


Observational Report



Opioid Tolerance – A Predictor of Increased Length of Stay and Higher Readmission Rates

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The increasing use of opioids to manage pain in the United States over the last decade has resulted in a subset of our population developing opioid tolerance. While the management of opioid tolerant patients during acute episodes of care is well known to be a challenge amongst health care providers, there is little in the literature that has studied opioid tolerance as a predictor of outcomes. We conducted a review on all admissions to Massachusetts General Hospital over a period of 6 months, from January 2013 to June 2013, and identified opioid tolerant patients at admission using the FDA definition of opioid tolerance. To compare risk adjusted groups, we placed opioid tolerant patients and control patients into groups determined by expected length of stay of less than 2 days, 2 to 5 days, 5 to 10 days, and greater than 10 days. Opioid tolerant patients were then compared to the control for outcomes measures including observed length of stay and readmission rates. Our results show that all opioid tolerant patients have a significantly longer length of stay and a greater 30 day all cause readmission rate than the control group ($P < 0.01$). This trend was found in the first 3 risk adjusted groups, but not in the fourth group where expected length of stay was greater than 10 days. The opioid tolerant population is at risk given the poorer outcomes and higher health care costs associated with their care. It is imperative that we identify opportunities for improvement and delineate specific pathways for the care of these patients.

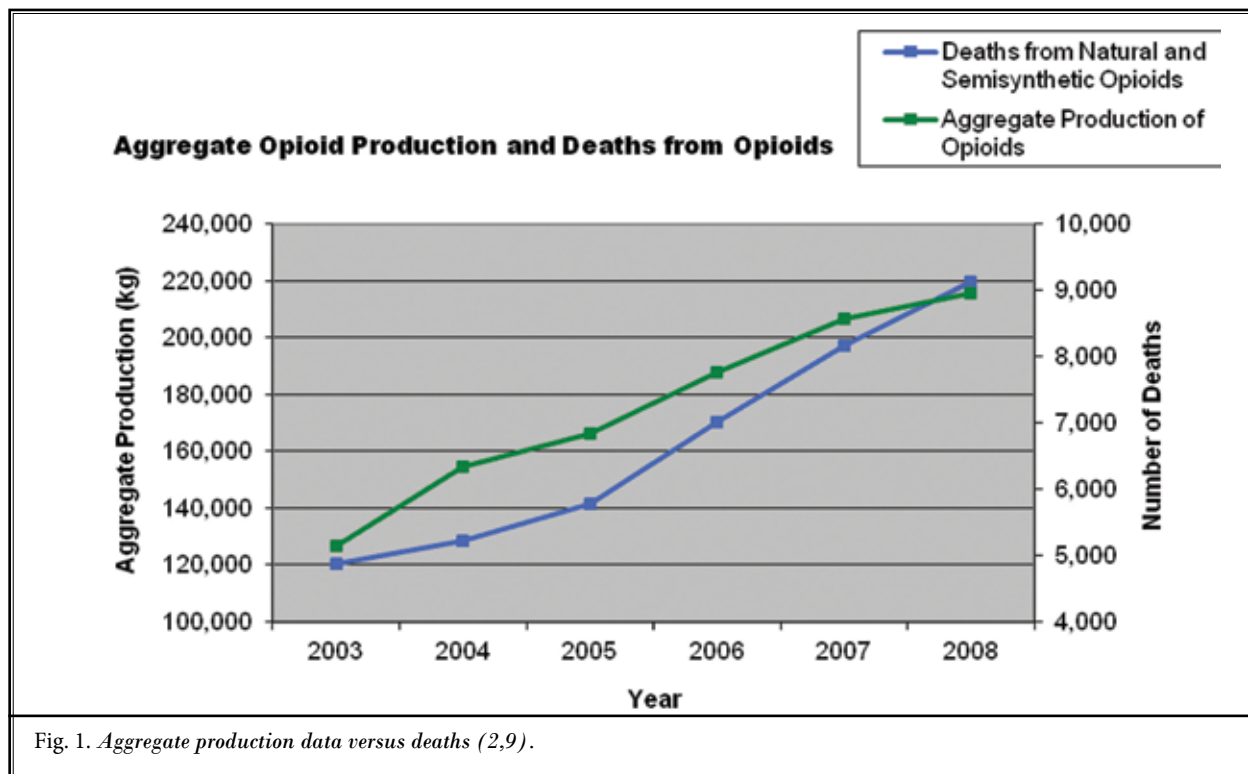
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Pain is a symptom that drives hospital admissions, and pain management is required by most patients during their inpatient stays. In 2001, The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) advocated for pain assessment as the “fifth vital sign” and for its management (1). Over a decade later, use of opioids to manage pain is increasing exponentially every year as seen by the production of opioids in the United States (2). However, it is unclear if increased opioid use has resulted in proportional improvements in the management of pain. In the interim, there are increasing concerns

about adverse events associated with opioid therapy as highlighted by the JCAHO sentinel alerts (2012) (3). There is also a real and alarming concern with ever-increasing prescription drug abuse and deaths, as seen in Fig. 1 (4).

