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Original communication

Post-mortem toxicology: A pilot study to evaluate the use of a Bayesian network to assess the likelihood of fatality

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ABSTRACT

The challenge of interpreting post-mortem drug concentrations is well documented and relies on appropriate sample collection, knowledge of case circumstances as well as reference to published tables of data, whilst taking into account the known issues of post-mortem drug redistribution and tolerance. Existing published data has evolved from simple data tables to those now including sample origin and single to poly drug use, but additional information tends to be specific to those reported in individual case studies. We have developed a Bayesian network framework to assign a likelihood of fatality based on the contribution of drug concentrations whilst taking into account the pathological findings. This expert system has been tested against casework within the coronial jurisdiction of Sunderland, UK. We demonstrate in this pilot study that the Bayesian network can be used to proffer a degree of confidence in how deaths may be reported in cases when drugs are implicated. It has also highlighted the potential for deaths to be reported according to the pathological states at post-mortem when drugs have a significant contribution that may have an impact on mortality statistics. The Bayesian network could be used as complementary approach to assist in the interpretation of post-mortem drug concentrations.

1. Introduction

The role of post-mortem toxicology is important with respect to establishing the contribution of drug(s) to the cause of death. The issue of which drug is primarily responsible remains a confounding factor given that most cases involve multiple drug use. Compilations of the usual therapeutic, toxic and fatal drug concentrations have been published[1,2] and it seems that these are the standard 'go to' sources to provide a meaningful interpretation of the drug concentrations found in individual cases. Since the early 1990's, the understanding of post-mortem toxicology has evolved significantly with recognition of the phenomenon of post-mortem drug redistribution,[3] site to site variability of drug concentrations,[4] influence of tolerance, free:total drug concentration ratios,[5–7] gender bias[8] as well as, more recently, the influence of genetic polymorphisms.[9–11] It has now been established and has become common practice, that peripheral blood should be obtained from a femoral vessel,[4,12] yet it remains that the extent of redistribution artefacts is an unknown quantity. Whilst markers for the extent of redistribution have been evaluated[13] it still remains a challenging factor in the interpretation of post-mortem toxicology. Similarly the published reference data has evolved from that reported in serum samples to include whole blood[14] as well as distinguishing from data derived from a single drug to that in combination with alcohol and/or other drugs. Further publications have addressed other physical attributes such as age and body mass index[15,16] as well as those reported in specific case studies, usually as a consequence of a fatality due to the emergence of a new drug (whether it be a designer or new pharmaceutical drug) or unusual cases.[17]

Drug contribution in forensic and coronial casework interpretation is further compounded by underlying pathological conditions such as chronic obstructive pulmonary disease, liver disease (alcohol and non-alcohol related), pneumonia or coronary artery atheroma. The contribution of drugs in these cases will naturally be taken into account, yet the published tables of toxicological data that are consulted may not indicate the presence/absence of natural disease. Of further note is the disparity on how a death is recorded in cases in different coronial jurisdictions.[18] A review of coronial services suggested a failure to identify deaths where drugs were deemed to have contributed,[19] yet it does not address how to resolve the issue associated with drug related deaths where drug

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testing is not always routinely carried out.[20,21] The Shipman Inquiry in 2003 proposed changes to the process of death certification but also noted that greater use of toxicological analyses should be adopted in the death investigation process.[22]

It is of note that 506,740 deaths were registered in England and Wales in 2013, of which 227,984 deaths were reported to coroners, reflecting a less than 1% increase (263 deaths) from 2012.[23] Of these coroners cases, 94,455 post-mortem examinations were instructed, a decrease of 359 from 2012. Furthermore, only 13,285 (14.0%) included toxicological analysis,[23] but nevertheless it does see an increase from 13.3% of cases in 2012.[24] This data appears to indicate that toxicological analysis was performed on 5.8% of the cases reported to the coroner but only 2.6% of all deaths registered in England and Wales in 2013 and as such suggests that toxicological examination has not seen a significant increase in routine implementation in death investigation since the Shipman Inquiry in 2003.

According to the Office for National Statistics,[24] there were only 2597 drug poisoning deaths, of which 1496 were classified as drug misuse deaths. Of the total drug poisoning deaths, 65.6% were male with an age demographic of 30–39 having the highest mortality rate.[24] The demographic of specific drug type mentioned on death certificates indicates that the opiates (heroin, morphine, codeine, dihydrocodeine) and opioids (methadone, tramadol) drug groups were by far the most prevalent, followed by the antidepressants (tricyclic, selective serotonin reuptake inhibitors and others) and benzodiazepines (of which diazepam was most prevalent in this category) See Fig. 1.

