Promoting Excellence in Symptom Management Case Series

Case Study: A New Intervention for Rapid End-of-Life Symptom Control in the Home Setting

Kathryn Paez, BSN, RN, CHPN  ○  Meegan Gregg, NP, CHPN  ○  Charlea T. Massion, MD  ○  Brad Macy, BSN, BA, RN, CHPN

The oral route is compromised for nearly all patients at the end of life (EOL). This article reviews the benefits and burdens of the usual alternative routes of medication delivery when the oral route fails and presents a case study on the use of a new innovation for the rectal delivery of medication to control EOL symptoms. A 62-year-old male hospice patient with end-stage metastatic prostate cancer presented with severe symptoms (Face, Legs, Activity, Cry and Consolability scale score, 9/10) that were uncontrollable with medications given via oral or sublingual routes. The patient goals were to remain at home with optimal symptom management. Rapid relief of symptoms was accomplished by the administration of medications already present in the home delivered with a new rectal catheter that provides discreet access for ongoing medication administration. Significant relief was noted within 20 minutes of dosing. The patient died peacefully 18 hours later, meeting his EOL goals, and the family was empowered to provide effective care for the patient at home. The family found the intervention easy to use. This case demonstrates how this new innovation can be used to ensure rapid symptom management and decreased burden of care by facilitating immediate and easy use of medications already present in the home.

KEY WORDS
Macy Catheter, rectal medication, sublingual medications, suppository, symptom management

Almost every hospice patient loses the ability to swallow medications in the last hours to days of life. For most of these patients, symptoms are well managed with the administration of sublingual (SL) medications. However, the SL route is ineffective for many patients in controlling symptoms. Whereas the precise percentage of hospice patients who die with poorly controlled symptoms is unknown, symptom control challenges at the end of life (EOL) are well known and documented.

A comprehensive literature review done by Kehl and Kowalkowski1 evaluated the prevalence of symptoms in the last 2 weeks of life. Of the 2416 patients in this review, the authors found that pain was present in 52.4%, dyspnea was present in 56.7%, and confusion was present in 50.1% of patients. Another literature review on symptom management in palliative care between 2004 and 2012 found that pain and other symptoms were inadequately assessed and managed at the EOL.2 A survey performed specifically on hospice patients by Coyle et al3 found that between 5% and 35% of hospice patients described their pain as “severe” in the last week of life and that 25% of the patients described their shortness of breath as “unbearable.”

When oral and SL routes are unavailable or ineffective and symptoms are active, establishing an alternative delivery route is essential. This article reviews the benefits and burdens of the common alternatives to oral delivery and presents a case study on the use of a new technology for rectal delivery to control symptoms at the EOL. This is the first case study published in the hospice and palliative care literature on the use of a catheter designed for administering ongoing medications via the rectum (Macy Catheter).
Alternative Routes of Medication Delivery in the Home Setting

When oral and SL routes fail to control symptoms, the interdisciplinary team (IDT) is challenged to find a route that is safe, rapid, effective, and easy for caregivers in the home setting. The National Consensus Guidelines (2013) state that the goal of symptom management in the hospice and palliative setting is the safe and timely reduction of symptoms to a level that is acceptable to the patient or patient’s surrogate if the patient is unable to self-report distress. Therefore, the choice of an optimal alternative medication route must consider the speed and extent of absorption, safety and comfort in the home setting, and ease of use by lay caregivers. The speed of initiating an alternative route is important because patients may have severe symptoms with little time before death. Waiting for medications to arrive while watching a patient suffering with symptoms can be a great burden to caregivers, especially if medications do not arrive in time to help, leading to a poor death outcome. Routes of medication administration available when the oral route fails include SL, rectal, subcutaneous (SQ), intravenous (IV), transdermal, transmucosal, epidural, and intrathecal. The more common alternatives used in the hospice setting are reviewed hereinafter.

The SL Route

The SL route is most frequently used in hospice care. Ease of access, simplicity for the caregiver, and the relatively low cost of medications make this route highly desirable. However, often, the SL route is ineffective or unfeasible in a patient’s final days. Clinicians must recognize when to switch to more effective routes of delivery. Skilled clinical assessment and an understanding of the limitations of the SL route will allow the clinician to anticipate when a patient will need an alternate route before symptom crises.

