Pro: indwelling pleural catheters cause harm to patients

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Indwelling pleural catheters cause significant harm without any advantage over talc pleurodesis for symptom control in MPE. The risks and benefits should be discussed with patients for a true "informed decision" about MPE management. https://bit.ly/4dUJPO5

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Abstract

Malignant pleural effusions (MPE) tend to recur and require definitive treatment with either chest drain and talc pleurodesis or indwelling pleural catheters (IPCs), which offer similar symptomatic benefits. In recent years, IPCs have become popular due to the presumed convenience of an outpatient procedure followed by home drainage leading to a misconception of IPCs being an ideal treatment for MPE. However, IPCs predispose the patient to multiple complications and have significant physical and psychological implications that are under-recognised. Patients require additional clinical reviews, hospital admissions and treatment for these complications related to IPCs. Additionally, there is a huge psychological impact of living with a home catheter that is a constant reminder of their cancer and this has been shown to affect quality of life negatively. Hence, IPCs should not be considered the "ideal" treatment for MPE management and clinicians should reflect the equipoise of the evidence for the benefits and accurately reflect the adverse effects of IPCs in their discussions with patients to facilitate informed decision making.

Introduction

We start with a scenario. A patient has been given 3–4 months' life expectancy and has to make a choice between two treatments for their recurring malignant pleural effusion (MPE): one which requires hospital admission for 4–5 days and still might not work *versus* a "one-off" procedure with home drainage. Which one sounds better? The decision might seem easy to the patient with a terminal illness, preferring the option of undergoing one procedure and prioritising staying at home surrounded by family. Sadly, the above statement detailing a "one-off" procedure, not infrequently used verbatim in clinical practice to describe the indwelling pleural catheter (IPC), is far from the truth, if not directly misleading.

IPCs have been around since the 1980s as a treatment option to manage recurrent MPE. IPCs were historically introduced for patients who have failed pleurodesis or who have a trapped lung to preclude pleurodesis [1]. Since the first randomised controlled trial (RCT) comparing the efficacy of IPC with a chest tube and pleurodesis with doxycycline in 1999 by Putnam *et al.* [2], there has been a series of large RCTs comparing the two treatments. The message from all of these studies is consistent: all have failed to show the superiority of IPC over chest drain and talc pleurodesis in symptom control, which is the primary aim of MPE management strategies.

However, it is not uncommon for a treatment to become embedded in daily practice over time to the extent that its harms and limitations are overlooked and accepted as such. There are some projected advantages that are better served as "out of sight, out of mind" for the physicians and we will tackle them in detail in the following point of view. In this debate we have taken a step back to critically evaluate the harms of IPCs, which are usually not the key focus of research on IPCs but have significant implications for patients, and have done so by challenging a number of key assumptions in the following sections.

IPCs reduce hospital admission

IPCs are projected to reduce hospitalisation as the treatment with an IPC, *i.e.* insertion, drainage and subsequent removal of the IPC is primarily offered as a day-case or outpatient procedure. In the AMPLE-1 trial, Thomas *et al.* [3] showed that IPC results in 2 fewer days in hospital compared with pleurodesis (median 10 days (interquartile range (IQR) 3–17 days) *versus* 12 days (IQR 7–21 days); p=0.03, Hodges–Lehmann estimate, 2.92 days (95% CI 0.43–5.84)) and 3.6 fewer days per patient respectively, which was a small percentage of their remaining life only. However, hospital stay was defined as admission for one or more days, excluding day-case procedures. This demonstrates physician bias in considering hospitalisation as significant only when a patient spends a night in hospital, without considering the burden of IPC-related visits to the hospital for both the patient and their accompanying relative or carer.

The patient burden of "outpatient" management was highlighted in a retrospective case series of 210 IPC patients by Asciak *et al.* [4], demonstrating that around 33.7% of patients require further review specifically related to their IPC and 23% require more than one review. This highlights that while patients with IPCs are not "hospitalised", they are most certainly "medicalised" as they are living with a permanent catheter with a high probability (one in three) of requiring at least one hospital visit to address an issue or complication specifically relating to the catheter. This is in addition to the healthcare contacts that occur for each home drainage (median n=96) as well as additional community nurse reviews, thus accumulating a highly significant treatment burden.

