Lymphology 53 (2020) 157-161

EDITORIAL

MORBIDITY MANAGEMENT AND DISABILITY PREVENTION: AN AGENDA FOR DEVELOPING NATIONS INITIATED IN INDIA

S.R. Narahari, T.J. Ryan

Institute of Applied Dermatology (SRN), Kasaragod, Kerala, India and Emeritus Professor of Dermatology (TJR), Green Templeton College, Oxford, UK

ABSTRACT

Treatment of patients with lymphedema focuses on reducing limb volume with more recent recognition of the importance of quality-of-life issues. Perhaps due to the incidence of filariasis-related lymphedema compared to breast cancer-related lymphedema in the western world, the Institute of Applied Dermatology (IAD) in Kerala, India has developed a low-cost and culturally acceptable treatment with quality-of-life focus that works well in that area. Worldwide, there is also recognition of chronic edema as a potential co-morbidity and the recent advances in genetic analysis continue to shed light on lymphedema development that may be important in filariasis-related lymphedema. Although improvement in treatment outcomes by surgical means has been shown, there is often conventional treatment mixed in the therapy and no randomized controls of any therapy exist. In addition, these techniques require supermicrosurgical skill not available in many areas of the world. The WHO has documented the need in filariasis for both universal health care and innovative care for chronic conditions. The IAD has addressed these issues with its integrative model of treatment with patient quality-of-life at the forefront to incorporate traditional practice to involve the patient more fully in family and community support for an additional therapeutic tool.

Keywords: lymphedema, filariasis, therapeutics, quality of life, integrative medicine

Since the publication of the first ISL consensus document in 1995 (1), lymphedema management and advocacy has advanced, with the Quality of Life of Patients increasingly used as a tool for measurement of effectiveness (2,3). Lymphologists, nurses, manual lymph drainage therapists and the views of patients have led to publications of research priorities (4,5). All adhered to the basic principle of reducing limb volume, lowering the frequency of inflammatory episodes, better skincare and emphasis on the role of movement and breathing.

At the Institute of Applied Dermatology in Kerala, India, a low-cost, culturally acceptable, locally available treatment *Integrative Medicine Treatment for Lymphedema* (IML) evolved from ISL consensus documents on Combined Physiotherapy(CPT) and compression as well as Vaqas and Ryan's analysis in

The Filaria Journal of traditional Indian Ayurveda medicine and Yoga (6) with the addition of modern dermatology's drug treatment of bacterial entry points. Due to its many patient-centric features (7) it has become popular among urban and rural outreach patients as a self-care, family member assisted home-based care. This evolution of this treatment took place while in Europe, USA, and Australia thoughts on causation were dominated by breast cancer and in India it was filariasis.

M Witte and Bernas, in a 2007 editorial (8), stimulated by description of an Indian therapeutic initiative in the journal, questioned "why not consider other treatments for lymphedema and dissect out components of combination therapies ('shotguns') until a 'silver bullet' drug arrives?" Such a question needs to take into account over the next decade changing views on causes and classification of edema.

The International Lymphedema Framework argued that lymphedema is increasing worldwide and that the number of persons with lymphedema in the world could exceed HIV and Tuberculosis put together. Moffatt et al (9) as a result of LIMPRINT study, which was an international multi-site population-based study to determine the prevalence and functional impact of chronic edema in the adult population, identified people with chronic edema throughout the health and social care systems, and proposed that the definition of lymphedema should include other causes of edema arising from damage to the venous system, the effects of gravity, immobility, and systemic disease. LIMPRINT data provide evidence for defining chronic edema as "any edema persisting for more than three months, including conventional lymphedema." It would highlight mortality and morbidity associated with complications, such as cellulitis, necrotizing fasciitis and septicemia and would shed light on health-related quality of life.

Lymphedema has long been associated with the sign of non-pitting or being brawny. The recent Indian study of up-regulation of collagen type III gene transcription may confirm that lymphedema should be distinguished biochemically from chronic edema (10). In India, the recognition of non-filarial lymphedema and its associated complex syndromes has been another reason for paying greater attention to genetics. Gordon et al (11) provide the new guidelines to make a precise diagnosis of the genetic causes of lymphedema. This group has identified and reviewed the literature of multiple genes associated with familial lymphedema and highlighted a number of rare syndromes. Their pilot observations in India, a nation having the most prevalent lymphedema, and also common cousin marriages, indicate that not every case of lymphedema in endemic areas may be due to filariasis alone (12).

