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Short paper / Article court

Deaths related to cocaine consumption: southern spanish experience

Décès liés à la consommation de cocaïne : l'expérience de l'Espagne du sud

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Abstract – Introduction: In the last few years, cocaine has emerged as a major cause of morbidity and mortality in our country. The objective of this study was to get an insight into the presence of cocaine and related compounds in forensic cases received in the Department of Seville of the Spanish National Institute of Toxicology in 2005. **Materials and Methods:** Toxicological analyses were performed in all samples received, following our laboratory normal procedures. Ethanol was analysed by means of headspace GC-FID. Screening of drugs of abuse was performed by means of CEDIA®. Extraction was accomplished by SPE (Bond-Elut, certified) and the extracts were analysed by gas chromatography with NPD and gas chromatography-mass spectrometry (GC-MS). **Results:** Cocaine and its metabolites were detected in 76 of the blood samples analysed and in 119 (61.57%) of the studied cases, only the metabolites were detected. Ethanol and ethylbenzoylecgonine were detected in 12 cases. Cocaine blood concentrations ranged from 0.02–7.24 mg/L. In 41 cases blood cocaine concentration was below 0.1 mg/L, in 25 was between 0.1–0.5 mg/L, in 9 cases between 0.5–1 and in 8 cases over 1 g/L. **Conclusions:** As it has been stated before, it seems that with the exception of massive drug exposure, cocaine-related deaths occur for the major part after prolonged drug use and it is almost impossible to correlate a specific blood concentration to toxicity. However, our results some differences between blood cocaine concentrations in people who died in road accidents and those who died in a different manner.

Key words: Cocaine, drug-related death

Résumé – Introduction : Au cours des dernières années, la cocaïne est devenue une cause importante de pathologies et de mortalité dans notre pays. L'objectif de cette étude était d'obtenir un aperçu du rôle de la cocaïne et de ses dérivés dans les cas de décès enregistrés en 2005 par la division de Séville de l'Institut National de Toxicologie (Espagne). **Matériels et Méthodes :** Des analyses toxicologiques ont été effectuées dans tous les échantillons reçus, suivant les procédures habituelles du laboratoire. L'éthanol a été dosé par HS-GC-FID. Le screening des stupéfiants a été réalisé par immunochimie (procédé CEDIA®). L'extraction a été faite par SPE Bond-Elut (certifié), et les extraits analysés par chromatographie gazeuse avec NPD et chromatographie gazeuse avec spectrométrie de masse (CG-MS). **Résultats :** La cocaïne et ses métabolites ont été détectés dans 76 des échantillons de sang analysés. Dans 119 cas (61.57 %), seuls les métabolites ont été détectés. L'éthanol et l'éthylbenzoylecgonine ont été détectés dans 12 cas. Les concentrations en cocaïne dans le sang se sont échelonnées de 0.02 à 7.24 mg/L. Dans 41 cas elle se situait sous 0.1 mg/L, dans 25 elle était entre 0.1 et 0.5 mg/L, dans 9 cas entre 0.5 et 1, et dans 8 cas elle était de plus de 1 g/L. **Conclusions :** Comme exposé précédemment, il semble qu'excepté dans les cas de surdose massive, les décès liés à la cocaïne surviennent majoritairement après un usage prolongé, et il est presque impossible d'établir une corrélation entre concentration dans le sang et toxicité. Quoi qu'il en soit, cette étude révèle des concentrations de cocaïne dans le sang différentes entre les sujets décédés d'accidents de la route et ceux décédés dans d'autres contextes.

Mots clés : Cocaïne, décès dû à la consommation de stupéfiants

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1 Introduction

According to data released by the European Monitoring Centre for Drugs and Drug Addiction, an increase in cocaine consumption has been recorded in Spain. In the last few years, cocaine has emerged as a major cause of morbidity and mortality, being cocaine consumption one of the issues that arises higher concern in our society. Nowadays, cocaine-related death is a serious and possibly increasing problem in European countries. Despite the limitations of the available

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data, cocaine seems to have played a determinant role in 1–15% of drug-related deaths reported by the European Monitoring Centre for Drugs and Drug Addiction [1].

Except in the case of drug couriers ("body packers") with massive drug exposure, death is not dose related, and cocaine blood levels cannot be used to predict toxicity [2]. Cocaine-related deaths occur for the major part after prolonged drugs use and mere presence of cocaine in fluids or tissues does not prove that death was due to cocaine consumption.

The objective of this study was to get an insight into the presence of cocaine and related compounds in forensic cases received in the Department of Seville of the Spanish National Institute of Toxicology in 2005.

