. He concluded that the studies demonstrate conclusive physiologic benefit from IPC and that IPC may be used in patients with severe peripheral arterial disease who are poor candidates for surgery or percutaneous angioplasty. The low cost of treatment and home use of IPC devices are indirect benefits of this treatment modality. Required now are large scale, randomized, trials to clarify the most clinically beneficial regimen.

Preliminary results of our current study measuring changes of endothelial activity (EA) in connection with ICP in patients with peripheral arterial disease shows a statistically significant increase of EA. The activation of synthesis of the most powerful endogenic vasodilator - nitric oxide could be thus detected.

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