The United States stands second only to Canada in regards to opioid consumption, as measured by morphine equivalence use per capita in the world (5). There is wide variation in opioid use across nations and even amongst the developed countries. This spiraling use of opioids in the United States has led to a new clinical problem called the “opioid tolerant” patient.



The US Food and Drug Administration (FDA) defines opioid tolerance as the use of greater than or equal to 60 mg of oral morphine equivalents per day for a period 7 days or longer (6).

The management of these opioid tolerant patients during hospitalizations for acute issues is well known to be challenging amongst health care providers. However, there is limited data in the literature as to the course and outcomes of opioid tolerant patients during acute care episodes compared to opioid naive patients admitted for similar conditions.

Our hypothesis was that opioid tolerant patients were likely to be our high resource utilizers in that they had a higher than expected length of stay and thereby would benefit most from clearly defined pathways of care.

METHODS

Definition of Cohort

Medications at the time of admission were reviewed for all patients admitted from January 2013 to June 2013. Patients who were on opioids at the time of admission were further analyzed to identify opioid tolerant patients per the FDA definition. Using the

opioid equianalgesic dose chart (Table 1), we converted their opioid use to oral morphine equivalents. Our assumption was that patients on 60 mg of oral morphine equivalents or more per day, on the day of admission, were likely to have been on that dose for at least 7 days prior given their admission and hence met the FDA definition of opioid tolerant patient. This study has received approval from the Massachusetts General Hospital Institutional Review Board. All patients not on opioids or those on opioids less than 60 mg of morphine equivalents per day or where we could not make the determination of opioid tolerant doses were treated as the control group.

Risk Adjustment

University HealthSystems Consortium (UHC) Clinical Data Base/Resource Manager (CDB/RM) is an alliance of 118 academic medical centers and 298 of their affiliated hospitals. This database accounts for more than 90% of the not for profit academic medical centers in the United States.

UHC reports expected length of stay for every patient in their database which is a multivariate regression model based on factors that include patient age and gender, risk of mortality as estimated by the

APR-DRG (3M model), number and type of comorbid conditions, transfer from an acute care institution, and socioeconomic status. This is superior to APR-DRG Severity of illness alone in that it accounts for other variables and is based on data from similar academic medical institutions.

To compare risk adjusted groups, we stratified them as expected length of stay of less than 2 days, 2 – 4.99 days, 5 – 10 days, and greater than 10 days (Table 2). This stratification was based on clinical relevance and an analysis of average expected length of stay for each of the severity of illness categories 1 through 4.

Analysis of Outcomes

For each of the 4 risk adjusted categories above we then compared the actual or observed length of stay and 30 day all cause readmission rates between the opioid tolerant cohort and control population of the non-opioid tolerant. These were then analyzed for statistical significance.

RESULTS

Identifying Opioid Tolerant Patients

Out of 25,836 admissions at Massachusetts General Hospital (MGH) during this time, 3,418 patients (13%) were on opioids. Two thousand and ninety-six admissions met opioid tolerant criteria, which is 1 in 12 patients for total admissions. Five hundred seventy patients, 17% of patients on opioids during admission, were not opioid tolerant. Opioid tolerance, or lack of, could not to be determined in 754 patients, which is 22% of the total patients on opioids during admission.

Length of Stay and Readmission Rates

In evaluating length of stay and 30 day all cause readmission rates between the opioid tolerant patients and control for each risk adjusted group, we found overall that opioid tolerant patients had a longer length of stay and greater 30 day all cause readmission rate than the control group ($P < 0.01$). Again this was borne out in the first 3 risk adjusted groups but not in the fourth group with expected length of stay > 10 days. The average length of stay for the control patients was found to be 5.66 days observed for 5.07 days expected, in comparison to the opioid tolerant patients whose average length of stay was 7.02 days observed for an expected 5.86 which was statistically significant ($P < 0.01$).

The 30 day all cause readmission rate overall for the control patients was 9%, while the rate for opioid toler-

Table 1. *Equianalgesia table (10).*

Drug	Morphine Equivalent mg (oral)
Buprenorphine (oral)	25
Buprenorphine patch	2.4
Codeine (oral)	0.15
Fentanyl patch 25mcg/hr	50
Fentanyl buccal (oral)	2.4
Fentanyl injection 500mcg (200mcg=30mg Morphine)	75
Hydrocodone (oral)	1.5
Hydromorphone (oral)	4
Hydromorphone 1mg/ml	4
Hydromorphone epidural.iv (1:5)	20
Meperidine (oral)	10
Meperidine (parenteral)	2.5
Methadone (oral)	4
Methadone parenteral (X1.3=oral methadone)	5.2
Morphine (oral)	1
Morphine 1mg/ml	1
Oxycodone 1mg/ml	1.5
Oxycodone (oral)	1.5
Oxymorphone (oral)	3
Pethidine (oral)	10
Propoxyphene (oral)	0.2
Tapentadol (oral)	0.4
Tramadol (oral)	0.2
Vicodin (oral)	1

