Interpretation of Morphine Concentrations in Trauma Cases

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Introduction

Many trauma cases have been submitted to our laboratory over the past year. In several of these we detected high morphine concentrations, which led to enquires from pathologists as to why this should be. One such case was that of a young man who died after being admitted to hospital following a road traffic accident. Toxicological analysis of his ante-mortem (AM) blood revealed a morphine concentration of 0.75mg/L.

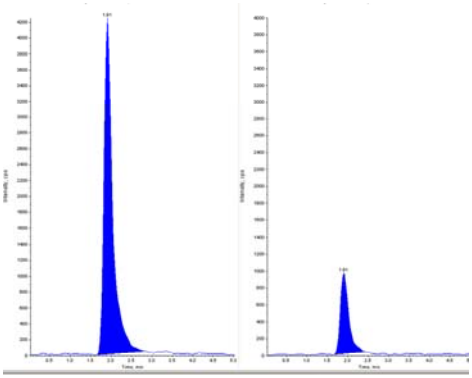

Figure 1: Chromatogram from the case, showing Morphine peak on the right and Internal Standard, Morphine D3, on the left.

Traumatic injury is the leading cause of death among individuals under 40 years of age. [1] Following such an incident, patients may be administered a variety of medications including anaesthetics, analgesics and sedatives. [1] The intravenous administration of morphine is widely accepted as the preferred method of emergency acute pain relief.

International guidelines recommend an initial dose of 0.1mg/kg, followed by a second dose of 0.05mg/kg, depending on Injury Severity Score (ISS) [2] [3]

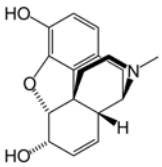

Figure 2: Chemical Structure of Morphine

In post-mortem (PM) toxicological analysis, these cases can often test positive for morphine at concentrations greater than the therapeutic range. At first instance this may appear to be medical negligence or opiate abuse. However, studies have demonstrated that trauma may limit morphine clearance and volume of distribution. [4]

In healthy volunteers the morphine clearance and volume of distribution were found to be 33.5 ± 9mL/kg per minute and 5.16 ± 1.41L/kg respectively, whilst in trauma patients they were much lower at 5.7 ± 2.3mL/kg per minute and 0.16 ± 0.691L/kg. [4]

Patients with burn injuries were found to exhibit similar tendencies, with the half-life of morphine extending to 123 ± 24 minutes, compared to 89 ±18 minutes for control subjects, and the volume of distribution remaining low at 2.2 ± 0.4L/kg. [5]

This is a result of the decrease in serum alpha acid glycoprotein (AAG), which binds basic drugs such as morphine, following acute trauma. [2] Liver function also changes leading to decreased hepatic blood flow which can alter the metabolism of morphine as this drug is metabolised primarily by the liver. [3]

Data from our laboratory, over the period January 2006 to November 2009, was analysed to compare morphine concentrations from trauma cases, known heroin abusers and suspected heroin/morphine overdose cases to determine whether our data supports this premise.

Results

Data was filtered from our database and grouped on the basis of 'trauma' using keywords such as burns, multiple injuries and road traffic collisions. All positive morphine cases falling within these designated causes of death were considered for the purpose of this study. For comparison, cases over the same period that stated suspected heroin/morphine overdose or IV drug abuse were also filtered and grouped as 'other'.

The average concentration of morphine for 39 'trauma' patients was found to be 0.22mg/L. The average for the 64 'other' was 0.40mg/L. These were broken down into AM and PM blood as shown in the graph below. The average morphine levels in PM blood for both 'trauma' and 'other' were similar at 0.28mg/L and 0.31mg/L respectively. This was not the case with the AM samples, however only three samples were available in the 'other' group i.e. most AM samples were derived from trauma cases.

The therapeutic range as set out by TIAFT is 0.01-0.12mg/L, the toxic range is 0.15-0.5mg/L and the fatal range is 0.05-4mg/L. [6]

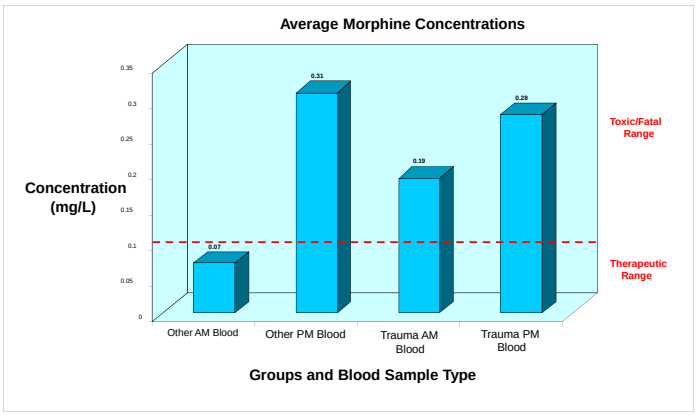

Figure 3: Average concentrations of morphine groups against the therapeutic and toxic ranges.

Conclusions

Based upon toxic morphine concentrations, medical negligence or opiate abuse might be viewed as contributing factors to death in trauma cases. However, as previous studies and our own findings suggest, caution must be applied with interpretation, as elevated concentrations of morphine may be due to the decrease in drug clearance and volume of distribution as well as the extension of its half-life.

The fact that the other studies in clinical laboratories use serum or plasma, whereas our post-mortem toxicological analyses usually involve whole blood should be considered before making direct comparisons between them. However, other factors such as PM distribution or metabolism have been shown to have little effect on morphine levels. [7]

Care should be taken when studying AM concentrations as there is the possibility of blood sampling occurring at the same site as drug administration. Another consideration is the time between death, sampling and analysis of PM samples due to the possibility of hydrolysis of morphine glucuronides. [8]

To make our study more comprehensive, information such as the time between initial administration and sample collection would be needed. It would also be helpful to have paired AM and PM blood samples from each case for comparison purposes, as the majority of our cases involved only one or the other.

References

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