Some medications for EOL comfort are poorly absorbed sublingually. Dose volumes of approximately 1 mL or less are optimal. Larger volumes can be too large for the limited surface area of the SL and buccal mucosa and are many times swallowed or aspirated or may drip out of the mouth. The SL absorption of medications is also highly dependent on oral pH, the amount of time in contact with the mucosal surface, and the moisture and secretions within the oral cavity.

Assessment of Patient Types for Whom the SL Route Is Ineffective

Patients with a history of severe pain requiring either high doses of opioid analgesics and/or adjuvant medications to manage pain are typically unmanageable via the SL route. If a patient is receiving large doses of an opioid analgesic and loses the ability to swallow, these doses cannot be effectively absorbed on the relatively small SL mucosa. In addition, hydrophilic opiates such as morphine, oxycodone, and hydromorphone are poorly absorbed sublingually. For example, the bioavailability of SL morphine is very low compared with those of other routes. In one study, mean (SD) SL morphine absorption was demonstrated to be only 9% (11.9%) compared with an intramuscular dose.

If dose volumes are too high or too frequent, silent aspiration can occur because medication administered in very low volumes will not always stimulate a swallow reflex, especially in patients with altered levels of consciousness. Furthermore, when a patient transitions to an actively dying state, the swallowing reflex may be impaired, escalating the risk of aspiration. When aspiration occurs, patients often have respiratory distress and more secretions, which increase patient discomfort and caregiver angst at the EOL. The clinician should assess for silent aspiration by asking caregivers whether they are noting any coughing or gurgling sounds after SL dosing.

If a patient requires adjuvant pain medications such as nonsteroidal anti-inflammatory medication, dexamethasone, antiseizure medications, or antidepressants, either these medications must be stopped, or another route must be found when swallowing fails because they are not absorbed sublingually. For patients with severe or complex pain management needs, abruptly stopping these medications when the oral route fails can result in a pain crisis. Another route of delivery may be needed to continue these medications. Therefore, a patient who has a history of complex or severe pain should be monitored carefully, and the IDT team should have a plan in place for how to deliver adjuvant pain medication quickly to patients when the oral route fails.

Terminal agitation is another symptom in which the SL route often fails. Agitation is one of the most common EOL symptoms and one of the most distressing for caregivers to witness. Agitated patients commonly will not cooperate with taking orally administered medications. Severe dyspnea or pulmonary crises requiring larger doses of narcotic analgesics or sedatives for palliative sedation are also poorly managed via the SL route. Other examples of symptoms that are difficult to manage with SL medications include seizures, fever, nausea, and vomiting.

Parenteral Route (IV and SQ)

Once IV access is established and medications are available, IV therapy is the most rapid delivery method available and allows for quick titration of medication to control severe symptoms. Most medications for EOL symptom control can be given intravenously. For multiple reasons, IVs are not commonly used in the home hospice.
setting. There is a significant delay in time to establish IV access and obtain medications and supplies, which equates to delayed symptom relief. In addition, IVs can cause pain and other problems at the site, and agitated or confused patients can pull out an IV. Complications such as infection, venous access issues, IV site infiltration, and higher burden of care for both the clinical team and caregivers to manage can make IV care in the home a challenge. Intravenous medication costs are also much higher than other routes of delivery.

The SQ route is considered a rapid and effective means of medication delivery. Studies on this route of delivery in the hospice setting indicate that discomfort and complications are minimal and that caregivers can effectively manage SQ therapy in the home. One downside of SQ delivery is that finding and managing an effective site of delivery can be challenging, especially with cachectic patients. Another downside of SQ delivery is the cost of supplies and medications, which are significantly more expensive than oral preparations. Finally, as vascular perfusion to the SQ tissue decreases during the dying process, medication absorption may decrease. Possibly, the greatest downside to both the IV and SQ routes in the home is the delay in the initiation of treatment due to the time needed for the delivery of medications, pumps, and supplies. This lag time can translate to a patient waiting several hours or more to achieve symptom relief, a significant burden when a patient may only have hours to days left to live. Freedom from pain and suffering is a patient right, and any interventions that require a delay in symptom management should be considered suboptimal if options exist to initiate more immediate treatment.