Table 2. *Population distribution in risk adjusted groups*

	<2	2 to 4.99	5 to 10	>10	Total
Control	879	13,594	4,997	1,708	21,178
Opioid Tolerant	72	1,109	619	239	2,039

ant patients was 16.3% ($P < 0.01$) (Table 3). Again the first 3 risk adjusted groups showed a similar difference of statistical significance while in the fourth group with expected length of stay > 10 days it was not of statistical significance (Table 3).

DISCUSSION

Opioid use has grown significantly over the last decade in the United States. Most health care providers would point to the management of acute issues in the opioid tolerant patient population as challenging. Our

Table 3. Length of Stay and Readmission Rates

Readmission Rate	<2	2 to 4.99	5 to 10	>10	TOTAL
Opioid Tolerant	12.68%	13.49%	21.13%	18.32%	16.17%
Control	4.91%	10.17%	14.42%	17.11%	11.51%
<i>P</i> Value	0.0136	<0.01	<0.01	0.7458	<0.01
Average Observed Length of Stay	<2	2 to 4.99	5 to 10	>10	TOTAL
Opioid Tolerant	2.46	4.60	8.29	16.34	7.02
Control	1.71	3.69	7.52	18.27	5.69
<i>P</i> Value	<0.01	<0.01	<0.01	0.1429	<0.01

study helps address the paucity of data on the course of opioid tolerant patients when hospitalized for acute issues when compared to the control populations.

The data illustrate the significant percentage of patients who meet the criterion for opioid tolerance on admission to the hospital and outlines a hospital course for these patients with outcomes less favorable than the control population.

We found opioid tolerant patients in our cohort to have a longer length of stay in the hospital by 1.7 days, more than a 100% higher all cause 30 day readmission rate, and their average days to readmission is 0.7 days sooner. As a result, these patients have higher health care costs as they utilize more of a hospital's resources.

All these findings were true for the first 3 risk adjusted categories that correspond with lesser severity of illness patients. For patients in the fourth category which corresponds with the sickest patients, no statistical difference was found.

Further research is warranted into factors that make this subset of the population at risk for prolonged stays and readmission. A hypothesis is that opioid tolerant patients may not be well controlled from a pain management perspective for their chronic pain, and the additional need for acute care may mean they stay longer or come back sooner to optimize their pain management. Earlier intervention with multimodal analgesia and the involvement of pain specialists to help manage this may be of value. Patients on chronic opioids are known to be prone to androgen deficiency which could potentially lead to decreased muscle mass and fatigue leading to prolonged recovery after an acute care episode (7). Chronic opioids have been implicated with immunosuppression which may make these patients more prone to infections (8). All of this could contribute to the prolonged stay and higher readmission seen in this population. Early recognition and prophylaxis may well lead to more optimal care for this at risk population.

A limitation of the study may be our inclusion criteria for the opioid tolerant group. We made an assumption that patients admitted on 60 mg of oral morphine equivalence or more per day were likely to also have been on the dose for at least 7 days. While this is extremely likely as most patients would not have been prescribed these doses as a first prescription, it is likely there may have been exceptions. The study is also limited to a single large tertiary care center.

The opioid tolerant population is at risk given the poorer outcomes and higher health care costs associated with their care. It is imperative that we identify opportunities for improvement and create specific care paths for the care of these patients. The first challenge is to identify opioid tolerant patients by standard criteria at time of initial visit to the hospital care setting be it the emergency room, the pre-admission testing area or direct admissions. These patients should be flagged for early evaluation by a pre-identified group of triage specialists who can then determine if they are candidates who may benefit from early intervention with the use of multidisciplinary teams.

CONCLUSION

During their hospital course it is critical that an evidence-based multimodal algorithm be employed for the management of their pain. At the time of discharge it is equally important that a specific pain management plan be elucidated in their discharge instructions which should be communicated to their designated outpatient physician. In addition, the patients should schedule an appointment with their outpatient providers before discharge when possible. Frequently, immediately after discharge many of these patients in their subacute phase present to their primary care physicians or surgeons for ongoing issues with pain management. In most circumstances these providers are not equipped to manage the spe-

cific needs of opioid tolerant patients and therefore the patients end up going back to the emergency room and hospital care system. We propose that the creation of a rapid response team consisting of health care providers with expertise in managing this

population in an acute or subacute outpatient setting, such as anesthesiologists and pain physicians, may well reduce the high readmission rates in this population by providing a smoother transition to their baseline state.

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