Could hydrocephalus shunts have a role in the treatment of lymphoedema?

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ABSTRACT

Lymphoedema is a consequence of impaired lymphatic drainage. Available treatment options vary in efficacy and impact on the individual. Whilst all are useful in reducing the extent and impact of lymphoedema, there are confounding factors such as patient compliance, financial and physical costs and unpredictably variable outcomes. There seems to be no single treatment that is affordable, effective and sustainable for patients with lymphoedema.

This review introduces the novel idea of a modified hydrocephalus shunt as a surgical alternative to treat (and perhaps prevent) lymphoedema.

Hydrocephalus shunts allow cerebrospinal fluid (CSF) to circumvent an obstruction during periods of impaired absorption, removing the build-up of fluid that causes hydrocephalus, working on a low pressure system.

Lymphatic pumping pressures in failing arm lymphatics have been recorded as approximately 25 mmHg[1]. In early stage leg lymphoedema, pressures have been recorded around 70mmHg (diastolic) and 100mmHg (systolic), whilst late stage lymphoedema has been recorded as 20mmHg, though often these lymphatics are very difficult to cannulate.

As hydrocephalus shunts work on pressures as low as 15-25mmHg at flow rates as low as 5ml/hr it is plausible that they could be used to facilitate normal flow, but importantly prevent retrograde flow of lymph in failing or failed lymphatics, thereby reducing lymphoedema.

Keywords: Lymphoedema, hydrocephalus, shunt, intralymphatic pressure.

INTRODUCTION

The lymphatic system is a low pressure vascular network that has a major role in the maintenance of fluid homeostasis and immune system regulation and defence in the human body[2] and is often at risk of damage through illness, surgery, radiotherapy, infection and day-to-day life.

There is a net, low-level filtration of plasma from both the arterial and venous ends of capillary beds, resulting in accumulation of plasma in the interstitium[3]. This ultra-filtrate comprises fluid, proteins and small molecules which are able to filter out of the capillaries and into the interstitium[4] and this interstitial fluid is then taken up into the lymphatic system by the terminal lymphatic capillaries[5].

Lymphoedema is a process of either congenital (primary lymphoedema) or acquired (secondary lymphoedema) abnormalities of the lymph vessels that result in impaired lymphatic drainage and fluid accumulation in the tissues[6,7]. Damage to lymphatic vessels can result in degenerative changes such as hyperplasia of endothelial cells, thickening of sub-endothelial collagen fibres, decreased number of collagen fibres and eventual total occlusion of the lymphatic lumen[8]. These changes result in an initial deceleration of flow, which causes overloading of the lymphatics and increased intra-lymphatic pressure with subsequent dilation and incompetency of unidirectional valves and retrograde lymph flow. Eventually, due to lack of contractility of lymphatics there are no effective pressures produced by the lymphatics sufficient to propel lymph and as the outflow for lymph is blocked, muscle contractions are unable to empty excess lymph[8]. This reduction in lymph flow often predisposes patients to poor wound healing, causing further complications.

In developed countries, the greatest cause of lymphoedema is obstructive lymphoedema caused mainly from the treatment of cancer; such as those patients who have received mastectomies and lumpectomies[6]. Outside of developed nations the most common cause of lymphoedema is lymphatic filariasis, which affects approximately 120 million

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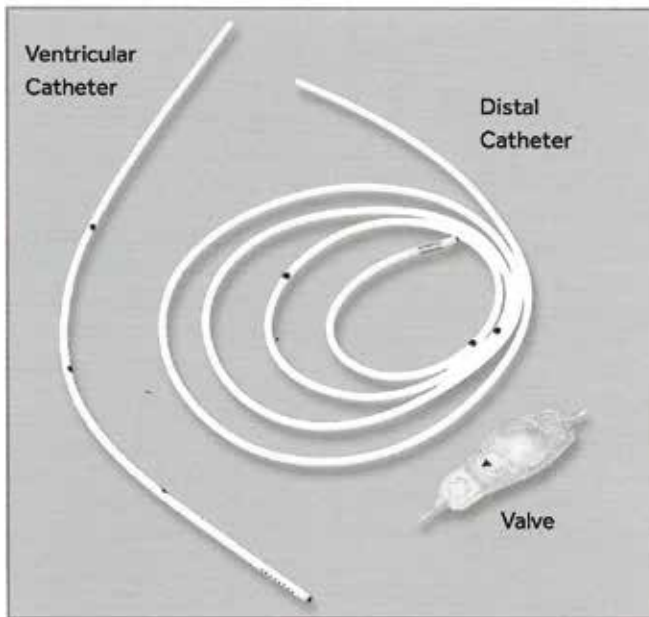
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Figure 1: Main components of a hydrocephalus shunt[14]

