

Research Article

Analysis of Medication-Related Deaths in Denmark

Lars Dahlgaard Hove,¹ Johannes Bock,² and Jens Krogh Christoffersen²

¹ Department of Anaesthesia, Hvidovre Hospital, University of Copenhagen, Kettegaard Alle 30, 2650 Copenhagen, Denmark

² Gynaecology and Obstetrics, The Danish Patient Insurance Association, Nytorv 5, 1450 Copenhagen, Denmark

Correspondence should be addressed to Lars Dahlgaard Hove; ldhove@hotmail.com

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Objective. To investigate the circumstances associated with medication-related deaths. **Design and Setting.** This retrospective study investigated closed claims concerning medication-related deaths from 1996 to 2008 registered by the Danish Patient Insurance Association (DPIA). **Results.** A total of 80 were patients registered as having died because of an adverse event or error associated with a medication, and 37 of these cases were considered to have been preventable. The circumstances of the 37 deaths are described in detail in this report. Orthopaedic surgery, anaesthesiology, and internal medicine were the specialties involved in the majority of the deaths. Incorrect dosing was the cause of 17 deaths, and the use of the wrong drug caused 11 deaths. The administration of a drug despite a known allergy/intolerance or contraindication caused 6 deaths. Other 5 deaths were caused by anticoagulation medications. Methotrexate given daily by mistake caused 2 deaths. **Conclusion.** This study describes the circumstances of 37 preventable deaths caused by medication. Drug administration despite a known allergy, opioids, sedative, anticonvulsive medicine, and incorrect dosing and incorrect use of anticoagulants are the most important areas to be addressed in the development of future patient safety measures to reduce patient deaths caused by or related to medications.

1. Introduction

In Denmark, patients may file a claim if their medical treatment results in an injury or an unexpected side effect. The independent Danish Patient Insurance Association (DPIA) considers these claims. The DPIA operates on a no-blame no-fault basis and does not take any legal action beyond assessing damages. As a result, patients may file a claim with the DPIA free of charge with the sole purpose of seeking financial compensation. Thus, the injured patient is spared the expense of legal fees and the trouble of going to court.

In general, financial compensation may be granted under any one of the following criteria: (1) an experienced specialist would have acted differently, whereby the injury could have been avoided; (2) defects in or failure of the technical equipment was of major concern with respect to the incident; (3) the injury could have been avoided by using alternative treatments, techniques, or methods if these were considered to be equally safe and to potentially offer the same benefits;

and (4) the injury was rare, serious, and more extensive than what the patient should be expected to endure.

Claims granted based on criterion (1) are associated with events considered possibly preventable (substandard treatment).

Compensation is calculated based on the extent of pain and suffering, reduced income, reduced ability to work, and medical expenses, as well as whether the injury could be expected to be permanent. Compensation is rendered if the calculated amount exceeds €1,500. The government pays the compensation. After the decision has been made, the patient may file an appeal with the Patient Damage Appeal Board, as well as with the courts of law. From 1996 to 2008, the DPIA received 45,953 claims; 39% of these were approved.

Drug-related errors are the most common single cause of medical errors. The incidence of adverse drug events is between 0.7 and 6.5% of hospitalised patients, and up to 56.6% of these events are preventable [1]. There is evidence that the death rate from medication errors is increasing.