Elaborating on previous articles on entry points for bacteria it was suggested by Ryan, influenced by studies on podoconiosis, that it was not just fissuring of skin and interdigital clefts that needed attention but aspects of epidermal cell turnover and trans-epidermal water loss (13) providing stimuli, to the two vascular systems, blood vascular and lymphatic, in the upper dermis, such as Vascular Endothelial Growth Factor (VEGF).

During this time, surgical treatments have also advanced from de-bulking surgeries to current liposuction and micro- and super-micro anastomosis of lymphatics to veins and to each other. Most surgeons continue to use conventional CPT before and after surgery, thereby increasing the chances of a drastic reduction in disability and possibly permanent recovery. Liposuction is indicated when pitting is absent or minimal. If pitting is greater than 8 to 10 mm, then CPT is done to reduce the edema to a non-pitting state on the assumption that adipose tissue is responsible for the swelling (14). Several authors have discussed the relationship between the structural changes in the lymphatic system and adiposity, i.e. chronic edema and adipose tissue proliferation (15). Multiple lymphatico-venous and lymphatic-venous-lymphatic anastomosis microsurgery is most effective when performed early in the disease along with CPT. This is given a new term *complete lymphedema functional therapy*. However, it

requires additional complex staging analysis based on immunohistologic, lymphoscintigraphic, and other peripheral and central lymphatic imaging, clinical and physical disability parameters. Autologous lymphatic grafts are performed effectively in a few isolated lymphatic injury sites. Lymphaticovenular anastomosis generally requires supermicrosurgical skill. This and vascular lymph node transfer are surgical treatments and can in some instances promise a permanent cure without the requirement of CPT. However, to think of providing lymphatic microsurgical preventive and curative 100% healing on a large scale is utopian because of its expense and the want of surgical expertise as well as the skillfulness of these techniques. Chylous and non-chylous reflux syndromes associated with peripheral lymphedema may benefit from CT- or MR-guided sclerosis, other interventional radiology techniques, or operative ligation of visceral dysplastic lymphatics. We are in an era of Evidence-Based Medicine and CPT is part of all surgical treatments (16) and confounds the outcomes. Systematic reviews have not recorded any randomized control trials of surgical treatments and any form of CPT.

Approaching four decades have gone by since the concept of elimination of LF was first discussed and the Global Alliance (later program) for the Elimination of LF was launched (GA(P)ELF). GPELF backed national programs have included hydrocelectomy. However, a prospective surgical study in bancroftian filariasis endemic areas of Recife, Brazil, showed that hydrocele operations in patients with lymphedema require a specific surgical technique, to avoid recurrence of the disease, and consequently, to avoid additional damage to the testicle (17). The testicular artery exposed during the surgery is at risk of damage, and urology surgical expertise is essential to guide such operations. Urologists find ultrasound an essential tool. The Urology speciality, in our opinion, should guide large-scale genital surgery, mainly to avoid complications cited in the prospective study and guarantee that the answers to questions raised by patients about the effect of surgery on fertility are backed by the evidence of no testicular atrophy in the long term.

Recently some lymphologists have suggested that known causes such as breast cancer and filariasis must interact with genetic susceptibility to explain who develops lymphedema. Lymphedema designated as a genetic disease (18) and LF as a tropical disease (19) have both evolved since the time Ryan & Mortimer wrote of the neglect of the lymphatic system (20). It has been exciting to appreciate that the three drugs used to break the transmission of microfilaria to the mosquito are achieving the goal of *Elimination of Lymphatic Filariasis* in many parts of the world. Less successful has been morbidity control. Many distinguished lymphologists visiting the Institute of Applied Dermatology in Kerala, India, have recognized that IML has succeeded in creating it as a model for managing advanced cases of lymphedema at the primary health care level (21) with a much-simplified regimen for early stages of lymphedema. Both fit into the WHO's models of MMDP for LF (22), Universal Health Care (23) and Innovative Care for Chronic Conditions (24).