people worldwide[6,9]. There are functional, psychosocial and emotional aspects of lymphoedema which impact greatly on the quality of life of sufferers, some of which are associated with the treatment regimens prescribed[10].

CURRENT TREATMENT OPTIONS

As with most interventions, a multidisciplinary approach to the treatment and management of lymphoedema is most effective, currently referred to as complete decongestive physiotherapy or treatment[6,11]. For lymphoedema, current research dictates that an approach that involves exercise and movement, swelling reduction and maintenance, skin care, risk avoidance and management of pain and psychosocial issues offers the best outcomes for lymphoedema sufferers[6]. There is currently an array of non-surgical and surgical treatment options available that offer varying degrees of relief for patients.

Physical therapy combined with compression is considered the standard treatment aiming to reduce fluid outflow into the interstitium by reducing venous pressure and flow[11]. This has been shown to reduce the size of the oedema by 40–60%, with compression garments achieving a size reduction of 46% individually[6]. However, this treatment is merely a maintenance treatment, not a cure, and one which relies heavily on long-term patient participation and compliance[6].

Manual lymphatic drainage is a form of massage developed with the aim of directing fluid towards functioning lymphatics and thereby bypassing damaged or obstructed lymphatics in order to drain an area of congestion[6]. Extensive studies have demonstrated that it is not beneficial as a stand-alone treatment, and that if done inappropriately (that is, too forcefully) can actually damage lymphatic vessels and

increase capillary filtration, which will only worsen oedema. As such, it is a treatment that should only be performed by trained operators, be that therapists, caregivers or the patients themselves[6,11].

Pneumomassage, or intermittent pneumatic compression (IPC) involves compression supplied by an external pump and compression stockings to reduce oedema[6]. This form of intervention is limited by patient compliance, risk of lymph obstruction, and lack of suitability for those with renal or congestive heart failure, and active metastatic disease. There is also a risk of damage to more superficial structures if the pressures in the pump are set too high[6].

Liposuction in the treatment of lymphoedema aims to remove fat in the affected limb in order to reduce the appearance and symptoms of lymphoedema[6]. It is indicated when other, non-surgical treatment options have been exhausted and there is significant discomfort in the affected limb due to weight[12]. It is, however, not a treatment option for patients with pitting oedema and requires high levels of patient compliance post-surgery with the use of compression garments and wound care[6].

Anastomoses can either be lymphatic to lymphatic (lymphatic-lymphatic bypass), lymphatic to vein (lymphaticovenous bypass) or lymph node to veins and arteries (microvascular lymph node transfer)[6]. These interventions aim to bypass the obstructed lymphatic. Whilst these surgical interventions have been shown to reduce lymph clearance time, there are potential complications, such as the development of lymphoedema at the site of lymphatic harvest and large surgical scars, combined with the fact that there is limited standardised data on the efficacy of such interventions[6].

HYDROCEPHALUS SHUNTS

Hydrocephalus shunts traditionally allow cerebrospinal fluid (CSF) to circumvent an obstruction in its normal pathway during periods of impaired absorption, removing the build-up of CSF that causes hydrocephalus. These shunts usually comprise three components: an inflow catheter which drains CSF directly from the ventricles or subarachnoid space; a valve which regulates flow and pressure within the catheter; and an outflow catheter, which connects either to the peritoneal cavity, heart or other drainage site and allows CSF to flow out into this space (Figure 1)[13].