**Transdermal Route**

Although transdermal gel preparations have become more popular in the last decade, there is currently very little evidence to support the effectiveness of most compounded transdermal preparations used for EOL symptom management. Smith et al. (2011) conducted a study on the absorption of lorazepam, diphenhydramine, and haloperidol gel. They tested blood concentration levels of volunteers to whom the gel was applied and demonstrated that haloperidol and lorazepam were not absorbed in high enough concentrations to be detectable and that diphenhydramine was absorbed slowly and erratically and in low concentrations. As patients decline in the last hours to days, blood flow to the skin generally lessens causing a reduction in blood flow to the medication reservoir, thus decreasing the bioavailability of medications. As with IV and SQ medications, there is a lag time to deliver transdermal medications to the home. Finally, it is impossible to dose for breakthrough symptoms with transdermal preparations.

**Rectal Route**

The rectal route is a good alternative for hospice patients when the oral route fails. The walls of the rectum are highly vascularized and quickly and effectively absorb many of the medications used for EOL symptom control. Medications delivered to the distal one-third of the rectum partially avoid the first pass effect through the liver, allowing greater bioavailability for some medications compared with the oral route.

**Suppositories**

There are numerous downsides to the use of rectal suppositories. Suppositories can be uncomfortable to insert and can even cause trauma to the rectal tissue. They demand repeated invasion of privacy with each dose and can be embarrassing for both the patient and the caregiver. If inserted incorrectly into stool and not placed directly against the mucosa, they will be ineffective. Suppositories involve frequent repositioning of the patient with each dose, which can exacerbate symptoms for the patient and can be difficult and unsafe for caregivers. Many suppositories need to be compounded, which can be expensive. In addition, like IV and SQ interventions, symptom control is delayed during the time it takes for suppositories to be prepared and delivered. Finally, suppositories require a relatively moist rectal environment to dissolve and need to spread over the rectal mucosa for quick and effective absorption. Actively dying patients are many times quite dehydrated, and the rectum can be very dry. If the medication cannot dissolve, it cannot enter the bloodstream and will eventually be broken down by bacteria causing a decrease in bioavailability.

**The Macy Catheter**

The MC (Hospi Corporation) is a relatively new Food and Drug Administration–cleared rectal catheter designed solely for administering ongoing medications and fluids to the rectum. The catheter is composed of a 14F silicone shaft with a 15-mL balloon (Figure). The catheter is placed into the distal one-third of the rectum in a nonsterile procedure. It can remain in place for up to 28 days for the ongoing administration of medication by the caregiver. A medication port rests on the patient's leg. One benefit of this intervention compared with suppository is that medications can be given repeatedly without moving the patient or repeatedly needing to invade the patient's privacy every time a medication is needed. Undoubtedly, the greatest benefit of this intervention is that symptom control can be immediately initiated with medications already present, avoiding a delay in patient comfort.

Once inserted, a balloon is inflated with 15-mL water to hold both the medication and the device in the distal rectum proximal to the anal sphincter. Oral medications in solid form that are known to be absorbed rectally can be
crushed, suspended in 10-mL water, and injected into the rectum. The catheter is then flushed with 3-mL water. The catheter is designed to be expelled when a patient defecates and will not impair bowel movements. One downside of the catheter is that, if expelled by the patient during defecation, it needs to be reinserted.

