Risk Factors for Acetaminophen Overdose

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Why is Acetaminophen Important?

- One of the most commonly used analgesic/antipyretic drugs worldwide – in the U.S. ~20% of the adult population takes an acetaminophen-containing product in any given week
- An ingredient in hundreds of products
  - Many products available over the counter – consumers decide what and how much to take without medical supervision
- Generally safe when taken as directed, but overdoses can lead to potentially fatal liver damage
  - Tens of thousands of ER visits attributed to acetaminophen annually
  - Intentional (suicide attempts) and unintentional overdoses – also a problem in children

There is ongoing concern about safety from FDA and consumer advocates, affects millions of users
Background and Objectives of Behavioral Surveillance Program

- **Purpose of behavioral surveillance:**
  - Quantify acetaminophen dosing behavior
  - Understand current knowledge/attitudes/behavior and other consumer characteristics related to dosing
  - Assess knowledge, attitude, and behavior changes following interventions

- **Data collection**
  - *Acetaminophen Patterns Study* provided an initial look at dosing patterns and characteristics of users (August 2010) – basis for most results shown*
  - *Low Education/Low Literacy Study* focused on a low SES population (October-December 2011)*
  - *Ongoing Surveillance* with similar methodology (2011-2016)

- **Sponsored by McNeil Consumer Healthcare**

*Results have been published.*
Methodology of Behavioral Surveillance Program

- Web-based data collection from internet panels
  - Telephone-based in low literacy study with subjects recruited by mall intercept
- 7-day diary, completed daily – acetaminophen products taken, details of use hour by hour
  - Key feature: list-based prompting with product names – subjects did not need to know their products contained acetaminophen
- Exit survey – knowledge of ingredients and label directions, attitudes toward medication use, label-reading behavior, medical history, demographics
End-Point: Exceeding 4 Grams Acetaminophen in a Day

- Maximum daily dose per label
- Allows for considerable margin of safety – *the large majority of “overdoses” do not result in liver damage*
- **Person-level** analyses:
  - What proportion of users exceed 4 grams?
  - Who are the individuals who exceed 4 grams?
- **Day-level** analyses:
  - What patterns of use lead to exceeding 4 grams?
HOW OFTEN IS 4 GRAMS EXCEEDED AND BY WHOM?
Prevalence of Exceeding 4 Grams Among Acetaminophen Users in Patterns Study

- 3,618 total users
- 163 (4.5%)* exceeded 4 grams
  - 73 (2.0%) took >4 grams on 1 day only
  - 15 (0.4%) took >4 grams all 7 days
- 26 (0.7%) exceeded 8 grams

*In ongoing Surveillance conducted year-round, the prevalence was 6.3%.
Prevalence of Exceeding 4 Grams According to Race/Ethnicity

*These results are statistically indistinguishable. There were not enough subjects to evaluate nonwhite racial/ethnic groups separately with statistical confidence, but no meaningful differences emerged.
Prevalence of Exceeding 4 Grams According to Health Literacy*

*Data from a separate diary study with 756 subjects recruited by mall intercept in low income areas and information obtained by telephone interview. The REALM is a commonly used test of health literacy.
Prevalence of Exceeding 4 Grams According to Knowledge of Acetaminophen as an Ingredient

*Subjects who identified acetaminophen as an ingredient in all products taken were considered to have correct knowledge.
Factors That Independently* Distinguish >4 Gram from ≤4 Gram Users

• Attitudes
  • “Choose my dose” *(directions on labels are just guidelines; I know what works for me)* ↑
  • “Start lowest dose” *(it is best to start with one pill and then take a second only if needed)* ↓

• Knowledge
  • Acetaminophen is an ingredient in the products taken ↓
  • Maximum amount to take at one time or in 24 hours ↓

• Pain and disability
  • Prevalence of chronic and other ongoing pain ↑
  • SF-12 physical component scores ↓

• Medical contact
  • ≥10 health care provider visits in past year ↑

*Based on unconditional logistic regression.
HOW IS 4 GRAMS EXCEEDED?
ANALYSIS OF WITHIN-DAY DOSING PATTERNS
Prevalence of Exceeding 4 Grams on Acetaminophen Usage Days in Patterns Study

- 13,852 usage days
  - Median dose = 1.0 gram
- 4 grams exceeded on 3.1% of days
  - Median dose = 5.5 grams
### How is 4 Grams Exceeded?

Through Other Deviations from Label

<table>
<thead>
<tr>
<th>Specific other deviations (not mutually exclusive)</th>
<th>&gt;4 gram use (n=431 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concomitant use (second acetaminophen med within dosing interval of first)</td>
<td>59%</td>
</tr>
<tr>
<td>Re-dosing too soon (re-dosing same med before recommended interval)</td>
<td>72%</td>
</tr>
<tr>
<td>Too much: exceeding labeled single dose</td>
<td>34%</td>
</tr>
<tr>
<td><strong>At least 1 deviation</strong></td>
<td>92%</td>
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</tbody>
</table>
How is 4 Grams Exceeded?
Through Combining OTC and Rx Products

% of days exceeding 4 grams

Medication types used

OTC Only
Rx Only
OTC+Rx
How is 4 Grams Exceeded?
By Combining Single-Ingredient and Combination OTC Products

<table>
<thead>
<tr>
<th>OTC medication types used</th>
<th>SI+Combo</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of days exceeding 4 grams</td>
<td>16%</td>
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</tbody>
</table>

- Single ingredient: 2%
- Combination: 0%
- SI+Combo: 16%
Key Points - 1

How often is 4 grams exceeded, and by whom?

- 4 grams exceeded by 5-6% of acetaminophen users
- Linked to poor knowledge of medication ingredients and directions
- Associated with attitudes of choosing-your-own-dose, and *not* trying lowest dose first
- Associated with ongoing and chronic pain, disability
- Associated with multiple medical visits and daily smoking
- Associated with very low health literacy
- Minimal differences according to race/ethnicity, but data were insufficient to permit a detailed evaluation
Key Points - 2

How is 4 grams exceeded?

- Almost always by deviating from label directions for one-time dose, dosing interval, and avoidance of concomitant use
- By use of multiple medication types

Suggestions for mitigation

- Widespread consumer education initiatives focusing on improving knowledge of product ingredients and label directions
  - Identify and address needs of specific communities
- Icon to identify acetaminophen products
- Engage health care providers to help focus their patients on responsible use of acetaminophen
Thanks to My Colleagues

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