



## **Reducing Adverse Drug Events Related to Opioids:**

### **An Interview with Thomas W. Frederickson MD, FACP, SFHM, MBA**

#### **Pat Iyer**

Hi, this is a podcast from the Physician-Patient Alliance for Health & Safety. The podcast that we are presented today is about the society of hospital medicine guide to reducing adverse events related to opioids.

Welcome to our podcast. My name is Pat Iyer. I'm a nurse and I have with me today Dr. Tom Frederickson, who is the medical director for the Hospital Medicine of CHI Health. He is the lead author of a 2015 publication called "Reducing Adverse Drug Events Related to Opioids". This was published by the Society for Hospital Medicine.

Dr. Frederickson earned his medical degree and Masters in Business Administration, and he achieved the marks of distinction of a fellow of the American College of Physicians and senior fellow in hospital medicine.

Tom, please give us some frame of reference for the purpose of this publication. Why was it written? Who is it written for? What does it cover?

#### **Tom Frederickson**

Pat, thank you very much for having me on today. It really was a pleasure to create this guide, Reducing Adverse Drug Events Related to Opioids (or the RADEO guide). I got the opportunity - really had a wonderful opportunity - to work with the Society of Hospital Medicine and with a number of really good colleagues in anesthesia and pharmacology and hospital medicine to create this guide.

It's really intended to be a comprehensive guide to quality improvement in the area of decreasing adverse events related to opioids in the inpatient setting. But it also encompasses making sure that transitions of care to the outpatient setting are safe as well.

The intended audience really is anyone who is interested in working in QI in this area. So that would really usually start with the chief medical officer; but very importantly it also includes all the frontline staff that will be working on creating and implementing the implementations, and anything that the team decides to do to make the environment in the

hospital safer with reference to prescribing opioids. So, that is usually the anesthesiologists, surgeons, hospitalists, nurses and respiratory therapists. So, I really think all would be interested in reading this guide and implementing some of the recommendations in order to make things safer in the hospital.

**Pat**

And I know when I saw the guide I realized it was very comprehensive. In order to focus in on our talk today, we've picked two of the many areas that the publication covers. And we'll be discussing first identifying patients at risk for opioid induced respiratory depression, which is a particular concern of the Physician-Patient Alliance for Health & Safety.

In looking at that topic of identifying at risk patients: let's talk first about the risk factors.

I'd like to give you a clinical scenario. An anesthesiologist sees an obese patient for a pre-op evaluation. Why should that patient's size raise a concern about respiratory depression?

**Tom**

Well, in a word: sleep apnea. Sleep apnea, or obstructive sleep apnea, is very common. In the adult population, perhaps as common as 7 to 22 percent of the adult population has some degree of sleep apnea. In addition to being common, it is also very under diagnosed.

Now in the patient you describe who has obesity, obesity greatly increases the risk for sleep apnea and morbid obesity (those with a body mass index greater than 35) are at significantly increased risk.

Sleep apnea is the number one risk factor for respiratory depression associated with the use of opioids. So, therefore, this patient, who has obesity, is at greater risk and care needs to be taken by the health care team to make sure we know who those patients are.

**Pat**

And certainly in today's health care with the focus on bariatric patients and the American population struggle with weight issues, it is a real clinical concern that we have to be attuned to.

**Tom**

Absolutely.

**Pat**

In thinking about respiratory depression, which is a very important concern to us, there's a deadly pattern that develops between respiratory depression and respiratory arrest that occurs in patients with obstructive sleep apnea (which I may refer to as OSA). Could you share with our listeners what that deadly pattern is?

**Tom**

Absolutely.

Patients with obstructive sleep apnea are dependent upon their arousal mechanism in order to avoid respiratory depression and eventual respiratory failure. When these patients receive

opioid medication, it decreases this ability for arousal. That puts them at risk for a sudden spiral that includes respiratory insufficiency and respiratory arrest. This can happen very quickly and part of the risk is that the traditional monitoring for sedation that we use in the hospital - that is on a periodic basis and depends upon nursing interventions and questioning - really becomes much less effective in this patient population that can have a respiratory arrest, because of failure to arouse, very quickly. So, a monitoring regimen that takes place every 60 minutes is likely to be ineffective.

**Pat**

Yeah, and that's a real concern when you think about the typical staffing on post-operative units and the frequency with which med-surg nurses can see their patients. Is there any way to identify patients with OSA in advance when they're receiving opioids?

**Tom**

Absolutely.