Lymphedema counseling and patient education sessions are crucial to improving the treatment adherence in CPT and IML. Empathetic relationship with the patient is often more successful in producing treatment outcomes when nurses and therapists lead the lymphedema program. Recently Dunbar et al emphasized the anti-inflammatory and vagal effect of friendship acting through the brain (25,26). The questionnaires used at the IAD have the holistic approach of integrative medicine and are administered with smiles. The counseling at the IAD is intensive, very friendly and incites an exceptional degree of patient participation

A case study conducted in Togo in Western Africa in collaboration with Centers for Disease Control and Prevention, emphasized sustainability through training of health care workers. The Togo program's sustainability heavily relied upon the requirement that all new health staff be trained in lymphedema management (27). The WHO document advo-

cates for the capacity building of health care workers and strengthening of health systems (22) at all levels to successfully implement a nationwide lymphedema program. The focus on the best possible data collection and its analysis have been fundamental to understand clinical differences and thereby providing leads to advances in the understanding and management of lymphedema. The IAD adopted the MySQL platform of open access www.bahmni.org for their electronic medical records (EMR). Bahmni's customized version has several tables through a single computer interface to record data from treatment activities of lymphologists, nurses, therapists, compression therapists, masseurs and other care providers such as Ayurveda doctors, Yoga trainers and physiotherapists. The Bhamni based EMR (28) with its technological limitations is adaptable worldwide for uniformity in data capture to assess the improvement of lymphedema patients, especially in resource-poor populations where lymphedema prevalence is maximum. IML can be initiated at select endemic areas, possibly in available leprosy facilities or AYUSH teaching/training centers and scaled up country-wide (29). The Bill and Melinda Gates Foundation seek to contribute to the morbidity management of Lymphedema in India and having located in their view a system that has satisfactorily treated 5,000 patients with good evidence of effectiveness, and they have found the Indian Government is a partner willing to support the IAD. It will be a collaboration that follows the WHO strategic goals (22) which are 1) to alleviate suffering of people with LF-related disease; 2) to promote improvements in the quality of life of people with chronic LF-related disease; and 3) to prevent debilitating and painful episodes of ADLA among people with lymphedema.

This editorial concerns "Morbidity Management and Disability Prevention," as an agenda initiated in India and as described very recently in the *Annals Ayurvedic Medicine* (29). It has a perspective quite unlike any so far published on this topic. It is the perspective of Integrative Medicine emphasizing that biomedicine may be enriched by taking note of traditional practices that are centuries old. It is also the perspective of a government that recognizes the value of ancient traditions in Medicine and makes it part of its Health Service policy, https://www.nhp.gov.in/nhpfiles/national_health_policy_2017.pdf.

By adding to these traditional practices some of what modern biomedicine has to offer they become more effective. In resource poor countries where evidence-based studies employing double blind randomized controlled trials demanding very large numbers of subjects are unaffordable, it is possible to collect and analyze large amounts of data proving effectiveness. It is also possible to provide culturally acceptable locally available and low cost therapy in resource poor rural villages (21). As suggested in the *Annals Ayurvedic Medicine* when the morbidity being managed is causing an inability to work or participate in social events, friendly partnerships involving participation of patient, family, and local community as individuals or supporting societies may be an additional therapeutic tool.

CONFLICT OF INTEREST AND DISCLOSURE

The authors declare no competing financial interests exist.

REFERENCES

1. The diagnosis and treatment of peripheral lymphedema: The consensus document of the International Society of Lymphology. Lymphology 28 (1995), 113-117.
2. Cornelissen, AJM, M Kool, XHA Keuter, et al: Quality of life questionnaires in breast cancer-related lymphedema patients: Review of the literature. Lymphat. Res. Biol. 16 (2018),134-139.
3. Thomas, C, SR Narahari, KS Bose, et al: Comparison of three quality of life instruments in lymphatic filariasis: DLQI, WHODAS 2.0, and LFSQQ. PLoSNegl. Trop. Dis. 8 (2014), e2716.
4. Narahari, SR, MG Aggithaya, C Moffatt, et al: Future research priorities for morbidity control of lymphedema. Indian J. Dermatol. 62 (2017), 33-40.
5. Underwood, E, M Woods, K Riches, et al: Lymphedema research prioritization partnership: A collaborative approach to setting research priorities for lymphedema management. Lymphat. Res. Biol. 17 (2019), 356-361.
6. Vaqas, B, TJ Ryan: Lymphedema: Pathophysiology