Both anecdotal evidence and research have shown this intervention to be comfortable for the patient when placed and during medication administration. A recent study comparing MC-administered phenobarbital with the same dose given via suppository on healthy volunteers showed MC administration to be rated as “comfortable” compared with the suppositories, which were reported as “mildly uncomfortable.” The study further showed more rapid, reliable, and higher bioavailability of (MC) administered phenobarbital compared with the same dose given via suppository. Phenobarbital plasma levels achieved in 30 minutes with (MC) administered doses took close to 3 hours to achieve with suppository.18 A case study series (Christensen,19 2016) demonstrated that severe symptoms of pain and agitation were controlled within 10 to 15 minutes using this intervention in three end-stage hospice patients. Successful use of the catheter for hydration and medication administration has been reported in the emergency department and intensive care settings. In these studies, the catheter was used when IV access was difficult or when patients needed medication unavailable in IV form.20,21

**CASE STUDY**

**Patient Background**

A 62-year-old male patient diagnosed with end-stage prostate cancer metastatic to the liver and bone had been on hospice for 28 days. On admission, the patient was on a high-dose narcotic regimen for pain control, which included fentanyl transdermal patch of 300 μg/h, with breakthrough doses of oxycodone IR of 40 to 60 mg every 4 hours. He had reported ineffective pain control at these doses with recurrent pain in 2 to 3 hours. He stated that he had to take oxycodone every 3 hours, more frequently than ordered for the uncontrolled pain.

He was successfully switched to methadone and was titrated to 30 mg twice a day. This effectively managed his pain as evidenced by a significant decrease in daily oxycodone IR to one to three doses of 40 to 60 mg daily and self-reports of improved pain management. Symptoms remained managed for approximately 3 weeks. After months of incapacitating pain, he could once again play with his grandson.

**Patient Assessment**

During 2 days, the patient rapidly transitioned to actively dying. His medication abruptly became ineffective. Liquid methadone was started, but he began vomiting, and his pain escalated. The patient became cognitively impaired and unable to self-report his pain. The Face, Legs, Activity, Cry and Consolability (FLACC) scale was used per agency standard to assess his level of discomfort.22 The patient had an initial FLACC score of 9 of 10 as evident by grimacing, groaning, rolling from side to side, and kicking his legs and an inability to be consoled. He also was diaphoretic, with a thready pulse and rapid, shallow respirations at a rate of 32 with an SpO2 of 85%.

The patient also demonstrated frequent clonic muscle spasms of unknown etiology, possibly from hypoxia or an adverse narcotic reaction. Because he had been vomiting, his family wanted to discontinue the liquid methadone. The oxycodone IR was ineffective as evidenced by the patient’s high FLACC score. The family had been crushing and dissolving the oxycodone tablets in water to give sublingually. The patient was now also coughing after doses, signaling possible aspiration of SL drugs. The family was also administering 1-mg tabs of lorazepam SL every 4 hours without an apparent effect. On the basis of these observations, the hospice nurse assessed that SL medications were ineffective and that the patient was in desperate need of immediate symptom control.

**Intervention**

**Patient Goals**

The patient’s EOL goal of care was to die peacefully in his home with as little discomfort as possible. The patient’s spouse and children aligned strongly with his goal of a peaceful death in the home setting. The family was distraught by his sudden deterioration, the severity of his uncontrolled symptoms, and their inability to provide symptom relief. Because SL medications were ineffective to control his symptoms and the emergent need for a rapid solution, the hospice nurse decided to use the MC. She concluded this to be the best option to avoid unwanted
hospitalization and to quickly control his symptoms without the need to wait for other medications to be ordered and arrive. She decided that this intervention was the only way to ensure that the patient received immediate symptom relief because medications already in the home could be used.

Family Education
The nurse initiated a discussion of the intervention with the patient’s family, providing education on the benefits of the catheter: ease of placement, comfort, and use. She also reinforced that providing medication this way would allow achievement of the patient and family’s goals of pain and agitation control and that he could remain comfortably at home through the EOL. The family saw the value in this treatment option and agreed to the plan.

IDT Planning and Communication
The nurse contacted the medical director (MD) to discuss goals of care and a medication regimen for rapid symptom management. The physician agreed that the MC was the best option. The new regimen included oxycodone 60 mg, lorazepam 1 mg, and haloperidol 1 mg every 30 minutes until the patient became comfortable. Once comfortable, the nurse and MD would reevaluate ongoing orders.