There's a number of scales that are in common use. Probably the most common one, and the most effective one in terms of being sensitive, is the STOPBang tool. Many hospitals implement screening for sleep apnea using the STOPBang. It's an eight point questionnaire. The questions are easily answered by talking to the patient or with a questionnaire given to the patient. So, it's easy to calculate; with a score greater than three, or three, positive responses out of the eight questions means high risk for sleep apnea. So, it's an effective screen.

The issue as you know is when it takes place. So, it's certainly much more effective if it's done as part of a pre-operative evaluation or upon admission if the patient's likely to need sedating medications during their hospitalization.

There are other screens as well - the Berlin questionnaire and the Epworth Scale. And these are effective screens as well; and they tend actually to be a little bit more specific for sleep apnea. But they're less commonly employed, because they're not as sensitive.

**Pat**

So, it sounds like one of the factors that we would hope our listeners would receive from this podcast would be to consider using one of those scales to identify the patient at risk.

**Tom**

Absolutely.

That's an important intervention - to have a policy in your hospital to identify high risk patients and to screen those patients for sleep apnea - since it's the number one risk factor for opioid induced respiratory depression and failure.

**Pat**

And we've talked about this as an issue and I wanted to share another clinical scenario which is closer to home. My husband's surgeon told him he needed a colon resection for colon cancer. At that time my husband was obese. He was a smoker. He had bronchitis. And the surgeon said, in a sentence that I have never forgotten, - "It would be a very good idea if you were not a smoker next Tuesday on the day of your surgery." What's the reasoning behind that advice (and, by the way, my husband stopped smoking cold turkey that moment, which was a blessing, and he never resumed). What is the reasoning behind that advice related to risk factors for respiratory depression?

**Tom**

Well, you mentioned one right there which is a wonderful story in that patients can take this as motivation and an opportunity to quit smoking, which in and of itself is a huge benefit. But, in terms of specific risk factors certainly being obese is a risk factor, as we've already discussed. It's a risk factor in other ways as well in the post-operative period, such as increased risk for thromboembolism or decreased mobility post-operatively. But, also, smoking puts you at risk for pulmonary disease. You mentioned this complicating factor: bronchitis. Certainly respiratory ailments or acute respiratory illnesses need to be treated and completely controlled before any kind of surgery because that puts folks at risk as well.

There is some evidence that smoking reduces the oxygen reserve during anesthesia and also during the potential respiratory failure.

**Pat**

Let's change our focus a little bit and talk about the opioids themselves. We know that many of them are metabolized by the kidneys and liver, and that people come to health care with chronic kidney problems or liver failure. Which of those substances in terms of opioids are problematic when the patient has renal or liver failure?

**Tom**

Well, all the commonly used opioids are metabolized in the liver. So, first of all, folks with advanced liver failure. Now, folks with early liver disease, it tends to be not so much of an issue, although care should be taken in all patients. But, folks with advanced liver failure just tend to accumulate the medication itself; so dosing intervals and dosing amounts need to be monitored and altered. And this includes folks with hepatic failure.

Now, in some of the medications, the hepatic metabolite is very metabolically active and physiologically active. I'll talk about meperidine first. Meperidine has an active metabolite that's CNS toxic and is excreted in the kidney. And, really, I think, fortunately, most hospitals - probably almost all hospitals - have gotten away from using meperidine in the acute care setting to control pain - and that's a good thing. It's really not a particularly good medication in that environment, for that use.

Morphine has an active metabolite that is a CNS depressant - and that is also excreted in the kidneys. And morphine is probably not the first choice of medication for folks with renal failure.

On the other hand: hydromorphone. The metabolite of hydromorphone is not a CNS depressant, and is probably a bit safer in patients with renal failure. The problem with

hydromorphone, of course, which I think many patients and people have experienced, is the dosing. People just need to be cognizant of the correct dosing; it's six to eight times more potent than morphine and dosages need to be adjusted accordingly.

Fentanyl is probably the safest in renal failure. It has no metabolically active metabolites or no physiologically active metabolites. But, just the dosing intervals tend to be so short, and the half life so short, that it just makes it more difficult to dose in the acute care setting.

**Pat**

Yes, those are certainly important considerations and I have been involved in a number of situations where the dosing of dilaudid was not appropriate with the tendency, of course, for people to receive too much of that with some significant adverse effects. So, I'm glad you brought up that warning because that's a common issue that I have seen in situations that have resulted in untoward outcomes.