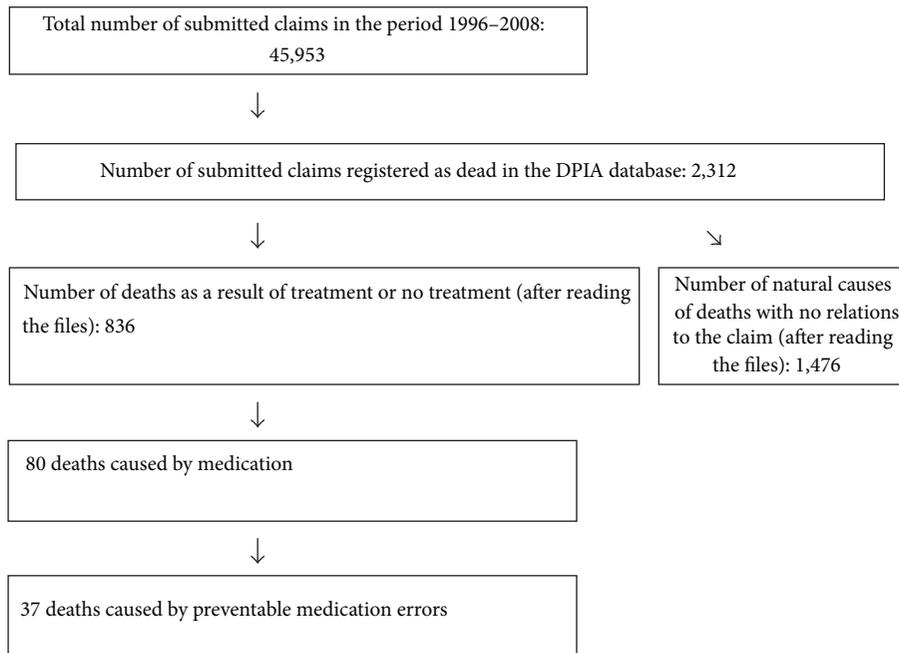


FIGURE 1: Flow diagram of the process of identifying the 37 claims associated with medication errors.

From 1983 to 1993, the number of deaths from medication errors and adverse reactions in US hospitals increased from 2876 to 7391 [2]. From 1990 to 2000, the annual number of deaths from medication errors in the UK increased from approximately 20 to just under 200 [3].

Malpractice claims, which include detailed information from disparate sources, may be used for systems analyses, which may in turn allow for the assessment of prevention strategies [4].

2. Design and Setting

For each claim, the DPIA creates a patient folder in which the documents of the case are kept; this information is then entered into a database in which all of the submitted claims are registered according to the diagnosis, treatment, and type of injury. Upon receiving a claim, the DPIA collects all of the medical records pertaining to the case. A lawyer evaluates the claim in collaboration with the medical specialists to determine whether standard practice (i.e., compliance with general recommendations and guidelines) was followed.

We reviewed the information drawn from the internal data system of the DPIA and conducted a detailed scrutiny of all of the patient folders and records. We used a retrospective design to investigate closed claims concerning cases in which patients were registered as having died from a medication-related cause. These closed claims were collected and analysed, and the decisions made by the DPIA, the appeal board, or the courts of law in cases of appeal were registered and used in this analysis.

3. Results

The total number of claims filed during the period from 1996 to 2008 was 45,953. Of these, 2,312 were associated with cases in which the patient had died.

We analysed these 2,312 claims and concluded that in 836 cases, the patient died as a result of treatment or lack of treatment. In 80 cases, the patients were registered as having died as a result of a medication, and 37 of these cases were judged as being associated with criterion (1) and therefore considered preventable.

Figure 1 shows a flow diagram of the process of identifying the 37 claims associated with criterion (1) from the original 45,953 claims.

Among the patients who had died, three were children (aged 1, 3, and 5 years), and the average age of adult patients who had died was 61.3 years.

Four patients were not financially compensated, and 33 patients were compensated with a total of €1.2 million, corresponding to an average compensation of €34,200 per case (range: €1,500–554,100).

Table 1 shows the distribution of deaths according to the associated specialties. Orthopaedic surgery, internal medicine, and anaesthesiology were involved in 19 of the 37 deaths.

Table 2 shows the distribution of the medication-related deaths according to the cause (incorrect drug, dose, formulation, route, strength, or timing). Cases of incorrect drugs or doses accounted for 28 of the 37 deaths. The category “incorrect dose” includes medications given at the incorrect dose, medications not given, and medications administered despite contraindications. The patients who died due to

TABLE 1: Specialty and number of preventable medication deaths.

Specialty involved	Deaths
General surgery (including surgical gastroenterology)	2
Internal medicine	6
Obstetrics	1
Orthopaedic surgery	6
General medicine	1
Cardiology	2
Anaesthesiology (including intensive care unit)	7
Thoracic surgery	1
Radiology	1
Neurosurgery	1
Oncology	2
Otorhinolaryngology	1
Paediatrics	1
Neurology	1
Haematology	2
Pulmonology	1
Nephrology	1
Total	37

TABLE 2: Causes of medication errors, examples, and numbers.

