

HIGH-RISK DRUG USE: EPIDEMIOLOGICAL PATTERN THROUGH HAIR TESTING IN THE FORENSIC CONTEXT

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ABSTRACT

Background: The basic sources of information on drug use are epidemiological surveys, although they have some limitations: their results may be conditioned by the lack of veracity of the responses and the sampling method makes it difficult to detect low-prevalence behaviours in target populations. This study aimed to establish the epidemiological pattern of drug use in the population undergoing drug testing in hair, in the framework of judicial investigations, in order to provide an additional approach to the knowledge of high-risk drug use.

Methods: A cross-sectional study on drug use was conducted on the population subjected to drug testing in hair (N=5,292) in the forensic context. Prevalence of cannabis, cocaine, heroin, ketamine, amphetamine (AP), methamphetamine (MA), 3,4-methylenedioxy-methamphetamine (MDMA), 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxy-N-ethylamphetamine (MDEA) and methadone uses were obtained. Association between drug use and demographics, and trends of prevalence over the period were analysed using the Pearson Chi-square test. Frequency distribution of drug concentrations in hair was obtained and it was assessed in relation to gender and age using the non-parametric Mann-Whitney U and Kruskal-Wallis H methods.

Results: During the period 2013-2015, prevalence of cocaine use was particularly high (49%), rating second among the population studied, after cannabis use (54%). Proportions of heroin, methadone, MDMA and amphetamine use ranged from 10% to 18%. There was a significant increase in prevalence of MDMA, heroin and amphetamine use during the period 2013-2015, as well as a significant decrease in methadone use. The rates of cannabis, cocaine and MDMA use were higher in men, whereas methadone use was higher among women.

Conclusions: Cannabis and cocaine are the most frequently abused drugs among the population undergoing drug testing in hair in the framework of judicial investigations over the three-year period, although the proportions of heroin, MDMA and amphetamine users show an increasing trend. Drug use patterns vary according to age and sex, with a decrease in cannabis and MDMA use and an increase in heroin and methadone use as age increased; cannabis, cocaine and MDMA use are more prevalent among men and methadone use among women.

Key words: Drug use, Hair testing, Drug testing, Epidemiology.

RESUMEN

Drogas y consumo de alto riesgo: patrón epidemiológico a partir de análisis de cabello en el contexto forense

Fundamentos: Las encuestas epidemiológicas son las fuentes básicas de información sobre el consumo de drogas, aunque presentan algunas limitaciones en este campo: sus resultados pueden verse condicionados por la falta de veracidad de las respuestas y el método de muestreo dificulta la detección de comportamientos de baja prevalencia en las poblaciones diana. El objetivo de esta investigación fue establecer el patrón epidemiológico del consumo de drogas en la población sometida a análisis de drogas en cabello en el marco de investigaciones judiciales, con el fin de aportar una fuente de información adicional al conocimiento del consumo de drogas de alto riesgo.

Métodos: Se realizó un estudio transversal de consumo de drogas en la población sometida a análisis de drogas en cabello en el contexto forense (N=5.292). Se obtuvo la prevalencia de consumo de cannabis, cocaína, heroína, ketamina, anfetamina (AP), metanfetamina (MA), 3,4-metilendioxi-metanfetamina (MDMA), 3,4-metilendioxi-anfetamina (MDA), 3,4-metilendioxi-N-etilamfetamina (MDEA) y metadona. Se analizó la asociación entre el consumo de drogas y los factores demográficos, así como de sus tendencias, mediante la prueba de Chi-cuadrado de Pearson. Se obtuvo la distribución de frecuencias de las concentraciones de drogas en cabello y se evaluó en relación con el sexo y la edad, utilizando los métodos no paramétricos U de Mann-Whitney y H de Kruskal-Wallis.

Resultados: En el periodo 2013-2015, la prevalencia de consumo de cocaína fue particularmente elevada (49%) en la población estudiada, próxima a la de cannabis (54%). Las tasas de consumo de heroína, metadona, MDMA y anfetamina resultaron entre un 10% y un 18%. Durante el periodo estudiado, se registró un aumento significativo del consumo de MDMA, heroína y anfetamina, así como una disminución significativa del consumo de metadona.

Conclusiones: Cannabis y cocaína son las drogas de abuso más frecuentes entre la población sometida a análisis de drogas en cabello en el marco de investigaciones judiciales en el periodo estudiado, si bien las proporciones de consumidores de heroína, MDMA y anfetamina muestran una tendencia creciente. Los patrones de consumo varían en función de la edad y del sexo, observándose disminución del consumo de cannabis y MDMA e incremento del consumo de heroína y metadona al aumentar la edad. El consumo de cannabis, cocaína y MDMA resulta más prevalente en hombres y el de metadona en mujeres.

Palabras clave: Consumo de drogas, Análisis de cabello, Análisis de drogas, Epidemiología.

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INTRODUCTION

The basic source of information on drug use -in Spain, Europe and worldwide- consists of epidemiological surveys carried out in general population or at school level. Performing drug testing on biological samples in addition to general surveys on drug use detects higher drug use than using only one of these methods^(1,2); however, this approach is not feasible in routine survey practice.

On the other hand, the study of chronic drug use through hair analysis has become a routine procedure in forensic toxicology, mainly due to the wider detection window in hair -from weeks to years- compared to traditional biological samples (blood, urine), which allows the retrospective investigation of drug use⁽³⁾.