It is pertinent to highlight that IPC is a lifelong treatment for the majority of patients; the AMPLE-1 trial showed that only 30% of patients achieved IPC removal during the trial study period hence the burden of healthcare contacts related to IPC continues for the rest of the patient's life. For this reason, early IPC removal has been an area of interest for pleural disease research and strategies such as aggressive daily drainage or talc instillation *via* IPC to accelerate pleurodesis, compared with standard symptomatic drainage, have been studied [5–7]. Despite this so called "aggressive" drainage strategy, the chances of successful pleurodesis are still <50% with daily IPC drainage (37% in AMPLE-2; 44% in ASAP trial) and talc *via* IPC (43% in IPC-PLUS trial) with no additional benefit in improving breathlessness, which is the main aim of MPE management. Additionally, providing daily drainage *via* district nurses is often difficult to achieve due to healthcare resource constraints and is cumbersome for the patients/carers who perform self-drainage. Thus, the pros and cons of "early IPC removal" need to be carefully discussed with patients.

Another important but often neglected outcome of "less hospitalisation" is a requirement for a robust outpatient IPC management pathway. This requires additional staff, resources and costs to cater for the lifetime needs of patients with IPC and can be challenging for hospitals with less developed service infrastructures. Unsurprisingly, this will result in variability in practice thus promoting health inequalities and poor patient care. As large-scale RCTs are often conducted in established pleural centres, the impact of health inequalities on MPE management strategies is not sufficiently highlighted and this remains an important focus of future studies.

IPCs have minimal complications

Davies *et al.* [8] demonstrated in the TIME-2 trial that patients with an IPC had a significantly greater risk of adverse events compared with chest drain and talc pleurodesis (OR 4.70 (95% CI 1.75–12.60); p=0.002) despite no benefit in dyspnoea, chest pain and quality of life (QoL) score at 6 weeks post-randomisation. Adverse events in TIME-2 were predominantly associated with IPC-related infections, but other notable complications included non-draining IPC due to catheter blockage or septated pleural effusion, IPC-fracture with a retained catheter fragment and IPC-site metastasis [9]. The management of these complications requires extra hospital visits for the patients, in addition to their planned treatment, which is physically and emotionally challenging when living with advanced cancer.

Amongst the complications, IPC-related infection is a major concern and it can be challenging from both diagnostic and treatment perspectives. IPC-related infections encompass catheter-site infection with or without pleural space infection with rates reported as high as 25% of all IPCs [10]. The diagnosis can be challenging both microbiologically to differentiate between contaminants and infection-causing organisms and biochemically in so-called "inflammatory malignancies". Although the catheter-site infection can be treated with oral antibiotics in most cases, pleural space infections related to IPCs usually require hospitalisation, intrapleural enzyme therapy and an average of 4–6 weeks of antibiotics [11]. The IPC may require removal in treatment-resistant or dual compartment infection, *i.e.* both the catheter-site and pleural space, thus resulting in more procedures, hospital visits and clinical reviews. Therefore, these significant complications must be appropriately reflected in patient discussions before MPE treatment decisions are made.

IPCs improve quality of life

Another common misconception amongst proponents of IPCs is that keeping patients out of hospital will positively impact upon their QoL. The published data, however, do not support this presumption.

A recent well-conducted randomised trial by Sivakumar *et al.* [12] (OPTIMUM) opted for QoL as the primary outcome, which the authors should be congratulated on given that our treatment intent is to improve QoL and previous large RCTs in MPE have not used QoL as a primary end-point. They randomised patients to either talc pleurodesis as an inpatient, or very active management of IPCs as outpatients, including daily drainage and outpatient talc *via* the IPC; arguably, their chosen IPC intervention was as aggressive as possible, and thus if there was any significant QoL signal, one would have expected to see it in a study of this design.

