Prescription Medication Deaths in Utah

Workgroup Meeting
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Summary of Findings

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Summary:

This workgroup was convened to address a substantial increase in deaths due to prescription pain medications in Utah. These meetings focused on defining the problem, identifying important unanswered questions, and identifying action steps that can be taken now to prevent further deaths.

A large increase in deaths due to opiate prescription pain medications occurred in Utah between 1999 and 2003. Preliminary analyses indicate that this problem has continued in 2004 and 2005. That increase primarily affected men and women ages 25 to 54 years of age and was widely distributed across Utah. While much remains to be learned, several conclusions about the causes of this problem emerged from the workgroup discussions.

Use of opiates for pain management has substantially increased during the past decade. Over a similar time period, abuse of these medications has also increased. Use of methadone for pain management has also increased in the past few years, motivated both by its efficacy and by its relatively low price. While having advantages for pain management, methadone also has complex, variable, and poorly understood pharmacologic properties that can lead to adverse outcomes, especially when used by inexperienced providers. Some of these deaths have involved patients using legitimately prescribed medications.

The most important question that must be answered to guide interventions will be to determine the proportion of these deaths that involve patients taking these medications under medical supervision and the proportion that involve individuals using them for non-medical purposes. In addition, it will be important to determine the specific factors contributing to death in patients prescribed opiates, the sources of medications used for non-medical purposes and the factors leading to non-medical use.

The workgroup identified three action steps that can be taken at this time to prevent further deaths: 1) educate health care providers about appropriate use of opiates for pain management, especially regarding methadone; 2) improve education provided to patients about appropriate use of opiates for pain management, and 3) educate the public about the risks of adverse outcomes of medical and non-medical use of opiates.

This workgroup focused on the immediate problem of deaths due to opiate use and on specific action steps that can be taken now. During that discussion other concerns emerged that cannot be addressed immediately by this process, but which deserve attention. One of these concerns was the overall increase in opiate use for pain management. It seems likely that this increased use, while intended to improve pain management, has led to 1) persons being treated with opiates in whom the risk of adverse outcomes is greater than the benefits, and 2) greater availability of opiate medications that are diverted to non-medical uses. A careful examination of how opiates are used in pain management is warranted. Any interventions that are intended to decrease use should be carefully designed to minimize the risk that those interventions will deprive people of needed access to these medications for treatment of pain.

The next step in this process will be to convene a second workgroup meeting to plan to implement the action steps identified in this summary.

Introduction

Over the past few years, the Utah Medical Examiner noted increasing numbers of deaths occurring due to overdose of prescription pain medications, such as oxycodone, methadone, and hydrocodone. Epidemiologic studies of data collected by the Office of the Medical Examiner confirmed that this was an important problem. On October 24 and 25, the Utah Department of Health convened a workgroup meeting to identify causes and potential solutions to this important public health problem. The workgroup included individuals with expertise in medical care, pharmacy practice, pain treatment, substance abuse prevention, poisoning prevention, public health, epidemiology, health care financing and other relevant areas. Two workgroup sessions were held to allow more participants to attend. At each session, an overview of the problem was presented and participants were asked to address three objectives:

1) Define current understanding of the causes of the epidemic of deaths due to prescription medications in Utah.
2) Identify important unanswered questions that can guide investigations leading to interventions to prevent deaths.
3) Identify action steps that can be taken now to prevent deaths from prescription medications.

Comments and conclusions by the workgroup members were recorded and used to prepare a draft summary of the discussions. That summary was reviewed by members of the workgroup and their suggestions were incorporated to produce this document which summarizes the conclusions of the workgroup.

Findings of the Workgroup

1) Current understanding of the problem

- **Deaths due to prescription narcotic pain medications have increased substantially in Utah. Similar trends have occurred elsewhere in the United States.**
  - Beginning in approximately the year 2001, deaths of Utah residents from non-illicit drug poisoning (unintentional or intent not determined) have increased from about 50 deaths per year in 1999 to over 200 in 2003. Preliminary analyses suggest the problem has continued in 2004 and 2005.
  - That increase was mostly due to increases in deaths from prescription opiate pain medications, including methadone, oxycodone, hydrocodone, and fentanyl. In an analysis of deaths from 1999-2003, methadone was implicated in 33%, oxycodone in 22%,

hydrocodone in 17%, and fentanyl in 5% of deaths[1] (1). Similar increases are known to have occurred in other parts of the country (2-3).

