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An Insight into Gabapentin and Pregabalin in Scottish Prisoners

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Abstract

The aim of this study was to evaluate the prevalence and abuse potential of antiepileptic drugs (AEDs) among prison populations in Scotland, UK. Participants consisted of all admitted and released prisoners over a 1 month period who consented to provide samples. Urine samples were collected and analyzed by liquid chromatography coupled with triple quadrupole tandem mass spectrometry using a method validated for the simultaneous quantification of 21 AEDs in urine. A total of 904 samples were collected. The samples were also screened for drugs of abuse by using point-of-care testing kits. A total of 18% of the samples were positive for AEDs. Gabapentin (GBP) was identified in 118 samples (13%) and pregabalin (PRG) in 32 samples (3.5%). Interestingly, 12 samples contained both drugs (1.3%). The concentrations ranged from 0.5 to 1,100 mg/L (median, 15 mg/L) for GBP and from 0.5 to 440 mg/L (median, 7.3 mg/L) for PRG. Four samples were found to have concentrations >400 mg/L, two samples for GBP and two samples for PRG. These concentrations are at least 20 times above the median concentrations. Other AEDs detected were levetiracetam (four samples), vigabatrin (four samples), lamotrigine (three samples), valproic acid (three samples), carbamazepine (two samples) and topiramate (one sample). Illicit or non-prescribed drugs were detected in 81% of urine samples of which 80% were from admitted prisoners and 20% from released prisoners. Benzodiazepines, opiates and cannabis were the most frequently detected drugs. Other drugs found in positive AED samples were methadone (26%), cocaine (18%), buprenorphine (17%), amphetamines (4%), methamphetamines (4%) and barbiturates (4%). This study shows a high prevalence of AEDs within the Scottish prison system, primarily due to GBP and PRG; however, due to the anonymity of the sample collection, it is unknown if these are prescribed or illicit drug ingestions.

Introduction

In recent years, there has been a growth in reports of antiepileptic drugs (AEDs) being misused on their own or in combination with other drugs of abuse in a variety of toxicological case types such as drug abuse, suicide, overdose and drug facilitated crime (1–6). The majority of these cases are due to the usage of pregabalin (PRG) and gabapentin (GBP), which have significantly increased among drug-using populations and prisoners since 1997 (2, 7–9). A report released by the National Health Service in 2018 showed that PRG alone, used to treat epilepsy and chronic pain, had the highest total gross ingredient cost at £36.38 million (10). Both medications are gamma amino butyric acid (GABA) analogues and are referred to collectively as "gabapentinoids" (Figure 1) despite the fact that neither binds to GABA receptors. Both drugs bind to the alpha2-delta site (an auxiliary subunit of voltage-gated calcium channels) in central nervous system tissues, reducing depolarization-induced calcium influx and thereby increasing GABA in the brain

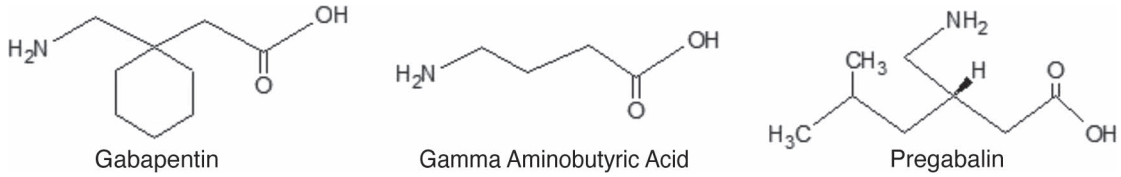

Figure 1. GBP, PRG and GABA structures.

in addition to reducing the release of excitatory neurotransmitters such as glutamate, noradrenaline and substance P (11, 12). As a consequence of their abuse liability, in April 2019, they were both reclassified as controlled medicines under the Misuse of Drugs Act 1971 (13). They are indicated for epilepsy, neuropathic pain and generalized anxiety disorder (14, 15). The latter two indications are the most common in primary care and prison settings.

Secondary to their widespread prescription in correctional facilities to treat cocaine and alcohol abuse during the recovery programs, reports have been published describing inmates who snorted GBP powder from capsules during their incarceration (7, 9, 16, 17). Gabapentinoids misuse was not only among prisoners and drug abusers; however, it was also reported to be intentionally misused among patients who have been prescribed these medications for neuropathic pain and psychological conditions such as generalized anxiety disorder (18).

Gabapentinoids have been reported by drug abusers to be ingested in combination with alcohol, prescription drugs (zopiclone and benzodiazepines), illicit/recreational drugs (marijuana and heroin/opiates) and with some "Legal High" drugs such as mephedrone and *Salvia divinorum* (2). Its tablets have been taken by different routes: orally (parachuting), intravenously after dissolving the tablets in water, rectally (plugging) and by inhalation (18). Users state that dose for dose, PRG outshines GBP; however, tolerance is gained more quickly (2).