Symptom Management Intervention and Ongoing Assessment
The nurse inserted the catheter, administered medications as ordered, and observed significant relief within 20 minutes. The nurse remained with the patient and family for the next 2 hours, administering doses every 30 minutes (for a total of four doses) until the FLACC was 0, as evidenced by the patient sleeping peacefully. Once complete comfort was achieved, the nurse collaborated again with the MD on a medication regimen to maintain comfort. This regimen included methadone 30 mg every 12 hours plus 240-mg oxycodone, 3-mg lorazepam, and 2-mg haloperidol every 4 hours around the clock. In addition, breakthrough doses of oxycodone 60 mg, lorazepam 1 mg, and haloperidol 1 mg every hour were available.

Emotional Support
During this time, the nurse talked with the family, providing emotional support, teaching the family how to administer medications through the catheter, and answering any questions about what to expect with the dying process.

Patient Outcome
Within 20 minutes after the initial medication administration, the nurse observed that the patient began to experience relief of both pain and agitation as evidenced by the calming of his body movements and the FLACC score decreasing from 9 of 10 to 5 of 10. The patient achieved an FLACC of 0 of 10 after 2 hours of receiving an additional three breakthrough doses.

The family continued to administer medications via the catheter every 4 hours until the patient died peacefully 18 hours later. The family reported that the patient remained comfortable throughout this time as evidenced by resting peacefully without grimacing, moaning, or agitation. The family felt confident administering the medications to him via the catheter, was greatly relieved that they could keep him comfortable, and expressed deep gratitude for the hospice care.

DISCUSSION
This intervention proved to be an excellent way to facilitate quick and effective symptom control. Most importantly, it allowed the patient to meet his EOL goals, spending his last hours in comfort surrounded by his family at home. Since February 2015, the agency presenting this case study has been using this method for medication delivery when the oral and SL routes are ineffective, with consistently excellent outcomes. Caregivers have reported confidence using the catheter to administer medications after less than 30 minutes of training and have been grateful for having the ability to quickly control symptoms in the home setting. Nurses carry a catheter kit with them to avoid delayed symptom control. After the initial training, nurses gained experience presenting the concept to patients and families. Although many nurses were initially uncomfortable with introducing the concept, once these nurses began to have experience with the intervention, they could discuss this option more easily.

Although the FLACC scale is the pain assessment tool currently used by the agency performing this study, this scale, like other available scales, has not been well validated in the hospice and palliative setting.23 A promising pain assessment tool known as the Multi-dimensional Observational Pain Assessment Tool has been tested in the inpatient hospice setting showing preliminary evidence of reliability, validity, and clinical use. It is currently being further studied in hospice settings. This scale looks primarily at the same four behavioral indicators of pain that were noted in the nurses’ assessment of the patient in this case study including restlessness, tense muscles, frowning/grimacing, and sounds. Each of these four behavioral indicators is rated in intensity from 0 (not present) to 3 (severe) for a possible total of 12 points. The Multi-dimensional Observational Pain Assessment Tool scale shows promise as a more valid and reliable scale for assessing pain in the hospice setting. It was reported by nurses in the study to be easy to use.24-26

The ability to control symptoms immediately has obvious benefits not only to patients and their caregivers
but also to clinicians, the hospice agency, and the entire health care system. Family satisfaction increases, whereas the cost and burden of care decrease resulting in a proverbial “win” for everyone involved.

As discussed earlier, symptom management still remains a challenge in the hospice setting in the United States. Unsuccessful symptom management can lead to inpatient admission, which may be counter to a patient’s EOL goals. The National Hospice and Palliative Care Organization’s facts and figures (2014 and 2015) showed that 31.8% of hospice patients died in an inpatient hospice setting in 2014, up greater than 5% from 26.4% in 2013. The data also show that an additional 9.3% died in an acute care hospital in 2014, up 2.3% from 7% in 2013. These figures translate to more than 40% of hospice patients in the United States dying in inpatient settings. It is safe to assume that a significant number of these inpatient admissions were for the management of symptoms that were considered uncontrolled in the home setting.