and management in resource-poor settings – relevance for lymphatic filariasis control programs. Filaria J. 2 (2003), 4.
7. Narahari, SR, TJ Ryan, PE Mahadevan, et al: Integrated management of filarial lymphedema for rural communities. Lymphology 40 (2007), 3-13.
8. Witte MH, M Bernas: Silver bullets and shotguns in lymphedema therapy. Lymphology 40 (2007), 1-2.
9. Moffatt, C, V Keeley, I Quere: The concept of chronic edema-a neglected public health issue and an international response: The LIMPRINT Study. Lymphat. Res. Biol. 17 (2019), 121-126.
10. Karayi, AK, V Basavaraj, SR Narahari, et al: Human skin fibrosis: Up-regulation of collagen type 111 gene transcription in the fibrotic skin nodules of lower limb lymphoedema. Trop. Med. Int. Health 25 (2019), 319-327.
11. Gordon, K, R Varney, V Keeley, et al: Update and audit of the St George's classification algorithm of primary lymphatic anomalies: A clinical and molecular approach to diagnosis. J. Med. Genet. 10 (2020), 653-659.
12. Zanten, MV, K Riches, V Keeley, et al: A diagnostic dilemma: Aetiological diagnosis of lymphoedema patients at an Indian multidisciplinary meeting. J. Lymphoedema 14 (2019), 43-46.
13. Ryan, TJ: Matts' hypothesis: How simple strategies can lead to better outcomes. J. Lymphoedema 11 (2016), 46-48.
14. Neligan, PC, J Masia, NB Piller (Eds.): *Lymphoedema (Complete Medical and Surgical Management).* 1st Edition. CRC Press Boca Raton. Florida, 2016.
15. Brorson, H, M Aberg, H Svensson: Chronic lymphedema and adipocyte proliferation: Clinical therapeutic implications. Lymphology 37(suppl) (2004), 153-155.
16. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus document of the International Society of Lymphology. Lymphology 53 (2020), 3-19.
17. Norões, J, G Dreyer: A mechanism for chronic filarial hydrocele with implications for its surgical repair. PLoSNegl. Trop. Dis. 4 (2010), 6- e695.
18. Mendola, A, MJ Schlögel, A Ghalamkarpour, et al: Lymphedema Research Group. Mutations in the VEGFR3 signaling pathway explain 36% of familial lymphedema. Mol. Syndromol. 6 (2013), 257-266.
19. Recognizing neglected tropical diseases through changes on the skin: A training guide for front-line health workers. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO.
20. Ryan, TJ, PS Mortimer, RL Jones: Lymphatics of the skin: Neglected but important. Int. J. Dermatol. 10 (1986), 411-417.
21. Narahari, SR, KS Bose, MG Aggithaya, et al: Community level morbidity control of lymphoedema using self care and integrative treatment in two lymphatic filariasis endemic districts of South India: A non randomized interventional study. Trans. R. Soc. Trop. Med. Hyg. 107 (2013), 566-577.
22. World Health Organization, Regional Office for South-East Asia: Morbidity management and disability prevention in lymphatic filariasis. WHO Regional Office for South-East Asia (2013). https://apps.who.int/iris/handle/10665/205539as accessed on 17th Nov 2020.
23. Health Coverage Collaborators: Measuring universal health coverage based on an index of effective coverage of health services in 204 countries and territories, 1990-2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet 396 (2020), 1250-1284.
24. Kaur, V: Silver bullets, shotguns, and integrative community-based approach to lymphedema from lymphatic filariasis in India. (Letter to the Editor) Lymphology 40 (2007), 87-94.
25. Dunbar, RIM: The anatomy of friendship cell press reviews. Trends Cogn. Sci. 22 (2018), 32-51.
26. Ryan, TJ: The nature of care in the management of lymphoedema: Not without laughter. J. Lymphoedema 14 (2019), 54-55.
27. Mathieu, E, AM Dorkenoo, M Datagni, et al: It is possible: Availability of lymphedema case management in each health facility in Togo. Program description, evaluation, and lessons learned. Am. J. Trop. Med. Hyg. 89 (2013), 16-22.
28. Raut, A, C Yarbrough, V Singh, et al: Design and implementation of an affordable, public sector electronic medical record in rural Nepal. J. Innov. Health Inform. 2 (2017), 862-878. doi: 10.14236/jhi.v24i2.862.
29. Narahari, SR, TJ Ryan: Mainstreaming of an Integrative Medicine Protocol for Morbidity Management and Disability Prevention of Lymphatic Filariasis: An opportunity for establishing AYUSH based National Health Programme. Ann. Ayurvedic Medicine 9 (2020),108-115.

S.R. Narahari, MD, DVD
Institute of Applied Dermatology (SRN)
Kasaragod, Kerala 671124, India
E-mail: srniad@gmail.com