Cause	Drug involved	Number
Wrong drug	Lidocaine, morphine	11
Wrong dose	Warfarin not paused, steroids paused	17
Wrong formulation	Methohexital	1
Wrong route	Contrast to nasogastric tube	1
Wrong strength	Thiopental	1
Wrong timing	Amiodarone, heparin	4
No drug despite indication	Insulin, glucose, and antithrombotic	2

an incorrect dose had typically received a 10–20-fold higher dose than that intended or recommended.

History. It describes the circumstances of the preventable medication-related deaths of the 37 patients. The administration of a drug despite a known allergy/intolerance or contraindication caused 6 deaths (incompatible blood transfusion, furosemide, penicillin, ibuprofen, diclofenac, and morphine). Other 5 deaths were caused by anticoagulation medicine. Methotrexate given daily by mistake caused 2 deaths. Interestingly, 1 death was caused by an incorrect dose in an electronic prescription system: a doctor prescribed a 5 mg bolus of terbutaline in the electronic prescription system, although 0.5 mg was the intended dose. The nurse administered 5 mg.

A 59-year-old woman had an elective operation for a cerebral aneurism. Her warfarin (given for an artificial heart valve) was mistakenly not paused, and she died of a major

subdural haematoma 2 days after the operation. The INR was 5.3 postoperatively. The notes in the medical record were confusing regarding the warfarin medication dosage.

A 73-year-old woman with Addison's disease was operated on for rectal cancer. Her steroid medications were paused during and after the operation, and she developed circulatory failure and died 4 weeks after the operation.

A 45-year-old man was treated with nitroglycerine for pulmonary oedema after an operation for correction of his nasal septum. A bolus of 50 mg nitroglycerine was accidentally given, causing severe hypotension. He died 2 days postoperatively due to a cerebral infarction.

A 1-year-old baby girl was scheduled for a CT scan because of recurrent pneumonia. Methohexital 8 mg was intended to be administered intravenously, but 80 mg was given. A 10% solution intended for rectal administration was confused with a 1% solution intended for intravenous administration. Cardiac arrest occurred shortly after the administration, and resuscitation was unsuccessful.

A 49-year-old man was intoxicated with an unknown substance after a suicide attempt. To obtain a secure airway, he was intubated. For this procedure, he was given a bolus of 2,000 mg thiopental (400 mg was intended). An anaesthetist had prepared the thiopental concentration as 125 mg/mL rather than the intended 25 mg/mL. Immediately after injection, the patient developed cardiac arrest, and resuscitation was unsuccessful.

A 43-year-old woman was scheduled for a scan of her stomach. The contrast was mistakenly injected into the subclavian catheter instead of the nasogastric tube as intended. She developed a severe anaphylactic reaction and died the same day.

A 54-year-old woman with lung cancer was scheduled for pericardiocentesis under anaesthesia. After initiating the anaesthesia, the patient was inadvertently given a bolus of 500 mg propofol. A new type of infusion pump was used, and it was adjusted incorrectly. Cardiac arrest occurred and resuscitation was performed, but the patient developed a cerebral infarction and died a few days later.

A 66-year-old man was admitted to a hospital with atrial fibrillation. Intravenous access was established, and the intended saline drip was confused with lidocaine. Lidocaine was given at a toxic dose. The patient went into cardiac arrest, and resuscitation was unsuccessful.

A previously healthy 5-year-old boy was treated for febrile seizures at home by an emergency physician. Within 15 min, the patient received 10 mg diazepam rectally, 20 mg diazepam intravenously, and 10 mg midazolam intravenously. The airway was not secured, and hypoxemia developed prior to hospitalisation. The patient died from hypoxic brain damage 4 days later.

A 72-year-old woman had a hemicolectomy of the right colon for colon cancer. Postoperatively, the patient (blood group A) received 2 units of group B erythrocytes. The patient developed disseminated intravascular coagulation. Three days later, she died of this incompatible allogeneic blood transfusion.

An 80-year-old man was observed in the recovery room after a minor operation on his oesophagus. A dose of

furosemide was given, despite a known allergy to this drug. He developed a severe anaphylactic reaction and died a few days later.