Analysis of drug use data from forensic context has great relevance to improve the interpretation of results and it reveals patterns of high-risk drug use (HRDU)-defined by the European Monitoring Centre for Drugs and Drug Addiction as *the use of psychoactive substances (excluding alcohol, tobacco and caffeine) by high-risk pattern (e.g. intensively) and/or by high-risk routes of administration in the last 12 months*⁽⁴⁾. From an operational point of view, it is considered that any drug user who has come into contact with the legal system has indeed a problem with their consumption pattern and is therefore a problematic⁽⁵⁾ or high-risk user.

The Drug Unit of the Madrid Department of the National Institute of Toxicology and Forensic Sciences (INTCF, Spain) analyses about 1,800 hair specimens per year, on judicial request in order to prove or dismiss a prior history of chronic drug use (cannabis, cocaine, heroin, methadone, amphetamine derivatives and ketamine), mostly in relation to delimitation of criminal liability and reduction of applicable penalties in certain cases, due to evidence

of detoxification and/or treatment of drug dependence.

This study overviews the drug tests performed on head hair samples at the mentioned Drug Unit in the period 2013-2015, with the aim of deepening the knowledge of the epidemiological patterns of high-risk drug use within the framework of judicial investigations.

SUBJECTS AND METHODS

Study design. This work is a cross-sectional study on chronic drug use in the forensic context, proven through hair testing. Tests were performed by the Drug Unit of the Madrid Department of the National Institute of Toxicology and Forensic Sciences (INTCF, Spain) -whose territorial scope comprises 9 regions and more than 19 million inhabitants-, during the period 2013-2015.

Subjects. A total of 5,292 hair specimens, consisting of proximal head hair segments, from individuals involved in judicial proceedings were included in this study.

In order to ensure the protection of personal data, the study was conducted on a database without information on the identity of individuals. For this reason, some cases of repetition of individuals are possible, due to the fact that during the period of three years more than one hair analysis was carried out on the same person, either because of their contact with Justice more than once or because of their periodic control to prove their detoxification and/or treatment of drug dependence, by court order. These circumstances represented in any case a small percentage in relation to the total number of hair samples analysed and therefore did not generate a relevant bias in the results.

Segmentation of head hair samples was performed depending on the requested covering

periods and the total hair length. In the absence of a specific request, the hair was not segmented if its length was less than 6.5 cm (77% of total specimens) and the proximal 6-cm-long segment was analysed otherwise. The most common lengths were 6–6.5 cm (25%), 3–3.5 cm (21%), 2–2.5 cm (19%) and 4–4.5 cm (15%).

Drugs tested. Hair tests were carried out to investigate use of cannabis, cocaine, heroin, methadone, ketamine, amphetamine (AP), methamphetamine (MA), 3,4-methylenedioxy amphetamine (MDA), 3,4-methylenedioxymethamphetamine (MDMA) and 3,4-methylenedioxyethylamphetamine (MDEA).

The tested substances were classified into three analytical profiles:

i) Cannabinoids Profile (N=4,631): Δ^9 -tetrahydrocannabinol (THC) and cannabinol (CBN).

ii) Coca-Opi-Mtd-Ket Profile (N=4,951):

– Cocaine and metabolites: methylecgonine, benzoylecgonine (BZE) and ethylbenzoylecgonine (generated when cocaine and ethyl alcohol are taken together).

– Opiates: heroin, 6-monacetylmorphine (MAM), morphine and codeine.

– Methadone.

– Ketamine and its metabolite norketamine.

iii) Amphetamines Profile (N = 4,334): AP, MA, MDA, MDMA and MDEA.

The three profiles were tested in 4,232 specimens.

Testing procedures and interpretation criteria. In all cases the analytical procedure involved

previous washing of hair with dichloromethane and detection, identification and quantification of drugs by gas chromatography-mass spectrometry using selected ion monitoring mode (GC-MS/EI), except for CBN, whose determination was only qualitative. For the Coca-Opi-Mtd-Ket profile, the method, based on previously published ones with some modifications^(6,7,8), consisted of incubation in methanol at 60 °C for 24 h in the presence of the internal deuterated standard (cocaine-d3), sonication in an ultrasonic bath and derivatisation with pentafluoropropionic anhydride (PFPA) and hexafluoroisopropanol (HFIP). The procedure for the other profiles included alkaline digestion of hair at 95 °C during 10 min, in the presence of internal standards (AP-d5, MDMA-d5 and THC-d3), liquid-liquid extraction of cannabinoids, solid-phase extraction and derivatisation of amphetamines with PFPA⁽⁹⁾.

Test results were interpreted taking into account the confirmation cut-offs proposed by the Society of Hair Testing (SoHT) to identify chronic drug use⁽¹⁰⁾, as well as detection and quantification limits of the analytical techniques. Thus, the following criteria were applied to confirm a positive case of chronic use:

i) Cannabis: THC \geq 0.05 ng/mg and identification of CBN

ii) Cocaine: cocaine \geq 0.50 and BZE \geq 0.05 ng/mg.

iii) Heroin: MAM and morphine, both \geq 0.20 ng/mg.

iv) Methadone: \geq 0.50 ng/mg.

v) Ketamine: ketamine \geq 0.50 and norketamine \geq 0.10 ng/mg.

vi) Amphetamine and related compounds: \geq 0.20 ng/mg of hair.

Negative results did not rule out sporadic use of the drugs tested in the time period studied.

Statistical análisis. The distribution by sex and age of the sample studied was obtained, expressing the results in frequency (N) and percentage (%).

For each substance studied, based on the qualitative results (positive vs. negative), the following analysis was performed:

i) Obtaining descriptive statistics for each year and for the whole period 2013-2015: total proportion of users and proportions of users by age and sex.

ii) Comparison of proportions of users in relation to year, age and sex by means of the Chi-square Pearson test. In cases where this test could not be applied because the expected frequency of a group was less than 5, this group was excluded from statistical analysis (e.g. samples of underage individuals, in the association between consumption and age). Given the large sample size (N=5,292), the Pearson Chi-square test was preferred over the Fisher exact test to adopt a more conservative approach in groups with small numbers of specimens.