In order to assess whether the use of hydrocephalus shunts would be appropriate in the treatment of lymphoedema, two brands of hydrocephalus shunts commonly used in Australia were considered: Medtronic® and Codman®. Both companies boast an array of shunt systems with catheters designed for various specifications and valves that may operate under single or adjustable pressures[15-17]. Comparing the pressure-flow rate settings of the Codman CERTAS® Plus Programmable valve and the Medtronic™ Strata™ adjustable valves it can be seen that both operate similarly under very low pressures and flow rates (Figure 2)[15,17].
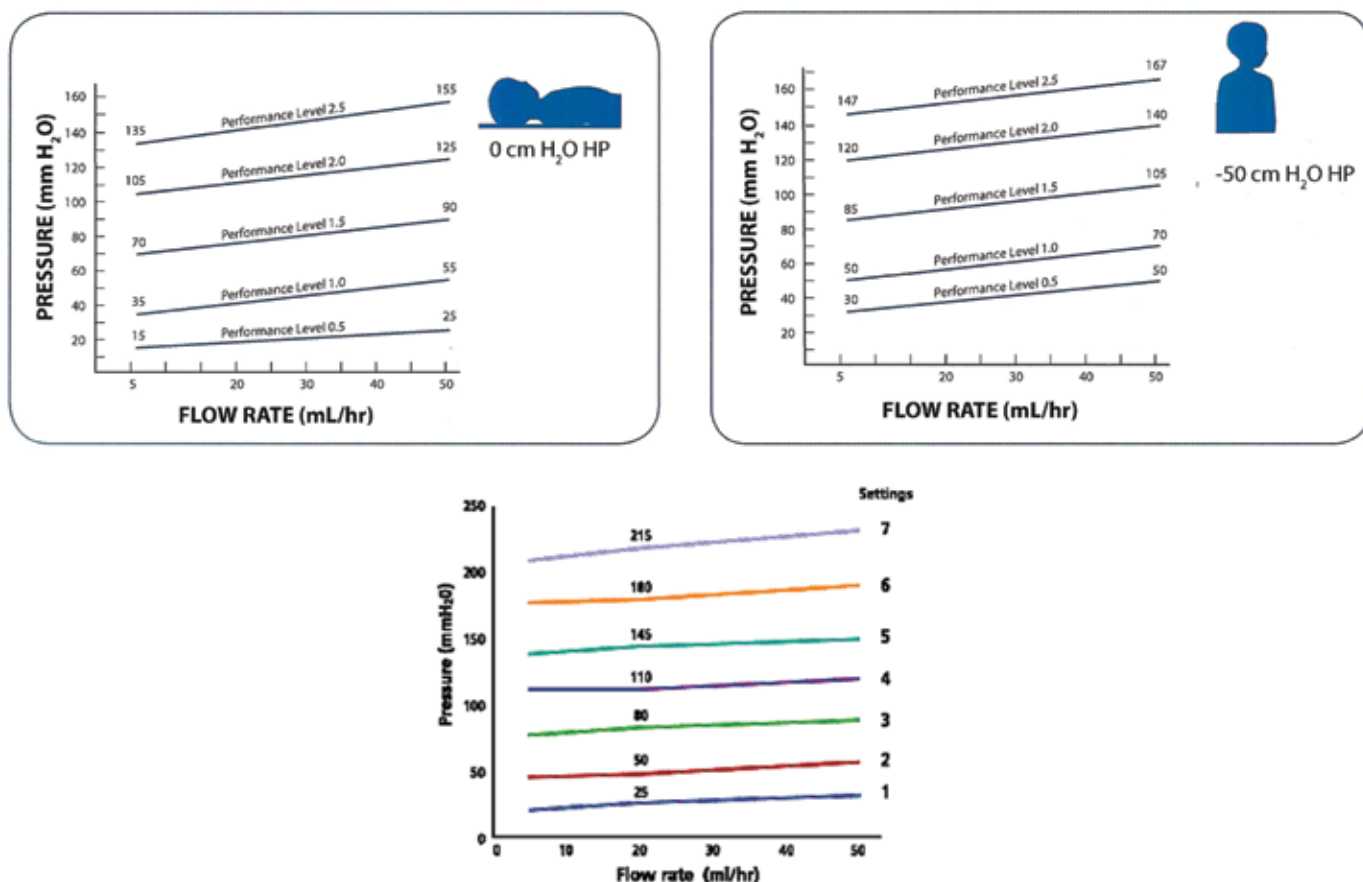
Figure 2: Top are the specifications for the Medtronic™ Strata™ adjustable valves and below are the settings for the Codman® CERTAS® Plus Programmable valve[15,17].