A 40-year-old man was treated for withdrawal symptoms with phenobarbital. The withdrawal symptoms stopped, but phenobarbital was given for 2 more days, constituting a total dose of 5,800 mg. The man was found in cardiac arrest, and despite successful resuscitation, he died shortly thereafter.

A 68-year-old man had previously developed an acute allergic nephritis due to dicloxacillin. He was admitted to the hospital for an infection in his artificial knee. Dicloxacillin was given by mistake, and he developed acute renal failure and died five days later.

A 71-year-old man with known chronic renal failure and atrial fibrillation was admitted for total knee replacement surgery. A few days after the operation, he developed a bleeding gastric ulcer and died. His coagulation parameters were severely irregular and were not treated.

A 73-year-old man was admitted for an unintentional acetaminophen overdose due to pain. He was treated with N-acetylcysteine. The N-acetylcysteine was mistakenly given at a 10-fold higher dose than recommended, and he developed a severe cardiovascular reaction and died.

A 61-year-old man with known chronic pulmonary disease was admitted for severe back pain. The dose of opioids was doubled from day 1 to day 2. He was prescribed morphine 30 mg \times 6 and time-released morphine 60 mg \times 3. He was found in a coma due to opioid overdose and died 3 days later.

A 3-year-old boy with known epilepsy was admitted with seizures. He was treated with fosphenytoin. The dose given was approximately 5 times higher than the recommended dose because the instructions were unclear. Cardiac arrest occurred shortly after administration, and resuscitation was unsuccessful.

A 55-year-old man with B-cell lymphoma was treated with a chemotherapy course (FLAG). This treatment was not indicated for this type of disease, and the patient died of side effects of the treatment.

An 89-year-old woman had been treated with methotrexate 10 mg weekly. She was admitted to a hospital where she was treated with methotrexate 10 mg daily. She died due to bone marrow depression.

A 64-year-old man was treated with methotrexate 10 mg weekly. He was admitted to a hospital where methotrexate was given daily for 5 days before the mistake was discovered. He died nine days later due to bone marrow depression.

A 39-year-old man with testicular cancer was treated for 5 days with carboplatin and etoposide phosphate. This was considered an overdose. He died 11 days later due to bone marrow depression.

A 67-year-old man had known heart and renal disease. His warfarin was paused before total knee replacement surgery and replaced by dalteparin 10,000 IU twice daily. A normal dose was considered to be 5,000 IU once daily. He died due to abdominal bleeding.

A 64-year-old man had an elective operation for an abdominal aneurysm. In the postoperative ward, there was confusion between two correctly connected infusion pumps. The first pump infused bupivacaine into an epidural catheter,

and the second infused dopamine through an intravenous line. A bolus of 5 mL bupivacaine was intended, but a bolus of 5 mL dopamine (21 mg) was given intravenously instead. The patient developed a cardiac infarction and died 3 days later.

A 25-year-old pregnant woman had acute cholecystitis. Morphine 10 mg was prescribed, but 10 mL (100 mg) was given intravenously by mistake. She developed respiratory failure and cardiac arrest. She was resuscitated but died 2 days later due to complications from the successful initial resuscitation in combination with the cholecystitis.

A 58-year-old woman was known to have lung cancer. She was treated with cisplatin, but the dose was 25% too high. She died 10 days later due to bone marrow depression.

A 70-year-old woman had chronic pulmonary disease. The doctor prescribed a 5 mg bolus of terbutaline in the electronic prescription system, although 0.5 mg was the intended dose. The nurse administered 5 mg. The patient developed cardiovascular collapse and died the same day.

An 81-year-old woman was having total hip replacement surgery. She had a known allergy to NSAIDs. Despite this, she was postoperatively treated with ibuprofen. She had an anaphylactic reaction and died.

A 68-year-old man with diabetes was having a nephrectomy. He was not treated postoperatively for his diabetes. He developed severe hypoglycaemia and died a few weeks later of complications related to this episode.

A 74-year-old woman with a known history of bleeding gastric ulcers was admitted to a hospital for a spine fracture. She was treated with diclofenac and developed a bleeding gastric ulcer. Despite an operation, she died 1 month later of complications due to the bleeding gastric ulcer. Diclofenac was considered contraindicated based on her past medical history.