Based on the quantitative results for THC, cocaine, MAM, methadone, AP and MDMA in the positive hair samples, the following operations were performed:

i) Obtaining frequency distribution of the concentration levels (ng analyte/mg hair). These distributions did not meet the normality criteria, but they were generally more pointed than the Gaussian distribution and showed positive asymmetry (the lowest values are the most frequent).

ii) Obtaining descriptive statistics: Median (Md) and 25th and 75th percentiles.

iii) Comparison of distributions by year, sex and age using non-parametric methods that do not require compliance with normality criteria: Mann-Whitney U for variables with two categories and Kruskal-Wallis H for variables with more than two categories.

The statistical analysis was carried out with IBM SPSS Statistics 21 software, using a 5% significance level.

RESULTS

Sex and age distribution of the population studied is shown in **table 1**. More than 88% of the specimens were taken from men. For both sexes, both age mean and age median were 35 years old and the age groups between 25 and 44 years old had the highest number of cases.

Qualitative results. Cannabis was the most widely used drug, with an average proportion of drug users of 54% in the period 2013-2015 (**table 2**). The prevalence of cocaine use was above 49%. Amphetamine and MDMA showed much lower values, 17% and 14%, respectively. Heroin and methadone presented similar proportions of users, reaching 10% and 11% respectively. Ketamine and methamphetamine showed less than 1% prevalence rates, MDA consumption did not reach 0.1%, and no cases of MDEA use were detected.

MDMA, heroin and amphetamine showed significant increases of use between 2013 and 2015, with relative increases of prevalence, respectively, of 48.6% ($p=0.0001$), 26.3% ($p=0.036$) and 18.4% ($p=0.008$) (**figure 1**). Methadone showed a relative decrease of 25.3% ($p=0.013$), whereas the increase of cannabis and cocaine use and the decrease of ketamine and methamphetamine use were not significant.

Table 1
Demographics of the study population, distribution by year and total.

| Sex | Age range (years) | 2013 | | | 2014 | | | 2015 | | | TOTAL | | |
|-------------------------------|-------------------|-------|-------|-------------|-------|-------|-------------|-------|-------|-------------|-------|-------|-------------|
| | | N | % | Age (years) |
| Men | <15 | 0 | 0.001 | 34.88 | 1 | 0.06 | 35.08 | 2 | 0.14 | 35.59 | 3 | 0.06 | 35.16 |
| | 15-24 | 204 | 12.30 | | 158 | 10.08 | | 152 | 10.53 | | 514 | 11.01 | |
| | 25-34 | 398 | 24.00 | | 383 | 24.44 | | 318 | 22.04 | | 1,099 | 23.54 | |
| | 35-44 | 428 | 25.81 | | 396 | 25.27 | | 350 | 24.26 | | 1,174 | 25.15 | |
| | 45-54 | 168 | 10.13 | | 152 | 9.70 | | 157 | 10.88 | | 477 | 10.22 | |
| | 55-64 | 25 | 1.51 | | 23 | 1.47 | | 32 | 2.22 | | 80 | 1.71 | |
| | >64 | 1 | 0.06 | | 2 | 0.13 | | 2 | 0.14 | | 5 | 0.11 | |
| Subtotal Age known | | 1,224 | 73.82 | | 1,115 | 71.16 | | 1,013 | 70.20 | | 3,352 | 71.81 | |
| St. Dev. | | - | - | 9.36 | - | - | 9.17 | - | - | 9.88 | - | - | 9.46 |
| Median | | - | - | 35 | - | - | 35 | - | - | 35 | - | - | 35 |
| Age unknown | | 434 | 26.18 | - | 452 | 28.84 | - | 430 | 29.80 | - | 1316 | 28.19 | - |
| Subtotal men | | 1,658 | 100 | - | 1,567 | 100 | - | 1,443 | 100 | - | 4,668 | 100 | - |
| Men % | | - | 89.86 | - | - | 87.93 | - | - | 86.67 | - | - | 88.21 | - |
| Women | <15 | 1 | 0.56 | 35.37 | | 0.00 | 35.85 | 4 | 2.04 | 35.58 | 5 | 0.86 | 35.60 |
| | 15-24 | 16 | 8.94 | | 15 | 7.25 | | 15 | 7.65 | | 46 | 7.90 | |
| | 25-34 | 53 | 29.61 | | 51 | 24.64 | | 48 | 24.49 | | 152 | 26.12 | |
| | 35-44 | 45 | 25.14 | | 49 | 23.67 | | 47 | 23.98 | | 141 | 24.23 | |
| | 45-54 | 22 | 12.29 | | 20 | 9.66 | | 22 | 11.22 | | 64 | 11 | |
| | 55-64 | 2 | 1.12 | | 4 | 1.93 | | 7 | 3.57 | | 13 | 2.23 | |
| | >64 | | 0.001 | | 1 | 0.48 | | - | 0.001 | | 1 | 0.17 | |
| Subtotal edad conocida | | 139 | 77.65 | | 140 | 67.63 | | 143 | 72.96 | | 422 | 72.51 | |
| St. Dev. | | - | - | 9.66 | - | - | 9.54 | - | - | 10.67 | - | - | 9.95 |
| Median | | - | - | 34 | - | - | 35 | - | - | 36 | - | - | 35 |
| Age unknown | | 40 | 22.35 | - | 67 | 32.37 | - | 53 | 27.04 | - | 160 | 27.49 | - |
| Subtotal women | | 179 | 100 | - | 207 | 100 | - | 196 | 100 | - | 582 | 100 | - |
| Women % | | - | 9.70 | - | - | 11.62 | - | - | 11.77 | - | - | 11 | - |
| Sex unknown | 25-34 | - | - | - | 1 | 12.50 | 40.50 | - | - | 39 | 1 | 2.38 | 39.75 |
| | 35-44 | - | - | | - | - | | 2 | 7.69 | | 2 | 4.76 | |
| | 45-54 | - | - | | 1 | 12.50 | | - | - | | 1 | 2.38 | |
| Subtotal age known | | 0 | 0.001 | | 2 | 25 | | 2 | 7.69 | | 4 | 9.52 | |
| St. Dev. | | - | - | - | - | - | 19.09 | - | - | - | - | - | 11.06 |
| Median | | - | - | - | - | - | 40.50 | - | - | 39 | - | - | 39 |
| Age unknown | | 8 | 100 | - | 6 | 75 | - | 24 | 92.31 | - | 38 | 90.48 | - |
| Subtotal sex unknown | | 8 | 100 | - | 8 | 100 | - | 26 | 100 | - | 42 | 100 | - |
| % Sex unknown | | - | 0.43 | - | - | 0.45 | - | - | 1.56 | - | - | 0.79 | - |
| Total | | 1,845 | - | - | 1,782 | - | - | 1,665 | - | - | 5,292 | - | - |

