UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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Palliative Care Pharmacy Team:

Clinical Pharmacy Specialist:

Maria Felton Lowry, PharmD, BCPS, BCGP
Assistant Professor
University of Pittsburgh School of Pharmacy, Department of Pharmacy and Therapeutics
Palliative Care Clinical Pharmacy Specialist
UPMC Palliative and Supportive Institute

Cell: 412-627-8473
Office: 412-864-2899
Email: lowrymf@upmc.edu

If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

Transdermal Fentanyl (TDF) use in Cachectic Cancer Patients

Background:
Fentanyl is a highly lipophilic opioid, which makes it suitable for intravenous, transmucosal, and transdermal administration. Fentanyl is ~70% protein bound (ie. albumin), and albumin is low in cachectic patients due to a leakage into subcutaneous and muscle interstitial spaces. Absorption of TDF is dependent on surface area of the patch, skin permeability, and local blood flow. Blood flow in subcutaneous adipose tissue depends on skin-fold thickness. Absorption can be increased by high temperatures, as seen in previous studies. Absorption has not been found to be affected by anatomical site of application (chest, abdomen, upper arm, and thigh). Oftentimes, cachectic patients with advanced cancer require high doses of TDF to achieve adequate analgesia.

Importance:
TDF is utilized widely for malignant pain, particularly in end-stage disease where progressive, chronic pain is prevalent. Palliative care clinicians should be aware of the pharmacokinetic and pharmacodynamic characteristics that potentially influence medication absorption and analgesia.

The Literature:
Pain. 2009 Jul;144(1-2):218-22.
Transdermal fentanyl in cachectic cancer patients
Objective: analyze the pharmacokinetic characteristics of TDF in cachectic and normal weight cancer patients
Methods: prospective cohort study; n=20; ten normal weight (mean BMI: 23kg/m^2) and ten cachectic patients (mean BMI: 16kg/m^2)
Outcomes: plasma fentanyl concentrations (adjusted for dose), local skin blood flow, skin temperature, local sweating, upper arm skin fold, pain intensity (VAS 0-100mm)
Results:

- Plasma fentanyl concentrations at 48- and 72-hour intervals were significantly lower in the cachectic patients then in the normal weight patients ($P < 0.05$)

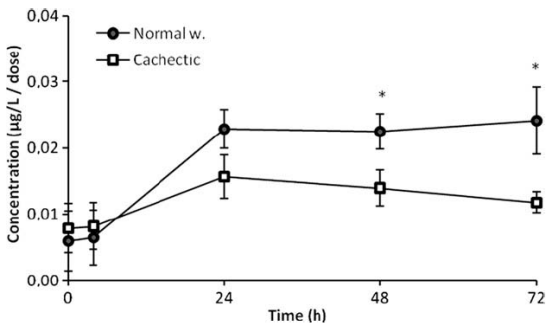


Fig. 2. Dose-adjusted plasma fentanyl concentrations in normal weight (filled circles) and cachectic (open squares) cancer pain patients during the 3-day treatment with transdermal fentanyl. Mean values ± SEM are given. $^*p < 0.05$.

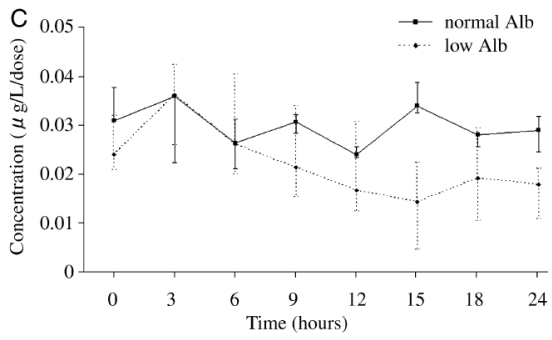
- Thinner upper arm skin fold in cachectic patients
  - Normal weight 4.3 ± 0.7 mm vs. Cachectic 2.0 ± 0.3 mm ($p < 0.01$)
- No difference between cachectic and normal weight patients in local skin blood flow, skin temperature, or local sweating

Conclusion:

- "Absorption of TDF is impaired in cachectic patients compared with that of normal weight patients with cancer-related pain"

Clin J Pain. 2013 Jun;29(6):487-91.
Serum concentration of fentanyl during conversion from intravenous to transdermal administration to patients with chronic cancer pain
Outcomes: efficacy, toxicity, and serum fentanyl concentrations at hours 3, 6, 9, 12, 15, 18, 24 after TDF administration
Methods: prospective cohort (n=18), classified into two study groups according to BMI and Alb
Results:

- During transition from IVF to TDF, no significant differences were observed in pain intensity or with number of rescue medications needed at each time point
- Dose adjusted serum fentanyl concentrations did not differ significantly between BMI groups at any time point
- Dose adjusted serum fentanyl concentrations were significantly lower in the low albumin group than the normal albumin group ($p < 0.05$) (no apparent edema or ascites present)



Conclusion:

- BMI did not seem to affect absorption of TDF in this study
- "Hypoalbuminemia was strongly associated with poor absorption from TDF delivery"

Bottom Line:

- Higher mean "normal" BMI in first study reported could be why they saw a significant difference in their BMI comparison groups
- Thickness of skin fold could be an indicator of adequate or inadequate blood flow in subcutaneous tissue
- Patients with low BMI, thin skin fold, or low albumin may be at risk for not fully absorbing total dose of TDF
- Consider alternative long-acting agent if patient has not responded to recent dosage increases in TDF that you would typically expect a clinical response based on other clinical factors (ie. PRN use, 50-100% dosage increase, etc)
- If patient has not responded to recent dosage increases in TDF, it may be wise to use the *last* known effective patch strength on which to base conversion calculations and be liberal with rescue opioid dosing

CLINICAL PEARL: It is possible that low BMI and/or low albumin impacts the absorption of fentanyl in TD delivery system. If patient has not responded to recent dosage increases of TDF, it may be reasonable to consider alternative long-acting opioid.