Not only is death in an inpatient setting much more expensive, more importantly, studies indicate that most patients would prefer to die in the home setting. In 2014, the Institute of Medicine published “Dying in America,” an analysis of EOL care in the United States. The report concluded that “the last few months of life are characterized by frequent hospital and intensive care stays.” The report also indicated that the EOL care in this country still falls far short of providing EOL care based on “the needs, values and preference of our patients.” The report concluded that health care expenditures related to unneeded and unwanted acute care services could otherwise be spent to improve the quality of EOL care. Allowing for quick control of symptoms with medication already in the home can decrease the need for emergency room visits and unwanted inpatient placement admissions related to symptom crises. As mentioned earlier, freedom from pain and suffering is a patient right. Symptom management interventions that require a delay in symptom management should be considered suboptimal if an option exists to initiate immediate treatment.

In conclusion, new technology in rectal delivery can be used to ensure rapid symptom management by allowing for the immediate initiation of symptom control with the use of medications already present. It can lessen the burden of care on families, frontline clinical staff, and clinical management. The ability to control symptoms in a greater number of patients dying in hospice could allow the hospice industry to achieve an even greater standard of care and excellence in symptom management than previously possible.

References

1. Kehl K, Kowalkowski J. A systematic review of the prevalence of signs of impending death and symptoms in the last 2 weeks of life. Am J Hosp Palliat Care. 2013;30(6):601-616.

2. Wilkie D, Ezenwa M. Pain and symptom management in palliative care and at end of life. Nurs Outlook. 2012;60(6):357-364.

3. Coyle N, Adelhardt J, Foley KM, Portenoy RK. Character of terminal illness in the advanced cancer patient: pain and other symptoms during the last four weeks of life. J Pain Symptom Manage. 1990;5:583-93.

4. National Consensus Project for Quality Palliative Care. The Clinical Practice Guidelines for Quality Palliative Care. 3rd ed. Pittsburgh, PA: National Consensus Project of Quality Palliative Care. https://www.hospice.org/multimedia/NCP_Clinical_Practice_Guidelines_3rd_Edition.pdf. Accessed August 23, 2016.

5. Marianne Matzo M, Sizerman D. Symptom Assessment and Pharmacological/Non-pharmacological Interventions In: Palliative Care Nursing, Fourth Edition: Quality Care to the End of Life. Edition 4. New York, NY: Springer Publishing Co; 2014:608.

6. Reisfeld G, Wilson G. Rational use of sublingual opioids in palliative medicine. J Palliat Med. 2007;10(2):465-475.

7. Narang N, Jyoti S. Sublingual mucosa as a route for systemic drug delivery. Int J Pharm Pharmaceut Sci. 2011;3(2):18-22.

8. Weinberg D, Inturrisi C, Reidenberg B, et al. Sublingual absorption of selected opioid analgesics. Clin Pharmacol Ther. 1988;44(3):355-362.

9. Marianne Matzo M, Sizerman D. Peri-Death Nursing Care In: Palliative Care Nursing, Fourth Edition: Quality Care to the End of Life. Edition 4. New York, NY: Springer Publishing Co; 2014:668.

10. Letizia M, Shenk J, Jones T. Intermittent subcutaneous injections of pain medication: effectiveness, manageability, and satisfaction. Am J Hosp Palliat Care. 1999;16(4):585-592.

11. Crane R. Intermittent subcutaneous infusion of opioids in hospice home care: an effective, economical, manageable option. Am J Hosp Palliat Care. 1994;11(1):8-12.

12. Marianne Matzo M, Sizerman D. Peri-Death Nursing Care In: Palliative Care Nursing, Fourth Edition: Quality Care to the End of Life. Edition 4. New York, NY: Springer Publishing Co; 2014:572.

13. Smith T, Ritter J, Poklis J, et al. ABH gel is not absorbed from the skin of normal volunteers. J Pain Symptom Manage. 2012;43(5):961-966.

14. Warren D. Practical use of rectal medications in palliative care. J Pain Symptom Manage. 1996;11(6):378-387.

15. Davis M, Walsh D, LeGrand S, Naughton M. Symptom control in cancer patients: the clinical pharmacology and therapeutic role of suppositories and rectal Suspensions. Support Care Cancer. 2002;10(2):117-138.