Table 2
Positive cases: distribution of drug concentration in hair (ng/mg)
in the whole period 2013-2015.

| Analyte | Concentration (ng/mg) | | | Positive samples (N) | Total tested samples | Positive samples (%) |
|-------------------------|-----------------------------|----------------------------------|-----------------------------|----------------------|----------------------|----------------------|
| | 25 th Percentile | Md (50 th Percentile) | 75 th Percentile | | | |
| THC | 0.20 | 0.63 | 2.01 | 2,499 | 4,631 | 53.96 |
| Cocaine | 3.53 | 10.94 | 35.72 | 2,436 | 4,951 | 49.20 |
| MAM (Heroin metabolite) | 1.13 | 4.02 | 14.52 | 491 | | 9.92 |
| Methadone | 5.42 | 9.43 | 16.47 | 553 | | 11.17 |
| Ketamine | 7.41 | 18.84 | 34.05 | 35 | | 0.71 |
| AP | 0.50 | 1.68 | 9.74 | 761 | | 17.56 |
| MA | 0.27 | 0.91 | 7.48 | 18 | 4,334 | 0.42 |
| MDMA | 0.57 | 1.82 | 4.52 | 598 | | 13.80 |
| MDA | 0.26 | 1.62 | - | 3 | | 0.07 |
| MDEA | - | - | - | 0 | | 0.001 |

Considering the whole period 2013-2015, it was found higher proportion of cannabis ($p=0.024$), cocaine ($p=0.002$), and MDMA ($p=0.007$) users among men, higher proportion of methadone users among women ($p=0.0001$) and non-significant differences in heroin and amphetamine use in relation to sex (figure 2).

Considering age and sex together, four different consumption patterns were observed:

i) Cannabis and MDMA showed the highest proportion of users in the youngest age group (aged 15-24) and a continued decrease in that ratio as age increased (figure 3.1). In relation to age, the differences in consumption were significant in men for both drugs ($p=0.0001$) between the 15-64 age groups, but there were no significant differences in women.

ii) Heroin and methadone showed a progressive increase in the proportion of users as age increased, reaching a peak in the 45-54 age

group (figure 3.2). Differences in the proportions of users in relation to age were significant for both substances in men between the 15-64 age groups ($p=0.0001$) and in women between the 15-54 age groups (heroin: $p=0.007$; methadone: $p=0.002$).

iii) Cocaine showed differences in the proportion of users among the age groups 15 to 64 years old in both sexes (men: $p=0.011$; women: $p=0.027$). The differences were higher among women, who showed the highest proportion of users at an earlier age than men (figure 3.3).

iv) Amphetamine did not show significant differences in relation to age, neither in men nor in women (figure 3.3).

Quantitative results. The differences between drug concentration values obtained from different populations and years require each laboratory to carry out its own statistical studies in order to interpret the quantitative results, so that

Figure 1
Prevalence of drug use among the studied population: evolution 2013-2015
(proportion of positive cases among analysed cases).

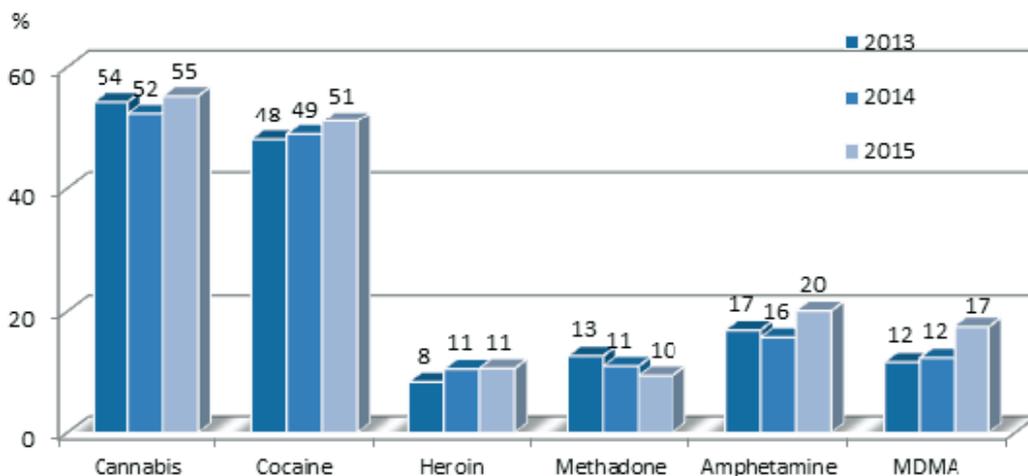


Figure 2
Prevalence of drug use among the studied population by sex, whole period 2013-2015
(proportion of positive cases among analysed cases).