- " Rates of death were highest for adults aged 25-54 (median age at death = 40), and somewhat higher for males than females, but similar in urban and rural Utah. Rates were higher for people who were overweight or obese.
- " Comparing 1991-1998 to 1999-2003, death rates from this problem increased for males and females and in urban and rural parts of Utah.
- " Methadone appears to have accounted for a disproportionate number of deaths compared to its frequency of use suggesting its use carries a particularly high risk of death.
- " Specific information was available from a review of 114 methadone deaths:
  - Methadone had been obtained through a valid prescription for 42%; evidence for diversion of the medication was found for 18%, and for 39% the source was unknown.
  - Other substances were involved in 60% of methadone-related deaths in 2004. Those substances included benzodiazepines, other opiates, antidepressants, alcohol, and other CNS depressants.
  - In the 44 deaths where a prescription was available to determine the onset of treatment, death occurred within 1 week of that prescription in nearly 70% of decedents.
  - For deaths where a prescription was found, the most common specialty board certifications noted for the prescribing physicians were family practice (32%), internal medicine (23%), and pain treatment (15%).

! **Use of opiates for pain management has increased in Utah and elsewhere in the U.S.**

- " Based on data from ARCOS[2] for the period 1997 to 2002, the amount of drugs distributed to Utah and the United States (in grams per 100,000 population) increased substantially for several of the prescription drugs described in this report, including methadone (Utah: from 269 g to 1,703 g; United States: 194 g to 954 g), oxycodone (Utah: 1,848 g to 9,804 g; United States: 1,668 g to 8,056 g), and hydrocodone (Utah: 4,754 g to 8,122 g; United States: 3,249 g to 6,777 g)
- " Several factors appear to have contributed to the increased prescribing of opiates for pain management, including availability of new pain medications and formulations of medications, marketing of those medications, and advocacy for improved pain management. (4-5)
- " While methadone accounts for a small proportion of all prescribed narcotic pain medications, the number of such prescriptions has increased substantially.

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[1] More than one medication could be implicated in a single death so these percentages should not be added.

[2] Automation of Reports and Consolidated Orders System (ARCOS) is a drug reporting system maintained by the Drug Enforcement Administration (DEA) that monitors the flow of DEA controlled substances from their points of manufacture through commercial distribution channels to points of sale or distribution at the dispensing/retail level.

! Abuse of opiate pain medications has increased in the U.S. and probably also in Utah (6).
  " In the 2002 National Survey of Drug Use and Health, 30 million people or 13% of the U.S. population (age 12 or over) reported non-medical use of a prescription pain medication at least once in their lifetime. From 1990 to 2002, the number of people who reported using prescription pain medications non-medically for the first time that year increased from 600,000 to over 2 million people (7).
  " The number of treatment admissions for substance abuse related to narcotic pain medications was relatively stable from 1992 to 1997, then increased substantially from 1997 to 2002 (1992 rate-14 per 100,000 persons age ≥12; 2002 rate-35 per 100,000). (8)
    - Utah was one of 31 states in the highest quartile with admission rates over 24 per 100,000.
  " Emergency Department visits for narcotic pain medications in the U.S. increased by 153% from 1995 to 2002, based on data from DAWN. The most common reason for these visits was dependence (9). Evidence from the Utah Emergency Department Database suggests Utah has experienced a similar trend (unpublished data).

! Methadone has complex pharmacologic properties that increase risk of adverse outcomes and that aren't widely recognized by practitioners or patients.
  " Long and variable half life (mean 24-36 hours; range 4-91 hours)
    - High inter-individual variability in metabolic breakdown rates
    - Variable within an individual over time because of interactions with other medications (including induction or inhibition of hepatic metabolism).
  " The timing of analgesic effect (peak and duration) does not match that of toxicity
    - Peak analgesic effect occurs at 1-2 hrs after an oral dose and lasts 3-5 hours, while stable levels of methadone in the body are not achieved for several days on a given dose.
  " Dosing of methadone does not have a linear or fixed relationship with that of other opiates.
    - The appropriate equivalent methadone dose to use when an individual is converted from use of another opiate to methadone is difficult or impossible to predict.
  " Tolerance for respiratory depression may not be equivalent to that for analgesic effects, especially in the first week or so of use in a patient (10).
  " Methadone is inexpensive relative to other opiate analgesic medications and financial incentives encourage providers to switch patients from other opiates to methadone.

! The increase in deaths due to methadone doesn't appear to have resulted from methadone treatment of opiate addiction
  " In 2001, policies for opiate treatment programs changed to liberalize use of methadone in pill form and allowance for take-home medication (10).
  " A national review of this question conducted by SAMHSA did not find evidence that opiate treatment was responsible for the increase in deaths due to methadone (10).
  " This workgroup did not find evidence that methadone treatment for opiate addiction had contributed to the increase in deaths from methadone (see also unanswered questions).

- Greater access to and use of comprehensive, multi-disciplinary pain management is needed.
  - Current reimbursement policies inhibit use of comprehensive, multi-disciplinary pain management.
  - Many providers have inadequate knowledge of the complete range of approaches to pain management.
  - Policy changes by insurers and DEA have led to more patients being treated for chronic pain in primary care settings and by mid-level practitioners.