2 Materials and methods

Reactives and solvents used were of analytical grade (Merck, Barcelona, Spain) and analytical standars were purchased from Promochem (Austin, TX, USA). Blood and urine specimens were collected by the coroner and kept in tubes with sodium fluoride as a preservative and calcium oxalate as antioxidative. On their arrival to the laboratory, all specimens were stored at 4 °C until their extraction.

Ethanol was analysed by means of headspace GC-FID, according to the Spanish Official Method for ethanol analysis in blood samples [3].

Screening of cocaine metabolite (benzoylecgonine) was performed by means of homogeneous enzyme immunoassay CEDIA® according to manufacturers' instructions in the case of urine. Blood samples were deproteinized with acetone prior to CEDIA® analysis [4].

All specimens were extracted by means of SPE (Bond-Elut® certified for basic compounds Varian Harbour City, CA, USA), following the normal procedure in our laboratory, which involves the employment of nalorphine as internal standard. Blood and urine samples were sonicated prior to extraction for 10 min and pH was adjusted to 9 with KOH 1N and centrifuged 10 min at 2500 rpm. Supernatant was extracted by means of SPE.

Preliminary analyte identification was performed by means of gas chromatography, using a Varian CP-3800 (Walnut Creek, CA, USA) gas chromatograph fitted with a NPD detector. The column used was a fused-silica Ultra-1 column (200 μ × 0,33 mm × 25 m) coated with methyl siloxane. Carrier gas was helium at a rate of 1.7 mL/min. Injector and detector temperatures were 280 °C and 300 °C respectively. Initial oven temperature was 60 °C, maintained for 2 min, increasing at 12 °C/min to 290 °C staying at this temperature for 10 min. Injection volume was 1 μL.

The presence of cocaine and its metabolites (ethylbenzoylecgonine, benzoylecgonine and methylecgonine) were confirmed and quantitated by GC-MS. Dry residues were heated 20 min at 70 °C with 50 μL of the derivatization reagent, BSTFA (N, O-bis (trimethylsilyl) trifluoroacetamide)) [5]. A Hewlett-Packard (Agilent Technologies, Palo Alto, CA, USA) gas chromatograph Model 5890 II equipped with a MS detector HP 5973 working in electron impact (EI) mode under selected ion monitoring (SIM) conditions. The column used was a fused-silica capillary Ultra 1 column (200 μ × 0,33 mm × 25 m) coated with methyl siloxane. Carrier gas was helium at a rate of 1,7 mL/min. Injector temperature was 280 °C. MS source and MS quadrupole temperatures were 230 and 250 °C respectively. Initial oven temperature was 60 °C, maintained for 3 min, increasing at 12 °C/min to 290 °C staying at this temperature for 10 min. Injection volume was 1 μL.

3 Results

In 2005, 5871 cases were analysed in the Chemistry Service of the Seville Department of the Spanish National Institute of Toxicology. In 3649 cases blood and urine were analysed and in 2231 blood was the only specimen analysed.

In 195 cases, cocaine or any of its metabolites were detected. Our results reflect the preponderance of males (78.60%) among these decedents, being the majority of them between 21 to 50 years old.

In 123 of these cases blood and urine were received. Cocaine was detected in 44 cases in both specimens. In 32 cases, cocaine was detected in blood but not in urine. Due to cocaine detection in blood, we can assume that cocaine detection was done shortly before death. Cocaine detection in blood has been estimated in 12 h [6]. However, when cocaine was not detected in urine we can suggest that probably the deceased took two cocaine doses in a short period of time. Alcohol was detected in a 48.91% of the cases.

Cocaine and its metabolites were detected in 76 of the blood samples analysed, and in 119 (61.57%) of the studied cases, only the metabolites (methylecgonine, benzoylecgonine or ethylbenzoylecgonine) were detected. Benzoylecgonine was the analyte most frequently present in analysed samples. Ethanol and ethylbenzoylecgonine were detected in 12 cases. Cocaine blood concentrations ranged from 0.02–7.24 mg/L (mean concentration 0.38 mg/L and median concentration 0.12 mg/L). In 41 cases blood cocaine concentration was below 0.1 mg/L, in 25 was between 0.1–0.5 mg/L, in 9 cases between 0.5–1 and in 8 cases over 1g/L. Benzoylecgonine blood concentrations ranged from 0.01–140.4 mg/L (mean concentration 6.27 mg/L and median concentration 1.25 mg/L).