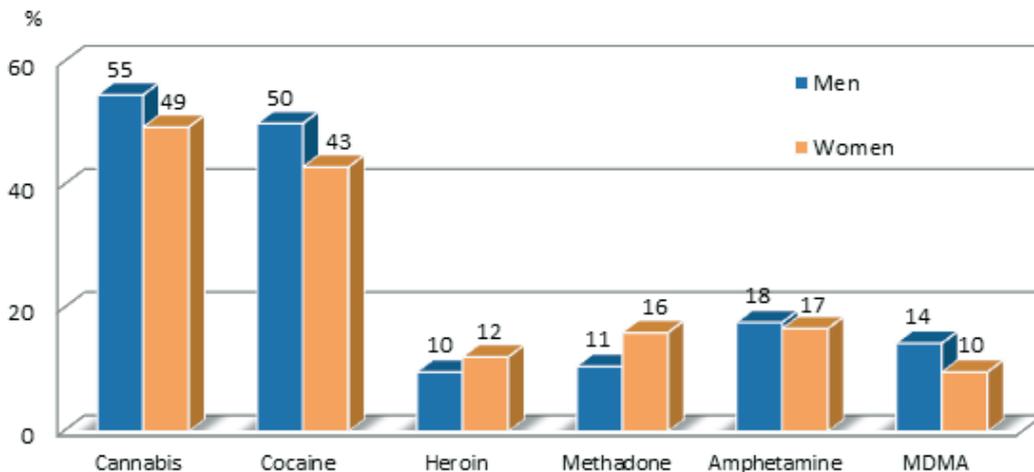
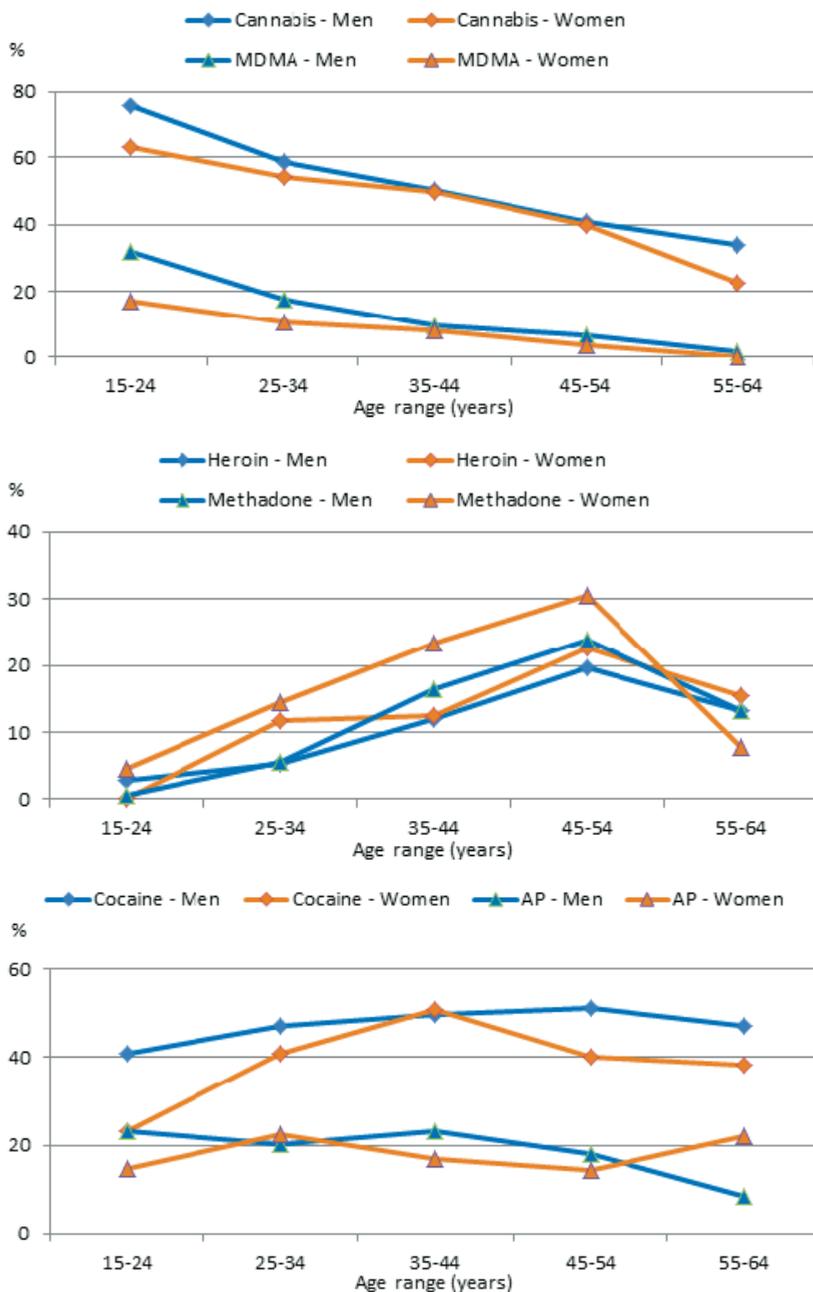


Figure 3
Prevalence of drug use by sex and age, whole period 2013-2015 (proportion of positive cases among analysed cases). From top to bottom: 3.1. Cannabis and MDMA, 3.2. Heroin and methadone, 3.3. Cocaine and amphetamine.



analyte concentration ranges could be established from the statistical distribution as follows:

- i) Low range: concentration lower than 25th percentile
- ii) Mid-range: concentration between 25th and 75th percentiles
- iii) High range: concentration higher than 75th percentile

Table 2 shows the 25th and 75th percentiles that delimit these ranges for substances with the highest prevalence of consumption, as well as the corresponding median values. Significant differences between distributions of drug concentration in hair over the period studied were only observed for THC and MAM.