2) Important unanswered questions:

- To what extent are deaths occurring in patients using opiate pain medications under the supervision of a health care provider vs. in persons who obtained the medications by some other means?
  - We know from the methadone study that some deaths are occurring among patients for whom methadone was prescribed, but we don't have similar information about deaths due to other opiates and the source of methadone is unknown for a substantial proportion of methadone deaths.
    - What proportion of deaths occur in patients who are using opiates under supervision by a prescribing physician?
    - What proportion of deaths occur in patients using opiates prescribed by a physician, but while not under physician supervision (e.g., saved from previous prescription)?
    - What proportion of deaths occur in persons using opiates non-medically?
  - What proportion of deaths are caused by opiates obtained through diversion from legitimate sources or otherwise obtained illegally?

- What factors contribute to deaths that occur while under the care of a physician?
  - What proportion of deaths are due to incorrect prescribing by physician?
    - due to inadequate knowledge by physician
    - due to prescribing or dispensing errors
    - due to inadequate patient education or failure to screen for risk factors such as use of other medications or alcohol
  - How is the risk of death due to opiates distributed among physicians according to specialty, training, location, age/duration of practice, and other variables?
    - Does the substantial proportion of deaths due to methadone prescribed by practitioners in primary care specialties reflect the distribution of physicians caring for patients who require pain medications or does it indicate greater risk of death for patients under the care of such physicians?
  - What proportion of deaths are due to patient mistakes in use of prescribed medication?
  - What proportion of deaths are due to misuse or abuse (e.g., incorrect dose, self-adjustment of dosing, use along with other CNS depressant medications or alcohol) by patient to whom medications were prescribed?

- What factors contribute to diversion and to non-medical use of opiates?
  - What factors contribute to initiation of non-medical use?
  - How do individuals using opiates for non-medical use obtain the drugs?
  - What steps can prevent diversion of medications into non-medical use?

- Has methadone used in opiate addiction treatment programs contributed to this increase?
  - While evidence was not found to indicate that methadone used in opiate addiction treatment programs was contributing to the increase in deaths, we didn't have information about methadone treatment conducted by private treatment facilities in Utah.
  - Since the source of methadone is unknown for many deaths, we should determine whether increased use of take-home methadone pills by addiction treatment programs could have increased availability of methadone for abuse and contributed to this problem.
  - A systematic approach to identifying whether deaths from methadone are occurring in patients receiving methadone for addiction treatment is needed.

- Information is needed about both provider and patient knowledge (and gaps in knowledge) about pain management and opiate use. Specifically, information is needed about:
  - Provider knowledge and gaps in knowledge about the appropriate role of opiates in pain management and of non-opiate approaches to pain management;
  - Provider knowledge and gaps in knowledge about pharmacology and risks of methadone for pain management; and
  - Information and education currently provided to patients about opiate use.

- To what extent have pharmaceutical marketing and government regulation or insurer reimbursement policies, contributed to this problem?
  - What factors have led to the increased use of opiates for pain management and how have those factors contributed to this increase in deaths?
  - What factors have led to the increased use of methadone and how have those factors contributed to this increase in deaths?

- What risk factors contribute to increased risk of death in patients being treated with opiates?
  - Role of obesity and sleep apnea?

3) Action Steps that can be taken now

- Education of providers about the appropriate use of opiates as part of pain management.
  - Education of providers about the risk of death during opiate treatment for pain.
  - Specific education of providers about the pharmacology and appropriate use of methadone.
  - Education of providers about comprehensive, multi-disciplinary approaches to pain management that include appropriate use of opiates along with other approaches.

- Patient education regarding prescription opiate use
  - Interventions that increase the provision of patient education regarding appropriate use of opiates (for patients to whom they are prescribed.)
  - Develop tools to facilitate patient education and screening.
    - e.g., patient information sheets, posters, etc.

- Public education regarding the risks of medical and non-medical use of opiates
  - Appropriate role of opiates in pain management
  - Risks of diversion and consequent non-medical use
  - Warning signs of non-medical use and of opiate dependence
  - Options for both pain management and for opiate dependence treatment

Next Steps

The next steps planned by the Utah Department of Health to address this problem include:

- Convene a meeting to develop a plan to implement the action steps identified in this report, including participants from this workgroup as well as other stakeholders that can help implement the action steps identified

- Continue the epidemiologic investigation of this problem, including:
  - Updating the trend data
  - Completing the investigation to better characterize this problem using the combined Medical Examiner and Controlled Substance Databases.
  - Consider a prospective investigation in which standard information is collected about each death related to prescription opiates.

- Contact other States that have experienced this problem and federal agencies involved in this issue (e.g., SAMHSA, CDC, DEA, FDA) to:
  - Learn from other experiences to enhance our response.
  - Learn about, participate in, or potentially stimulate a national or multi-state effort to address this problem.

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