

Serious Adverse Drug Events Reported to the Food and Drug Administration, 1998-2005

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FROM ABSTRACT

Background

The US Food and Drug Administration has operated the Adverse Event Reporting System since 1998. It collects all voluntary reports of adverse drug events submitted directly to the agency or through drug manufacturers.

Methods

We analyzed all serious adverse drug events and medication errors in the United States reported to the Food and Drug Administration from 1998 through 2005.

Results

From 1998 through 2005, reported serious adverse drug events increased 2.6-fold from 34,966 to 89,842, and fatal adverse drug events increased 2.7-fold from 5,519 to 15,107.

Reported serious events increased 4 times faster than the total number of outpatient prescriptions during the period.

In a subset of drugs with 500 or more cases reported in any year, drugs related to safety withdrawals accounted for 26% of reported events in that group in 1999, declining to less than 1% in 2005.

For 13 new biotechnology products, reported serious events grew 15.8-fold, from 580 reported in 1998 to 9,181 in 2005. The increase was influenced by relatively few drugs: 298 of the 1489 drugs identified (20%) accounted for 407,394 of the 467,809 events (87%).

Conclusions

These data show a marked increase in reported deaths and serious injuries associated with drug therapy over the study period.

The results highlight the importance of this public health problem and illustrate the need for improved systems to manage the risks of prescription drugs.

THESE AUTHORS ALSO NOTE:

"Serious adverse drug events (ADEs) have been estimated to account for 3.1% to 6.2% of admissions to hospitals studied."

"Among hospital inpatients, serious ADEs have been reported to occur at a rate of 1.9 per 100 admissions."

"In hospital emergency departments, ADEs of all levels of severity were estimated to account for 2.5% of all visits for unintentional injury in 2005-2006, of which 16.7% were severe enough to require hospitalization."

"A meta-analysis of inpatient hospital and hospital admission studies conducted over several decades estimated that ADEs were associated with 106,000 deaths in 1994."

"The Adverse Event Reporting System (AERS) of the US Food and Drug Administration (FDA) is the world's largest database of voluntary, spontaneous reports of adverse drug reactions and medication errors." It has been in operation since 1998.

"The objectives of this study were to measure any changes in the annual number of reported serious ADEs since 1998, identify drugs frequently implicated, and explore potential reasons for the changes observed."

"A serious event, in the FDA's regulatory definition, means an adverse event that resulted in a health outcome of death, a birth defect, disability, hospitalization, or was life threatening or required intervention to prevent harm."

"One feature of the study period was the introduction or increased use of biotechnology products, notably immunomodulators created through genetic engineering."

RESULTS

"In the 8-year period, 467,809 serious events met the study criteria for inclusion in this analysis."

"Serious ADEs reported to the FDA increased from 34,966 in 1998 to 89,842 in 2005, a 2.6-fold increase."

"Reported deaths increased 2.7-fold, from 5,519 in 1998 to 15,107 in 2005."

"The overall relative increase was 4 times faster than the growth in total US outpatient prescriptions, which grew in the same period from 2.7 billion to 3.8 billion." **[WOW, the number of out patient drug prescriptions increased by 1.1 billion in the US population in 7 years.]**

Over the 8-year period, adverse drug events caused the death of 80,880 patients, caused permanent disability or birth defects in 32,922 patients, and of the remainder, 354,007 patients had 1 or more of the other serious outcomes.

Death as the outcome accounted for 15.8% of events in 1998 and 16.8% in 2005.

A disproportionate share of adverse events occurred among elderly patients, which constituted 12.6% of the total US population but accounted for 33.6% of the serious adverse events.

"Among the 15 drugs most frequently named in fatal events, 7 were pain medications and 4 had primary effects on the immune system."

The number of serious adverse events associated with 13 prominent biotechnology products grew 15.8-fold during the period, from 580 in 1998 to 9,181 in 2005, including anti-TNF (anti-tumor necrosis factor) immunosuppressive drugs.

COMMENT FROM AUTHORS

"These data show that a nearly 3-fold increase has occurred in reported serious injuries, disability, and death associated with drug therapy in the 8-year study period."

"Among the most frequently reported drugs associated with fatal events, we observed a disproportionate contribution of pain medications and drugs that modify the immune system."

"This study shows that substantially growing numbers of patients are experiencing serious injuries from drug therapy."

KEY POINTS FROM DAN MURPHY

- 1) From 1998 through 2005, reported serious adverse drug events increased 2.6-fold from 34,966 to 89,842.
- 2) From 1998 through 2005, fatal adverse drug events increased 2.7-fold from 5,519 to 15,107.
- 3) From 1998 through 2005, reported serious events increased 4 times faster than the total number of outpatient prescriptions during the period.
- 4) From 1998 through 2005, serious and fatal adverse drug events were highest for new biotechnology drugs, growing by 15.8-fold.
- 5) Serious adverse drug events (ADEs) account for 3.1% to 6.2% of hospital admissions.
- 6) "In 1994, inpatient hospital and hospital admission studies indicated that ADEs were associated with 106,000 deaths."

- 7) "A serious event, in the FDA's regulatory definition, means an adverse event that resulted in a health outcome of death, a birth defect, disability, hospitalization, or was life threatening or required intervention to prevent harm."
- 8) "One feature of the study period was the introduction or increased use of biotechnology products, notably immunomodulators created through genetic engineering."
- 9) "The overall relative increase [of serious adverse drug events] was 4 times faster than the growth in total US outpatient prescriptions, which grew in the same period from 2.7 billion to 3.8 billion."
- 10) **[The number of out patient drug prescriptions increased by 1.1 billion in the US population in 8 years.]**
- 11) Over the 8-year period, adverse drug events caused the death of 80,880 patients, caused permanent disability or birth defects in 32,922 patients, and of the remainder, 354,007 patients had 1 or more of the other serious outcomes.
- 12) Death as the outcome accounted for 15.8% of events in 1998 and 16.8% in 2005.
- 13) A disproportionate share of adverse events occurred among elderly patients, which constituted 12.6% of the total US population but accounted for 33.6% of the serious adverse events.
- 14) "Among the 15 drugs most frequently named in fatal events, 7 were pain medications and 4 had primary effects on the immune system."
- 15) The number of serious adverse events associated with 13 prominent biotechnology products grew 15.8-fold during the period, from 580 in 1998 to 9,181 in 2005, including anti-TNF (anti-tumor necrosis factor) immunosuppressive drugs.
- 16) "These data show that a nearly 3-fold increase has occurred in reported serious injuries, disability, and death associated with drug therapy in the 8-year study period."
- 17) "Among the most frequently reported drugs associated with fatal events, we observed a disproportionate contribution of pain medications and drugs that modify the immune system."
- 18) "This study shows that substantially growing numbers of patients are experiencing serious injuries from drug therapy."