THC concentration increased between 2013 (Md=0.51 ng/mg) and 2014 (Md=0.72 ng/mg) ($p=0.007$). Higher concentration of THC was observed in men (Md=0.68 ng/mg) than in women (Md=0.36 ng/mg) ($p=0.0001$). As age increased, THC concentrations in hair progressively decreased in men ($p=0.003$), while in women the differences were not significant (**table 3**).

A higher concentration of cocaine was observed in men (Md=11.48 ng/mg) than in women (Md=7.41 ng/mg) ($p=0.002$). In relation to age, there were significant differences in the distribution of cocaine concentration in hair in men ($p=0.0001$). The lowest cocaine levels were found in the youngest group, while the highest levels were found in the 25-44 age groups. Among women, there were no significant differences related to age (**table 3**).

In relation to heroin use, MAM concentration in hair was lower in 2013 (2013: Md=2.49 ng/mg; 2014: Md=4.18 ng/mg; 2015: Md=3.35 ng/mg) ($p=0.040$). The MAM concentration

distributions showed no significant differences related to sex nor age (**table 3**).

The frequency distribution of methadone concentration in hair was very different from the rest of the substances studied. It was a very homogeneous distribution in all concentration ranges, instead of an asymmetric distribution with the highest proportions at the lowest values. The concentration of methadone in hair showed no significant differences related to sex nor age (**table 3**).

The distribution of quantitative values of amphetamine did not show differences by sex, while in relation to age there were significant differences in men between the age groups from 15 to 65 years old ($p=0.0001$). The highest value of Md resulted in the 45-54 year old age group (4.06 ng/mg). Among MDMA users, there were no significant differences in the distribution of MDMA concentration in hair according to sex or age (**table 3**).

DISCUSSION

In the period 2013-2015, cannabis and cocaine are the most commonly used drugs among the population subjected to hair testing for drugs in the context of judicial proceedings, although the proportions of users of heroin, MDMA and amphetamine show a growing trend. Consumption patterns vary according to age and sex. As age increases, both cannabis use and MDMA use decrease, while heroin use and methadone use increase. The use of cannabis, cocaine and MDMA are more frequent among men and methadone use is more common among women.

In relation to quantitative results of psychoactive substance concentration in hair, an increase of THC and MAM concentration is observed during the study period. The highest concentration of THC is found among the youngest men

Table 3
Positive cases: distribution of drug or metabolite concentration in hair (ng/mg)
by sex and age range, whole period 2013-2015.