**Tom**

Unfortunately, I think many of us have seen that, so it's excellent to keep that in mind.

**Pat**

Absolutely. And I know another factor that affects patients' ability to tolerate medications is this concept of people who are opioid naive versus experienced. Many people with chronic pain come into the health care setting with a history of being on a lot of medication. How does that effect their risks of respiratory depression?

**Tom**

Well, probably the most important thing to keep in mind first is that when patients are post-operative, or have a medical or trauma reason for pain, and to be in the hospital. Of course, pain is among the most common reasons to need to be in the hospital - they deserve and need to have their pain controlled. So, it's not a reason to under-treat or to not treat these folks if they have chronic pain or they've habituated to opioid medications.

But, having said that, as clinicians we need to realize that folks with chronic pain - whether they are habituated to opioids or not - we're likely to have as clinicians a more difficult time controlling those patients' pain. They're likely to need higher doses of opioids to control pain. And with the higher doses, come higher risks of sedation and eventual respiratory depression. So, it's good to have, you know, strategies. It's good to be including multi-modal strategies to and to use opioid sparing techniques in all patients - but particularly in this subset of patients.

**Pat**

While we're on the topic of the effects of medications, I'd like to ask you about the sedation risk from the additive effects of non-opioid medications. I've seen several clinical situations with tragic endings when health care providers combined opioids with medications that had sedating effects. Could you comment on the medications that have some of the biggest risks of those interactions?

**Tom**

Absolutely. The biggest risk are the benzodiazepines, and the reason that the benzodiazepines pose a risk are really two.

First is they're very common. Many patients come into the hospital taking benzodiazepines. They're commonly used for anxiety and other conditions as well. So, patients, who are already on benzodiazepines, habituated benzodiazepines, need to continue that medication in the hospital.

So, when you have an additive effect, or even more than an additive effect of adding an opioid medication to control pain, the sedating effects of the benzodiazepines, as well as the opioids, can be more than additive; and this really is a situation that requires an increased level of caution for providers and policies in place that include more heightened monitoring and such to avoid untoward events.

Certainly many other classes of medications would have similar precautions. It's common nowadays, and there is some pretty good evidence, that the gabapentinoids can be opioid sparing. But they are also a sedating medication, and that's important to keep in mind - especially in those who are elderly, who are naive to gabapentinoids, and who have renal failure. So, even though they can be opioid sparing, when folks are naive to both the classes of medications and receive them both during their hospitalization, it requires some caution.

Certainly there's lots of other classes that can be sedating. Another common class in the hospital are the anti-psychotics - particularly haloperidol - that's often used to control the symptoms related to delirium in the hospital; but, it's a sedating medication.

And, then the last class really common in the hospital are the antiemetics, particularly phenergan and compazine, which are sedating medications and can have additive sedating effects along with opioids.

**Pat**

This reminds me of walking through a little maze, making sure you're following the right path and not hitting walls trying to avoid all of the risks along the way.

**Tom**

Yeah, absolutely.

I think that you bring up a good point. That's how come a QI approach that involves policies, that involves making it easy for clinicians to do the right thing through appropriate tools and interventions, is so important in this realm; because the medicine and the patients can be complicated and clinicians need to have it easy for them to make good decisions and to treat their patients in a way that is going to be effective but safe.

**Pat**

Given all of these risks, is there a tool that our listeners could use to screen for the risk of respiratory depression?

**Tom**

You know, there really isn't one good comprehensive tool. Probably the most important screening we have already talked about, and that is screening for sleep apnea and being aware of patients - either post-operative patients or patients coming into the hospital - who are going to need pain control to find out whether they are at risk for sleep apnea and to intervene appropriately - whether that be with CPAP or monitoring. So, that's very important.

But, along with this, you need to monitor for organ system dysfunction - whether that be acute, related to the hospitalization, or chronic. And then, what we just talked about in terms of medications. It really needs to be a comprehensive approach. I think that these are the three most important - being on top of organ system dysfunction, particularly hepatic and renal insufficiency, be it acute or chronic; medications, chronic medications and acute medications; and then, most importantly, having some sort mechanism to know which of your patients are at risk for sleep apnea.

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*This concludes the first part of the discussion with Dr. Tom Frederickson. We hope that you have enjoyed this discussion about identifying patients at risk for opioid induced respiratory depression.*

*We invite you to listen to the second and concluding discussion with Dr. Frederickson on the importance of monitoring patients receiving opioids.*