The results clearly demonstrated no significant difference between the two groups at 30 days post-randomisation, and once again demonstrated more adverse events in the IPC group [12]. The patients included in the trial had a good performance status to comply with the study protocol, and yet despite this relatively active population who might be expected to maximise their "freedom" from an in-hospital treatment, there was no difference in the QoL measured using standard and well-recognised instruments.

Notably, some important aspects of living with an IPC are overlooked in the generic QoL questionnaires. This has been highlighted in a recent study by Mitchell *et al.* [13] specifically designed to understand patient perspectives on IPC. Although most patients reported improvement in their symptoms and QoL at initial follow-up, multiple adverse issues subsequently occurred: notably itching at the drain site (49%), difficulty in sleeping (39%) and IPC use reminding patients about cancer (63%). These are hugely relevant to patients but not explicitly reported as treatment-related adverse events in large RCTs [13]. This further demonstrates the limitation of our current understanding of the impact of IPCs on patients' QoL and this should be factored into the treatment decision-making with further RCTs and qualitative studies in this area prioritised.

IPCs are cost-effective

An IPC is often projected as a cost-effective treatment to hospitals compared with inpatient talc pleurodesis. Physicians are encouraged to consider outpatient/early discharge strategies in their clinical treatment and IPC seems a favourable option for managing MPE. However, the data suggest that IPC is a more costly treatment for healthcare services as a whole due to the need for repeated home drainages, irrespective of the healthcare costs of IPC-related reviews and complications. Hence, the proposed cost–benefit of "outpatient" IPC insertion is outweighed by the cost of equipment required for drainage 2–3 times per week. It becomes a significant financial burden in those countries where the patient has to purchase IPC drainage equipment. A cross-sectional survey from the USA aimed to understand the costs associated with IPC drainage and suggested that patients pay an average of USD 238 every 2–4 weeks in addition to their insurance coverage to cover the cost of IPC vacuum bottles and dressing kits [14]. Another study from Hong Kong reported that an individual drainage bottle costs a patient HKD 200 (USD 25) [15]. The US survey also found that around 12% of caregivers had to take time off work to help with the IPC drainage which has additional cost implications. These direct and indirect IPC costs are significant and should be discussed with the patient to ensure that the treatment is affordable and not an additional burden to contend with.

IPC home drainage has no environmental implications

The home drainage of an IPC is considered inherently safe and patients usually discard used equipment in the general waste bin at home. This raises an important issue of the carbon footprint related to weekly IPC drainage. On average, a patient needs to drain their IPC 2–3 times per week. Each IPC drainage pack weighs ∼300 g and contains single-use consumables, usually made with plastic. This has serious environmental implications as a three-times per week drainage strategy will produce almost 1 kg of plastic waste. As previously elucidated, IPC is a lifelong treatment for most patients who continue to live with the IPC and require regular drainage for the rest of their lives. Clinicians should be aware of this environmental aspect of IPC drainage, especially for patients with a longer life expectancy, who can be offered alternative treatments like talc pleurodesis. Patients should be allowed the opportunity to make a more environmentally conscious choice, should this be a priority to them.

What is the way forward?

Herein, we have presented arguments for why we believe that IPCs cause significant harm and should not be considered the "default" or "one-size-fits-all" treatment for MPE. The most obvious counterargument is that options are limited as talc pleurodesis may not be an option in a significant minority (including trapped

lung) with repeated thoracentesis and surgical pleurodesis only having a role in specific scenarios. We partially agree with this point of view but feel the priority for clinicians should be empowering patients towards making an informed decision through providing a balanced view of the risks and benefits of the two main treatment options in MPE that is in line with the equipoise of the evidence base, and not influenced by physician-centred convenience. Patients who opt for an IPC should be aware that this is not the "one-off outpatient" panacea as is usually portrayed, but rather a life-long treatment with a risk of clinical, psychological, financial and environmental implications. The future holds promise for hopefully obviating the need for a long-term MPE drainage strategy as targeted cancer treatments become commonplace with excellent patient outcomes. However, until the tap is turned off, we need to mop the floor wisely without biases.

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