| Analyte | Age range (years) | Concentration (ng/mg) | | | | | | Muestras positivas (N) | | p (comparison by age) | |
|-------------------------|-------------------|-----------------------------|-------|--------------------------------------|-------|-----------------------------|-------|------------------------|-------|-----------------------|-------|
| | | 25 th Percentile | | Median (50 th Percentile) | | 75 th Percentile | | | | | |
| | | Men | Women | Men | Women | Men | Women | Men | Women | Men | Women |
| THC | 15-24 | 0.32 | 0.20 | 0.90 | 0.38 | 2.76 | 2.23 | 363 | 27 | 0.003 | 0.788 |
| | 25-34 | 0.22 | 0.14 | 0.73 | 0.33 | 2.16 | 0.88 | 567 | 75 | | |
| | 35-44 | 0.18 | 0.16 | 0.60 | 0.44 | 1.88 | 1.12 | 514 | 63 | | |
| | 45-54 | 0.16 | 0.13 | 0.57 | 0.45 | 2.40 | 2.74 | 164 | 23 | | |
| | 55-64 | 0.22 | - | 0.53 | - | 1.55 | - | 22 | - | | |
| Cocaine | 15-24 | 2.77 | 1.62 | 5.94 | 4.43 | 15.04 | 12.37 | 187 | 10 | 0.0001 | 0.676 |
| | 25-34 | 4.10 | 2.68 | 12.80 | 6.68 | 31.30 | 19.34 | 479 | 60 | | |
| | 35-44 | 3.81 | 3.21 | 12.37 | 8.89 | 37.53 | 31.17 | 555 | 70 | | |
| | 45-54 | 4.32 | 2.61 | 11.38 | 11.30 | 45.39 | 20.72 | 232 | 25 | | |
| | 55-64 | 3.39 | 3.58 | 9.11 | 6.50 | 38.81 | 58.50 | 36 | 5 | | |
| MAM (Heroin metabolite) | 15-24 | 0.88 | - | 2.98 | - | 13.59 | - | 13 | 1 | 0.741 | 0.265 |
| | 25-34 | 1.29 | 0.77 | 3.30 | 3.20 | 9.22 | 5.55 | 54 | 17 | | |
| | 35-44 | 1.30 | 1.22 | 3.26 | 8.55 | 10.49 | 34.81 | 133 | 17 | | |
| | 45-54 | 1.41 | 0.78 | 3.83 | 3.05 | 14.42 | 13.84 | 89 | 14 | | |
| | 55-64 | 1.94 | 0.20 | 4.17 | 1.83 | 47.44 | - | 10 | 2 | | |
| Methadone | 15-24 | 2.49 | 2.60 | 17.63 | 3.07 | - | - | 3 | 2 | 0.763 | 0.273 |
| | 25-34 | 6.68 | 3.47 | 9.62 | 7.05 | 16.09 | 14.08 | 57 | 21 | | |
| | 35-44 | 5.60 | 4.42 | 10.31 | 11.14 | 15.83 | 16.99 | 183 | 32 | | |
| | 45-54 | 4.70 | 5.98 | 8.39 | 9.60 | 14.60 | 18.69 | 107 | 19 | | |
| | 55-64 | 1.63 | 7.25 | 10.54 | 7.25 | 19.90 | 7.25 | 10 | 1 | | |
| Ketamine | | 7.32 | 0.21 | 19.20 | 4.87 | 34.24 | - | 33 | 2 | - | - |
| AP | 15-24 | 0.43 | 0.52 | 0.98 | 2.14 | 3.23 | 17.14 | 99 | 7 | 0.0001 | 0.306 |
| | 25-34 | 0.49 | 0.57 | 2.51 | 1.45 | 14.35 | 3.49 | 192 | 29 | | |
| | 35-44 | 0.59 | 0.69 | 2.28 | 8.23 | 9.84 | >20 | 232 | 21 | | |
| | 45-54 | 0.61 | 0.75 | 4.06 | 6.35 | >20 | 11.13 | 67 | 8 | | |
| | 55-64 | 0.24 | 5.71 | 0.31 | >20 | 0.84 | | 5 | 2 | | |
| MA | | 0.28 | 0.20 | 0.91 | >20 | 5.44 | - | 16 | 2 | - | - |
| MDMA | 15-24 | 0.75 | 0.50 | 2.12 | 0.74 | 4.30 | 4.35 | 133 | 7 | 0.222 | 0.727 |
| | 25-34 | 0.58 | 0.36 | 1.77 | 0.58 | 4.54 | 6.70 | 158 | 14 | | |
| | 35-44 | 0.50 | 0.53 | 1.17 | 2.20 | 3.11 | 4.50 | 95 | 10 | | |
| | 45-54 | 0.68 | 2.47 | 1.45 | 3.87 | 6.68 | - | 25 | 2 | | |
| | 55-64 | 1.20 | - | 1.20 | - | 1.20 | - | 1 | - | | |
| MDA | - | 0.26 | 0.26 | 1.62 | - | - | - | 2 | 1 | - | - |

(15-24 years) and the highest concentration of cocaine among men aged 25-44 years.

Studies of drug use in specific populations based on medical examinations, diagnostic tests, admissions to treatment and hospital emergency departments for the use of psychoactive substances^(11,12), infections in drug users⁽¹³⁾, and drug-related mortality⁽¹⁴⁾, do not allow generally the direct estimation of prevalence in the general population, due to methodological limitations derived from the lack of randomization of sampling. However, these studies reveal very useful information for planning and providing services of health promotion, and disease prevention and treatment.

Data from health systems and official registries have the added advantage of avoiding bias due to untruthfulness of respondents. Different studies have shown the tendency of respondents not to recognize the use of certain drugs, such as heroin or cocaine, and, as a result, prevalence estimates may underestimate such use, especially in case of recent use^(15,16,17,18,19,20,21).

Just as the use of health systems by drug users is a common source of epidemiological data, this study raises the importance of using the contact between drug users and legal systems as a valuable source of information, given that data provided by drug testing on biological samples for legal purposes represent objective information on high-risk drug use that is not otherwise easily accessible.

In the period 2013-2015, the prevalence of drug use among the population subjected to hair testing for drugs in the context of judicial proceedings within the territorial scope of Madrid Department of the INTCF, is 8 to 100 times higher, depending on the substance, than the prevalence in general Spanish population, estimated from surveys⁽²²⁾.

Except for heroin, all drugs tested in hair show also higher prevalence of use in the group under study than among inmates in prison in the 30-day period before incarceration, also estimated from surveys^(23,24). These differences can be justified to some extent by the differences in sampling methods and in the methods used to prove drug use. In relation to this last aspect, the differences between the analytical tests and the responses to surveys -mainly due to the lack of veracity in the answers- have already been mentioned. Regarding sampling methods, the surveyed sample of 5,024 inmates is randomly selected among a total of 50,671 inmates, proportionally to the penitentiary centre and nationality, and in an appropriate manner by gender, overrepresenting women. In the study of drug testing in hair, sampling is not at random, but all 5,292 specimens whose proximal area was tested for drugs in the period under consideration are included in the study. In most of the studied cases, the interest of the analysis is focused on the assessment of the liability of the accused, given that positive results in the drug test in hair contribute to the demonstration of mitigating circumstances for criminal responsibility related to drug addiction, in accordance with the Criminal Code in force in Spain. As a result, the analysis of drugs in the hair - which is mostly requested by the defense of the accused - shows high percentages of positive cases.

The prevalence of cocaine use is particularly high (49%) among the population subjected to hair testing for drugs in the forensic context, and close to that of cannabis (54%), the most commonly used drug among the 10 substances tested. Although the populations are not comparable, the similarity of prevalence for both drugs contrasts with the general population, where cannabis use (6.6% during the last 30 days, in 2013) exceeded more than six times that of cocaine (1%)⁽²²⁾.