A 33-year-old male became paraplegic after a fall. Heparin was stopped after 4 weeks and before he was mobilised. He died of a pulmonary embolism 3 days after the heparin was stopped.

A 41-year-old woman was operated on for 5 hours for a cholesteatoma. No antithrombotic medicine was given, and she died of a pulmonary embolism 10 days after the operation.

A 69-year-old man had known severe heart disease. He was given medicines (metoprolol and felodipine) intended for another patient. He developed heart failure and died later the same day.

A 75-year-old woman had chronic pulmonary disease. She was mistakenly given 100 mg time-released morphine that was intended for another patient. She was transferred to the ICU but died 3 days later, likely due to aspiration.

A 55-year-old woman was admitted to a hospital for asthma. Morphine was given despite a known allergy to the drug. She went into cardiac arrest, and resuscitation was unsuccessful.

A 69-year-old man with known heart disease was being treated with amiodarone. Lung fibrosis was diagnosed after 6 months, but amiodarone was continued. It was considered contraindicated to continue amiodarone after the diagnosis of lung fibrosis. He died of respiratory failure.

A 54-year-old man was prescribed mirtazapine for depression. An ECG was not taken. He died of a heart attack 3 weeks later.

An 81-year-old woman was treated for arthritis with prednisolone. She developed severe depression and gastrointestinal bleeding a few weeks after the start of prednisolone. The prednisolone was not stopped. She died of bleeding and infection in her gut.

4. Discussion

Patient safety issues and medication errors are well studied, but there are only a few papers in which the circumstances of preventable medication-related deaths are described in detail. The definition and assessment of preventability remain unclear in many studies of adverse drug events. In this study, we used the decisions from the DPIA (or courts of law in cases of appeal) in the analysis. It is a known problem that preventability is judged in the eye of the reviewer and cannot be proven [5]. By describing the deaths, though in short terms, we provide the reader with the opportunity to develop his/her own opinion concerning preventability.

Fortunately, most medication errors are harmless; however, 1% of errors cause injury, and a small percentage of these errors are deadly [1]. Thus, our study describes a very small fraction of the total number of medication errors, but it is an important fraction. Safety tools should be implemented to reduce the number of these deaths. Our study showed that methotrexate caused 2 deaths. In the UK, the National Patient Safety Agency has linked 25 patient deaths and 26 cases of serious harm to the use of oral methotrexate in a community setting over a 10-year period in the UK. Action has been taken to develop a new packaging design that clearly shows that this drug is to be taken on a weekly rather than daily basis.

We found that the specialties of orthopaedic surgery, internal medicine, and anaesthesiology are involved in the majority of these deaths. Drug administration despite a known allergy, incorrect dosing, and the incorrect use of anticoagulation medicines are the most frequent causes of deaths. In our opinion, these are the areas that should be given the highest priority with regard to the implementation of patient safety measures for the prevention of medication errors.

The general view is that electronic prescriptions will reduce errors, but new technology can also introduce new types of errors [6]. We registered 1 patient as having died from a 10-fold drug overdose that was prescribed in an electronic system.

It is important to emphasise that in Denmark, Sweden, and the other Nordic countries, there is a no-fault no-blame system in which payment is made for any injury arising from a medical action, and the patients do not need to prove negligence or causation via litigation. This is in contrast to other countries where payment is dependent on the proof of a negligent act or omission on the part of the physician. This system results in an appreciable increase in the number of approved claims in comparison with a fault-based liability

system. Despite this no-blame no-fault system, studies have shown that the number of patients who are harmed by negligent care and actually file a claim may be less than 2%; therefore, the actual number of medication-related deaths remains uncertain, but it may be many times greater than reported [7, 8].

In this paper, we have described the actual circumstances of 37 patients who died from a treatment-related cause. Our purpose was to allow the reader to see these deaths not just as numbers but as individual cases, allowing reflection on each case. This paper is to be seen as a small contribution to the understanding of the often multifactor and complex circumstances of medical errors.

We hope that the presentation of these 37 patient deaths may facilitate the development of prevention measures in the future.

Abbreviation

CVC: central venous catheter;
MRI: magnetic resonance imaging.

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