Applying evidence-based symptomatic treatments from other clinical disciplines to palliative care

The evidence base for palliative care has seen a steady increase in the number of high-quality randomised controlled studies that have significantly contributed to improving patients' and caregivers' care in this setting. Adequately powered phase III studies are the gold standard in establishing a causal link between the intervention and the outcome. Ideally, studies conducted in other clinical disciplines (with comparable populations) would be repeated in palliative care populations to confirm the benefits and harms of any proposed non-pharmacological or pharmacological intervention but this is costly, time-consuming, resource intensive and may be difficult to justify ethically if the results from another clinical discipline can reasonably be applied to palliative care patients.

Many therapies for symptoms need an evidence base for safe and effective management. The evidence generated from studies conducted in palliative care populations is a fraction of potentially applicable knowledge currently available that has direct relevance to palliative care. There is already a large evidence base for symptom control developed in patient populations that may be analogous to those in palliative care. One way to complement the available evidence generated by palliative care studies to further improve clinical practice is to apply findings from symptom control studies conducted in other clinical disciplines. The careful extrapolation of findings from other clinical disciplines into palliative care can help advance the evidence base for improved palliative care clinical practice by addressing some current gaps in knowledge on symptomatic treatments.

In evidence-based practice, application of knowledge to clinical decisions relies on the researchers' ability to target a defined and reproducible population representative of broader populations or clinical care settings to optimise *generalisability*, and the clinicians' ability to determine sufficient similarities between the population studied and the individual patient to optimise *applicability*. Formal frameworks have been proposed to maximise the researchers' ability to describe the palliative care populations in their studies so clinicians can make more informed decisions when applying the findings to their practice.[1] There is a need for similar formal methods to maximise the clinicians' ability to make informed decisions about the applicability of interventions where the evidence has been developed in disciplines other than palliative care.

Applicability is applying research findings to a patient,[2] ultimately asking 'will this person react in a similar way to the intervention for a similar net clinical effect (benefits and harms)?'[1] Applicability of findings across disciplines (or "clinical transferability"[3]) relies on evaluating the therapeutic intervention in the context of the population and setting in which the intervention was studied.[1,3] Assessing applicability requires clinicians to have critical appraisals skills to interpret the relevance of each study's findings for the patients they serve, and incorporate relevant findings into their own practice.[1]

Applicability facilitates effective translation of relevant research into clinical practice. In palliative care, translating evidence into practice is challenging due to differences in patient characteristics (where lack of agreed referral criteria creates a heterogeneous case-mix in a specialty that relies on referral from a wide range of other clinicians); differences in the service profile (where time from referral to death can differ greatly[4]); or interventions that may have different effects late in life. Funding imposes further potential constraints[5] as do differing measures used to assess clinical outcomes.[6] Additionally, data in other disciplines

may be collected using disease-specific instruments with which palliative care clinicians may not be familiar. All of this means clinicians will need to "equate" the study results to their actual practice before they can apply the proposed treatments in the knowledge that such therapies are appropriate for their patients.

A way forward

Despite these challenges, applying evidence from other clinical disciplines into palliative care offers exciting opportunities to accelerate the evidence base for symptom control. If applying knowledge from other disciplines is desirable, what factors should guide this process and help clinicians to undertake this evaluation for their population with confidence? Furthermore, if knowledge has been applied from another discipline, how do we evaluate the subsequent net effect in palliative care without repeating the original studies?

Applying evidence from other clinical disciplines into palliative care requires a rigorous and transparent process to balance potential benefits and harms of the research findings when applied to palliative care patients. Several key factors should guide palliative care clinicians' evaluation of research findings from other clinical disciplines to help optimise the use of beneficial interventions and limit inappropriate interventions,[7] for individual patients and populations. ***First,*** *the study population*: this would include identifying the demographic and clinical profile of patients (or caregivers) in both the original study and those to whom it may apply in palliative care. General population descriptors can help determine similarities and differences between study and patient populations, and caregiver factors are important if the intervention requires supervision or caregivers to administer it. ***Second,*** *the symptom*: this would include identifying any similarities in the underlying pathophysiology between patients in the original study and those seen in palliative care, the clinical presentation of the symptom when compared to palliative care patients and the way symptoms are assessed in the disciplines under consideration. ***Third,*** *the intervention evaluated*: this should include details such as the time to onset of benefit and duration of benefit when evaluating its applicability in patients with limited prognosis and reduced physical reserve, the effect size seen with the proposed therapy and whether that would be acceptable for palliative care populations, any contraindications for the new target population, and risks of drug/drug or drug/host interactions in the palliative care population, given the patterns of prescribing for co-morbid diseases and for symptom control.[8] ***Fourth,*** *the quality and strength of the evidence*: this should include identifying confirmatory studies with the same direction and magnitude of net effects for the proposed intervention, or potentially contradictory studies for the same indication. ***Fifth,*** *the setting of care*: this should include identifying issues around safety monitoring and patient compliance and how similar those are between the original study and those seen in palliative care, or whether the trial setting can be replicated in routine palliative care, and findings applied across clinical settings (e.g. specialist vs primary care, inpatient vs community). ***Sixth,*** *the availability of the intervention*: this would include issues around cost and accessibility of the proposed intervention in palliative care. In addition to this assessment, quality measures of the originating study would have to be considered to assess risk of bias when exploring the study's internal validity.

A formal framework with this kind of clinical focus, similar to those guiding generalisability of clinical research,[1] would introduce a degree of rigour in navigating the effective translation of findings across disciplines in palliative care, potentially further improving patients' and caregivers' outcomes. Ideally, this would also be complemented with guidelines at the

service, funding and policy levels that would support a collaborative clinical research model for advancing the science and practice of palliative care.

Implications for clinical research and practice

Using existing evidence from other clinical disciplines to inform palliative care practice can be scientifically sound and cost-effective. Having made the decision to apply knowledge from another discipline, post-marketing frameworks can be used to monitor the direction and magnitude of net effects in palliative care patients. Post-marketing surveillance (phase IV) studies can be the first critical step in evaluating the net effect of findings applied from other disciplines into palliative care by monitoring real-world outcomes,[7] including drug interactions[9] and toxicities.[10] Using a rigorous methodology,[11] such studies can add to knowledge from the original phase III study when applied in the palliative care setting.

Patients and families deserve the best possible care when faced with a life-limiting illness and rapidly changing life circumstances. Irrespective of the delivery setting and models of care, palliative care clinicians should be able to quickly and confidently work with the available evidence to provide much needed symptom relief and support to their patients and caregivers. With many symptomatic treatments still in development and awaiting validation in palliative care populations, applying relevant findings from other clinical discipline systematically can facilitate more effective translation of research findings into clinical practice and help accelerate building the evidence base by bringing high quality symptom control studies in comparable populations into palliative care. Post-marketing studies also have an important role to play in ensuring such evidence translates into the expected patient (or caregiver) outcomes.

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