The proportion of cannabis users in the analysed sample is 16% higher than that found in the 2016 Prisons Survey (37.8% of inmates had used cannabis within 30 days before the admission⁽²⁴⁾), being cannabis also the most used drug among the inmates. Data from the 2011 Prisons Survey had been slightly higher: the 39.8% had used cannabis in the past 30 days of freedom⁽²³⁾.

The prevalence of cocaine use in analysed sample in the period 2013-2015 is 17% higher than that obtained in the prison population in 2016 (31.8% of the inmates had used cocaine in the 30 days prior to admission to the institution, 24.8% as powder and 16.2% as cocaine base)⁽²⁴⁾. The results obtained in the 2011 Prisons Survey were higher for powder cocaine (27.4%) and lower for cocaine base (18.5%)⁽²³⁾.

Prevalence of amphetamine use in the studied sample was higher than 17%, more than three times the prevalence of amphetamines use (PA and/or MA) among the Spanish prison population in 2016 (4.9% in the last 30 days before entry into prison)⁽²⁴⁾, and in 2011 (4.6%)⁽²³⁾. Between the two substances, amphetamine has always been the most common substance in Europe in general and in Spain in particular, so that the information provided by official statistics and reports in relation to amphetamines is mostly related to AP.

The proportion of MDMA (ecstasy) users in the study population is close to 14%, almost three times the prevalence of MDMA use in the Spanish prison population in the last 30 days of freedom in 2016 (4.9%)⁽²⁴⁾, and in 2011 (4.8%)⁽²³⁾.

The prevalence of heroin use in the sample analysed (10%) is lower than that of methadone use (11%) and is lower than the proportion of heroin users among inmates obtained by the 2016 Prisons Survey (12.2% in the 30 days prior to entry into prison)⁽²⁴⁾. Related to

methadone use, that survey only records the prevalence of non-prescription use (4.6% in the 30 days before entry into prison). The results from hair analysis include consumption of methadone with and without a prescription. Its higher value in relation to the figures obtained by the Prisons Survey may be related to the existence of a percentage of cases of suspension of prison sentences in the population studied, in which the subject's detoxication or treatment for drug dependence must be proven (although the number of individuals who may be in this circumstance is not known).

From 2013 to 2015, there was a significant increase in the prevalence of use of MDMA, heroin and amphetamine among the studied population, as well as a significant decrease in methadone use.

On the other hand, drug testing in hair for legal purposes detects drugs with prevalence of use lower than 1% in that context, such as MA, MDA or ketamine, which were only studied as groups of substances (e. g. amphetamines, hallucinogens) in surveys.

Drug use among people under judicial proceedings shows significant differences in relation to gender: cannabis, cocaine and MDMA had higher prevalence of use in men (with differences of 6, 7 and 4 percentage points, respectively), while methadone use was higher in women (difference of 5 percentage points). The data from 2016 Prisons Survey show that the prevalence of use of cannabis, cocaine, heroin, amphetamine and MDMA in the last 30 days in prison is higher in men, being the greatest difference in the case of cannabis (20.2% versus 8.7%). Only methadone without a prescription is most prevalent among women⁽²⁴⁾.

The differences of use of cocaine, heroin and methadone in relation to age are significant in both sexes among people under judicial

proceedings. However, the differences of use of cannabis and MDMA are significant only among men. Heroin and methadone show a progressive increase in the proportion of users as age increases, reaching a peak in the 45-54 age group. Conversely, cannabis and MDMA show the highest proportion of users in the younger age group (15-24 years) and a continued decline in prevalence as age increases.

Consumption patterns according to age are slightly different in prison. For cannabis, cocaine and amphetamine, the highest prevalence of use occurs among persons under 25 years of age in 2016, with a continued decline in the proportion of users as age increases. Heroin and MDMA use peaks among inmates aged 25-35, with a subsequent decline in prevalence as age increases⁽²⁴⁾.

The results from this study are not directly comparable with those reported in the few publications relating to large series of drug testing in hair, mainly due to the fact that the populations of origin are very different, with most of analyses carried out in the context of obtaining or recovering the driving license^(25,26,27).

In relation to the quantitative results of drug concentration in hair, it has been proposed to interpret them by comparison with previous results obtained in the same laboratory from a sufficiently large population, and analysed statistically⁽²⁸⁾. The increase in THC concentration between 2013 and 2014 reflects a possible increase in quantities consumed and/or in the frequency of the consumption and/or in the richness of the substances consumed.

On the other hand, the homogeneity of frequency distribution of the concentration of methadone in the hair shows that, by being a medicine, it can be dosed correctly. Even in cases of non-prescription use the consumer can

control the dosage of the product to achieve a certain effect.

To the best of our knowledge, this is the first study in which quantitative data from hair testing are used for epidemiological purposes to assess drug use patterns in relation to sex or age. Concentrations of THC and cocaine in the hair were higher in men, which was consistent with previous findings of more intensive use of those drugs or more frequently in men than in women^(29,30).

No information was available on the quantities of drugs consumed by the persons included in the study, nor on the frequency of consumption, nor on the form in which it was consumed (by example, marijuana versus cannabis resin or cocaine base versus cocaine hydrochloride). This limitation prevented the analysis of correlations between these parameters and the concentration of the substance in the hair, which would have been very interesting.

The study of drug use prevalence in the forensic context provides an additional approach to knowledge of high-risk drug use. Epidemiological information revealed through the study of large series of data from hair analysis carried out for legal purposes is particularly relevant in the case of drugs with low prevalence of consumption in general population. Consequently, based on data from Forensic Toxicology, Forensic Epidemiology provides informed knowledge about drug use that may be additionally useful in adopting appropriate Public Health measures, aimed at preventing drug use and minimizing its effects.

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