32 (16.24%) of the cases studied corresponded to people killed in road accidents. Cocaine was detected in only 10 of these cases, being benzoylecgonine detected in all of them. Cocaine blood concentrations ranged from 0.01–0.27 mg/L (mean concentration 0.06 mg/L and median concentration 0.03 mg/L). Benzoylecgonine blood concentrations ranged from 0.01–38.74 mg/L (mean concentration 2.07 mg/L and median concentration 0.29 mg/L). It is remarkable that in these cases along with cocaine or its metabolites ethanol was detected in 21 cases. In 90.47% of those cases, blood ethanol concentration (BAC) was over 0.5 g/L (legally admitted BAC for car drivers in Spain), in 66.66% of the cases BAC was over 1 g/L and in a 52.38% of the cases over 2 g/L.

4 Discussion and conclusions

The determination that cocaine is directly responsible for the immediate cause of death should be considered only when there is a reasonably complete understanding of the circumstances or facts surrounding the death. Another, more obvious and immediate cause of death must be absent, or, at least cocaine must be shown to be a significant contributing factor in the chain of medical findings that lead directly to the immediate cause of death. Knowledge of the past medical history of the individual, the results of a complete forensic autopsy and toxicological studies and an understanding of the current relevant forensic literature on this subject should be available to the reviewer prior to any interpretation of the significance of cocaine upon a specific death.

Except in the case of massive drug exposure (courier or "body packers"), where acute toxicity is dose-related and is characterized primarily by its sympathomimetic effects (tachycardia, hypertension and hyperthermia) [7], cocaine-related deaths occur for the major part after prolonged drug use [8]. Long term use of cocaine initiates a series of changes at molecular, cellular and tissue levels [9], many of which favour the occurrence of sudden cardiac death.

The interpretation of postmortem blood concentrations is even more complicated than attempts at making such correlations in the living. Only in eight of the cases in which cocaine was detected (299), we found a blood cocaine concentration higher than 1 mg/L. Before the current cocaine pandemic, blood concentrations of more than 5 mg/L were thought to be uniformly fatal. With more experience, it has become apparent that isolated postmortem blood concentrations cannot be used to determine the cause of death. Tolerance on a massive scale occurs, and concentrations well in excess of 5 mg/L can be encountered in cases of trauma death where the presence of cocaine is clearly an unrelated finding [8, 10].

The literature offers considerable toxicological data about cocaine-related deaths, and it is clear that correlation of a specific blood or tissue concentration with toxicity is not generally possible. For some authors, establishing the presence of cocaine in the blood, in the absence of other findings, may signify death by cocaine poisoning. Due to the fact that acute cardiac effects of cocaine are independent of the cocaine concentration in the blood, the presence of cocaine in the blood, in the absence of other findings, can allow a death to be certified as resulting from cocaine intoxication. However, others would undoubtedly insist that isolated cocaine levels couldn't be used to explain the cause of death. In fact the presence of low levels of cocaine are proof only of cocaine use, if the appropriate anatomical or histological changes are present, cocaine may be the cause of death even if it is not detectable in the blood. Benzoylecgonine presence in analyzed samples can establish only cocaine consumption prior to death [10–14].

One factor that potentially increases the risk of toxicity in drug abusers is the concomitant use of ethanol. Ethanol was detected in a nearly half of the studied cases (48.91%). These findings suggest that the concomitant use of cocaine and ethanol is widespread among population studied. Cocaine-alcohol produced greater euphoria and increased perception of well-being relative to cocaine. Heart rate significantly increased following cocaine-alcohol administration relative to either drug alone.

32 of the studied cases corresponded to people killed in road accidents. In these cases blood cocaine concentration is clearly lower than cocaine concentrations found in cases were death is not due to an accident, whereas, blood ethanol concentrations (BAC) were above 0.5 g/L in 29 cases. BAC was higher than 1 g/L in 19 cases and was above 2 g/L in 10 cases.

Therefore, it seems reasonably to think that cocaine consumption was done between 12 and 24 h prior to the accident, whereas alcohol was consumed at least 6 h before it [6, 15]. Ethylbenzoylecgonine was detected in only one of these cases. This fact points out that cocaine and ethanol consumption was not done simultaneously. However, it is important to underline that the effects of cocaine on performance persist once the period of acute stimulation had passed. Cocaine is particularly dangerous for road traffic because of the discrepancy between the subjective feeling of increased performance on the one hand and the actual fitness which objectively has not increased to the same extent on the other hand [16].

As it has been stated before, it seems that with the exception of massive drug exposure, cocaine-related deaths occur for the major part after prolonged drug use and it is almost impossible to correlate a specific blood concentration to toxicity. However, our results show some differences between blood cocaine concentrations in people who died in road accidents and those who died in a different manner.

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