There have of course been reforms of the coroners system in England and Wales; notably that in 2006 to improve the service for a more effective investigation into deaths[25] with legislation leading to implementation of structural and procedural changes in 2009, alongside the appointment of a Chief Coroner and the concept of a coroner's investigation into death where an inquest may or may not be required. These reforms appear to suggest an impact on the trends of cause of death reported in mortality statistics.[23] Whilst these reforms have taken place, there also remains a difference in practice by hospital, clinical and forensic pathologists in the cause of death coding (part 1a) as defined using the International Classification of Diseases, 10th revision. The wording that appears on death certificates ranges from those having named specific drug combinations (but no priority given to the recorded list of drugs e.g. combination effects of morphine, codeine and alcohol); drug overdose (with no reference to specific drugs); natural disease (when drugs are present but have been deemed not to have played a vital role in the terminal outcome).

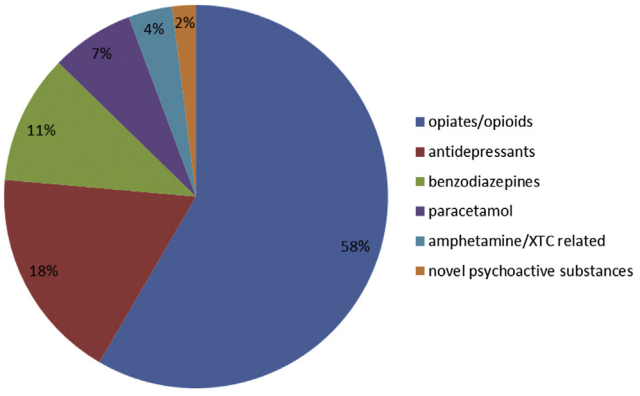

Fig. 1. Proportion of drug related deaths in 2012 where a named drug appeared on the death certificate. Modified from Office for National Statistics.[24]

Approximately 10% of the deaths reported in drug poisoning deaths had a generalised form of words on the death certificate (e.g. drug overdose or multiple drug toxicity).[24] It is also interesting to note that it has been previously reported that in cases where no natural disease was found at post-mortem, the cause of death can be attributed to a specific combination of drugs, yet in the presence of disease with the same combination of drugs, the cause of death was attributed to the disease rather than both having a contributory factor.[26] As a consequence much useful toxicological data in unnatural or indeed natural deaths remains unavailable for interpretation for post-mortem toxicology or even public health awareness (contra-indications/adverse drug combinations).

2. Bayesian statistics

The basic concept in Bayesian statistics is that of conditional probability; whenever a statement of probability (P) of an event A is given it is given under the condition of other known factors. This can be exemplified by the statement: “given the event B, the probability of the event A is x”.

The notation for this is $P(A|B) = x$.

Bayes theorem is defined as:

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)}$$

This defines the relationship between the probabilities of A and B and the conditional probabilities of A given B and B given A.Where;

P(A) is the prior probability i.e. the initial degree of belief in A
P(A|B) is the posterior probability i.e. the degree of belief accounting for B

This method is employed in a number of applications, where ‘reasoning under uncertainty’ is required e.g. medical diagnoses, stock market analysis and risk analysis, to name a few.[27] The advantage of using the Bayesian framework in such circumstances is that it can encompass both aleatory data (e.g. frequency data derived from direct experimental observation) and epistemic data (e.g. an assigned probability for an event, based upon published literature or personal experience).

Over the past two decades, a probabilistic approach has been introduced and developed as a framework for the interpretation and evaluation of forensic evidence as it has proved very useful in dealing with the evaluation of findings in the light of two competing propositions or hypotheses. Its use has been seen to be gathering momentum over the past few years[28–31] in for example DNA profiling,[32] individualisation,[33] bioforensics[34] and forensic entomology.[35] This approach has also been applied to the forensic autopsy[36] which, whilst limited to prediction of cause of death from war victims, does illustrate the potential for an expert system to be used as a viable probabilistic tool for cases if appropriate information pertaining to the case was added to the system.

In a forensic context, where the probabilities of two competing propositions (events) need to be considered (e.g. p(Hp) = the toxicology results account for death and p(Hd) = the underlying pathology accounts for death) through conditioning by the findings from an examination (E), and contextual information (I), Bayes theorem can be rearranged where the prior and posterior probabilities for each proposition are ratios, commonly referred to as ‘odds’ and the quotient of the probability of the evidence given the proposition becomes the likelihood ratio;