16. Van Hoogdalem E, de Boer A, Breimer D. Pharmacokinetics of rectal drug administration: part I. General considerations and clinical applications of centrally acting drugs. Clin Pharmacokinet. 1991;21(1):11-26.

17. DeBoer AG, Moollenaar F, de Leede L, Breimer D. Rectal drug administration: clinical pharmacokinetic considerations. Clin Pharmacokinet. 1982;7(4):285-311.

18. Lam Y, Lam A, Macy B. Pharmacokinetics of phenobarbital in micro- enema via Macy Catheter versus suppository. J Pain Symptom Manage. 2016;51(6):994-1001.

19. Christensen P. Utilizing the Macy Catheter to facilitate rapid symptom control in the home setting: a case series. Poster session presented online at the National Hospice and Palliative Care Organization. Virtual Conference 2016: Challenges on the Front Lines: Effective Approaches to Complex Cases (Poster). http://www.nhpco.org/utilizing-macy-catheter-facilitate-rapid-symptom-control-home-setting-case-series. Accessed August 26, 2016.

20. Honosage A, Parker B, Wesselhoff K, Lyons N, Kulsedt E. First use of a new device for administration of buspirone and acetaminophen to suppress shivering during therapeutic hypothermia. Ther Hypother Temp Manag. 2016;38(1):48-51.
21. Lyons N, Nejak D, Lomotan N, et al. An alternative for rapid administration of medication and fluids in the emergency setting using a novel device. *Am J Emerg Med*. 2015;33:1113.e5-1113.e6.

22. Voepel-Lewis T, Zanotti J, Dammeyer J, Merkel S. Reliability and validity of the face, legs, activity, cry, consolability behavioral tool in assessing acute pain in critically ill patients. *Am J Crit Care*. 2010;19(1):55-61.

23. McGuire D, Kaiser K, Haisfield-Wolfe M, Florence IF. Pain assessment in non-communicative adult palliative care patients. *Nurs Clin North Am*. 2016;51(3):397-431.

24. McGuire D, Harrold J, Kaiser K, et al. Measuring pain in non-communicative patients in the inpatient hospice setting: psychometric evaluation of the Multidimensional Objective Pain Assessment Tool (MOPAT). *J Pain Symptom Manage*. 2013;45(2):403-404.

25. McGuire D, Kaiser K, Soeken K, et al. Measuring pain in non-communicative palliative care patients in an acute care setting: psychometric evaluation of the Multidimensional Objective Pain Assessment Tool (MOPAT). *J Pain Symptom Manage*. 2011;41:299-300.

26. McGuire D, Reifsnyder J, Soeken K, Kaiser KS, Yeager KA. Assessing pain in nonresponsive hospice patients: development and preliminary testing of the Multidimensional Objective Pain Assessment Tool (MOPAT). *J Palliat Med*. 2011;14(3):287-292.

27. National Hospice and Palliative Care Organization. NHPCO facts and figures on hospice care in the US. 2015. http://www.nhpco.org/sites/default/files/public/Statistics_Research/2015_Facts_Figures.pdf. Accessed April 15, 2016.

28. National Hospice and Palliative Care Organization. NHPCO facts and figures: hospice care in America, 2014 edition. 2014. http://www.nhpco.org/sites/default/files/public/Statistics_Re search/2014_Facts_Figures.pdf. Accessed April 15, 2016.

29. Gomes B, Calanzani N, Gyseis M, Hall S, Higginson I. Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care*. 2013;12:7. http://bmcpalliatcare.biomedcentral.com/articles/10.1186/1472-684X-12-7. Accessed April 16, 2016.

30. Institute of Medicine. 2014. Dying in America: improving quality and honoring individual preferences near the end of life. http://www.nationalacademies.org/hmd/Reports/2014/Dying-In-America-Improving-Quality-and-Honoring-Individual-Preferences-Near-the-End-of-Life.aspx. Accessed April 15, 2016.