As demonstrated by Figure 2, these adjustable valves operate under pressures as low as 15 mmHg and flow rates as low as 5 mL/min[15,17].

HYDROCEPHALUS SHUNTS AND INTRALYMPHATIC PRESSURES

There is limited data available with regard to the pressures acting within human lymphatics; however, studies by Modi *et al.* and Olszewski and Engeset have shed some light on lymphatic flow rates and pressures under various circumstances. In this review, end lymphatic pressures are being focussed on, as this data will be most relevant to the potential use of a hydrocephalus shunt as treatment.

It is important to note that in healthy individuals, the rhythmic contractions of the lymphatics are the main factor in the generation of pressures sufficient to produce lymph flow, and therefore contractions of surrounding musculature, and external massage and compression of the lymphatics of healthy individuals do not greatly increase flow as the lymphatics are usually empty between pulsations[8,18,19] and the pulsations alone are sufficient to propel lymph. Whilst rhythmic contractions of surrounding leg muscles do not increase the mean pressure of normal lymphatics

between pulsations, it does create a slight increase in pulse pressure of 0.5–3 mmHg superimposed on the intrinsic pressures produced in both horizontal and upright healthy patients[8,20]. These contractions also increase the frequency of pulsations[8,18,20].

In individuals with obstructive lymphoedema, spontaneous contractions are irregular and ineffective, whilst muscle contractions, external compression of lymphatics through the use of elastic stockings and massage can produce lymph flow[19].

Several studies have demonstrated that a systolic pumping pressure of 5–25 mmHg in normal leg lymphatics is required for lymphatic pulsations to begin to occur[8,18,20], with most healthy lymphatics reaching systolic pumping pressures of 29–37 mmHg, sufficient to propel lymph, with a tendency towards higher pressures in larger vessels[8,20]. Diastolic pressures were usually around 0 mmHg between pulsations, during which time there is no flow of lymph[8,18,20]. In the upright position, normal leg systolic pressures were approximately 44.7 mmHg[8,20]; however, there have been other studies that have recorded no significant difference between supine and standing healthy leg pressures[20].

In early-stage lymphoedematous legs, Olszewski demonstrated that there was an increase in both diastolic pressure (70 mmHg) and systolic pressure (100 mmHg). Muscular contractions then elevated these pressures as high as 200 mmHg. In this early staging of lymphoedema, both the spontaneous lymphatic contractions and the contractions of surrounding musculature were sufficient to propel lymph; however, this was not always propelled proximally due to failed valves[8]. It is hypothesised that the dramatic increase in intra-lymphatic pressure with muscle contractions in these cases is due to the lymphatics being full of lymph in between lymphatic pulsations[19].

In advanced-stage lymphoedematous legs, Olszewski recorded end pressures as low as 20 mmHg with no recorded lymph flow due to incompetent valves; however, these lymphatics were often difficult to cannulate, if at all possible[8]. Muscular contractions did not help to increase lymph flow in these patients, neither did manual massage of the foot, compression bandaging at a pressure of 40 mmHg and pneumatic massage, as only rudimentary pulse waves could be detected due to fibrotic changes in the lymphatics[21].

Modi et al. demonstrated that the average pumping pressures in arms of healthy individuals was 39 mmHg (±14 mmHg) whilst average pumping pressures in lymphoedematous arms was 24 mmHg (±19 mmHg)[1]. This study had a small population size (16 people in each the healthy and lymphoedematous group), and patients were not separated and observed based on lymphoedema stage.

Taking into consideration these pressures, and the pressures under which hydrocephalus shunts work, it is our hypothesis that a hydrocephalus shunt, modified in size to be suitably inserted into a damaged lymphatic could take the place of the dilated, incompetent lymphatic valves. Then with the aid of local muscle contractions and, if necessary, massage, to force the lymph past the valves, will act in such a way as to prevent retrograde lymph flow, reducing and possibly reversing the process of lymphoedema and giving the lymphatics an opportunity to maintain normal pumping.

Von der Weid and colleagues have been researching the impact of lymph stasis on inflammation and hypothesise that stasis of lymph caused by impaired lymph drainage leads to inflammation[22]. Further studies have furthered this line of thought and hypothesised that this lymph stasis not only leads to inflammation, but also to fat accumulation and fibrosis and that these three attributes cause and exacerbate each other in a vicious cycle[22]. As a result, the use of modified hydrocephalus shunts in the treatment of lymphoedema may help to break this cycle, preventing lymph stasis and therefore also inflammation, fat accumulation and fibrosis, which, in turn, will improve lymph flow itself.

Lymphatic diameters vary, depending on their location in the body. Branches in the head and neck have recorded diameters of 0.1 mm in the anterior cervical branches to 1 mm in the supraclavicular and supratrapezoid branches[23,24]. In the upper limb, lymphatic diameters have been recorded as small as 0.2–0.5 mm in the fingers and hands, and as large as 1.2 mm in the arm above the elbow[23]. Lymphatics of the lower limb range in diameter from 0.2 mm in the toes and foot to 2.2 mm in the deep branches of the thigh[23-26]. Despite these small diameters, cannulas with an outer diameter of 1.1 mm have been used to cannulate lymphatics of the foot in the study by Stranden and Kramer[27]. Similarly Olszewski and Engeset cannulated leg lymphatics of diameters ranging between 0.1 and 0.4 mm using a polyethylene P60 Adams Clay cannula[20,28]. As the diameters of the catheters currently used with the CODMAN® and Medtronic® hydrocephalus shunts currently range between 0.7 mm and 1.4 mm inner diameter and 2.2 mm and 2.8 mm outer diameter[17,29], some adjustments will be needed to produce catheters of smaller diameter, suitable for use with the lymphatics. However, it is promising that catheterisation of vessels this size has already been accomplished. The catheters used by Medtronic® and CODMAN® also have features such as x-ray detectable dots and impregnation with antimicrobials[17,29], which may also be appropriate for use in the lymphatics.

CONCLUSION

Lymphoedema is a condition that affects a wide number and variety of patients, often causing a significant impact on the quality of life of its sufferers. Whilst there are a variety of treatment options available currently, none are curative and most impact the patient's quality of life and require a high level of compliance.

Damage to the lymphatics resulting in incompetency of unidirectional valves and subsequent retrograde flow of lymph is a key issue in the development of lymphoedema[8]. This paper introduces the hypothesis that the insertion of a shunt, with a functioning valve, joined on either end to functioning lymphatics, will help to bypass lymphatics with incompetent valves; thereby providing a replacement functional valve and system which should improve the removal of lymph from the drainage site of the damaged lymphatic. Despite the limited amount of data present on human intra-lymphatic pressures in patients with lymphoedema, the current research available suggests that the use of a modified hydrocephalus shunt, inserted into ineffective lymphatics could reduce and possibly reverse the process of lymphoedema. In patients with lymphoedema secondary to the treatment of cancer (that is, lumpectomies, mastectomies and lymph node removal) the focus of the treatment would be to improve lymph drainage from these damaged lymphatic areas and allow lymph flow through scarred tissue once cancer treatment has ceased, as the insertion of a shunt prior to cancer removal would be ineffective. In patients suffering lymphatic filariasis, the aim would be to determine the areas of damaged or dysfunctional lymphatics and cannulate through these. Whilst adjustments to the size of the catheters currently used in hydrocephalus shunts would need to be made for them to be appropriate for use in the lymphatics, the fact that researchers have been

able to catheterise the lymphatics already demonstrates that this is achievable. Figure 2 illustrates the low flow/pressure environment that the shunts currently operate under and demonstrate that it is conceivable that a correctly sized shunt could be appropriate for use when the lymphatics and their valves are dysfunctional.

It is hypothesised that the patients who are most likely to benefit will be those with early-stage lymphoedema. Generally speaking, in this group there are reasonable lymph pump pressures, pressure conduction through the tissues due to compression and muscle contraction is relatively good[8]. Also their lymphatics are easier to cannulate, (as is now evidenced by the tendency to move microsurgical interventions from the late stage of lymphoedema to the earlier ones) and the pressures generated will be more than adequate to pass through the shunt valve. However, for those with advanced lymphoedema where the lymphatics are difficult to cannulate[8], there may be an indication for larger/longer areas of shunt bypass in order to find viable lymphatics to connect to. This would not only have a major impact on the quality of life of individual sufferers, but greatly impact the health care burdens of countries worldwide.

Trials of this process remain to be undertaken but the process seems feasible and benefits could be significant.

CONFLICTS OF INTEREST

None.

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