In Scotland, drug and addiction services have raised concerns regarding these drugs being misused. A recent survey including 129 participants showed a 22% prevalence of GBP and PRG among drug addicts in Edinburgh (8). This study gives an indication of the prevalence of these drugs. However, an accurate response rate to the survey could not be determined as participants at the addiction clinics are often unregistered and turn up without appointments. In addition, participants may not provide correct information regarding their drug use, therefore providing misleading data.

In order to evaluate the prevalence and abuse potential of AEDs among prisoners in Scotland, a study was carried out in collaboration with the Scottish Prison Service (SPS) after obtaining ethical approval from the West of Scotland Research Ethics Service (WoSRES). The study included eight prisons in Scotland and to, our knowledge, the first of its kind to be carried out on such a large scale in Scotland. The prevalence and abuse potential of gabapentinoids and other AEDs were evaluated using urine analysis to assess drug consumption in individuals who were admitted into prison and other prisoners who were released within the same time period.

Methodology

Study design

Out of the 15 prisons in Scotland, 8 prisons participated in this study: Addiewell, Perth, Barlinnie, Polmont, Low Moss, Cornton Vale, Edinburgh and Greenock (Figure 2). All of these establishments are closed prisons with facilities in place to prevent escape. Community access is available to suitably risk assessed offenders from Barlinnie, Cornton Vale, Greenock and Polmont (19).

The prisons were chosen based on the number of prisoners and logistical constraints, with the exception of Greenock prison, which requested to participate in the study in spite of its small population. Participants were all consenting prisoners, male and female, admitted to and released from the selected prisons over a 1 month period (November 2013).

Urine samples were initially collected by prison staff within each prison as part of their annual screening for common drugs of abuse using a routine point-of-care testing device. All specimens and data were encoded with a serial number to protect the confidentiality of prisoners. After the samples had been tested at the prison by a commercial dipstick test, they were transferred to the Department of Forensic Medicine and Science and stored at −20°C until analysis for AEDs.

Chemicals and reagents

Eslicarbazepine acetate (ESL) was purchased from Santa Cruze Biotechnology. Lacosamide (LAC), PRG and tiagabine (TIG) were obtained from LGC Standards. *S*-licarbazepine (S-LC), ezogabine (RTG), phenobarbital (PBT), rufinamide (RFM) and gabapentin-d_{10} (GBP-d_{10}) were purchased from Cerilliant. GBP, vigabatrin (VIG), valproic acid (VPA), carbamazepine (CBZ), carbamazepine 10,11-epoxide (CBZO), oxcarbazepine (OXC), phenytoin (PHT), 5-(3-Hydroxyphenyl)-5-phenylhydantoin (p-HPPH), stiripentol (STP), levetiracetam (LEV), zonisamide (ZNS), topiramate (TPR), lamotrigine (LTG), tolbutamide (TUB), 10-11 dihydrocarbamazepine (CBZ-DiOH) and ammonium acetate (HPLC grade) were purchased from Sigma Aldrich. Methanol (HPLC grade) was supplied by VWR International Ltd. Double-distilled water was obtained from the in-house Millipore® System.

Calibrators, quality control and internal standards preparation

For qualitative method validation, stock solutions for AEDs were prepared in methanol for LEV, VPA and VIG at 10 mg/mL and at 1 mg/mL for all other drugs. Three working solutions were prepared by further diluting the stock solutions in methanol to obtain 1 mg/mL for LEV, VPA and VIG; 20 mg/L for RTG, TIG and OXC and 100 mg/L for the rest of the drugs. For quantitative validation, eight calibration standard solutions were prepared in methanol from the working solutions to achieve the target concentrations. Two quality control (QC) samples (low and high) were directly made in urine. QC levels were 7 and 45 mg/L. All QCs and stock solutions were stored at −20°C and working solutions were stored at 4°C.

Three internal standard stock solutions of TUB, CBZ-DiOH and GBP-D_{10} were prepared in methanol to give a concentration of 10 mg/L. A combined working internal standard solution was

Figure 2. Regional distribution and number of collected samples from participating prisons.

prepared in methanol at 2.5 mg/L for GBP-d_{10} and 5 µg/mL for TUB and CBZ-DiOH.

Calibration curves were extracted in duplicate by adding the following volumes to 100 µL of urine: 100 µL of the standards, 100 µL of the internal standards mix solution and 200 µL of methanol (methanol total volume 400 µL). The standards were vortexed for 30 s and centrifuged for 10 min at 10,000 rpm. An aliquot of 200 µL of the supernatant was transferred to an LC vial and diluted with 500 µL of deionized water. A 5-µL aliquot of the diluted supernatant was injected and analyzed by LC–MS-MS.

Urine sample preparation

A 100 µL aliquot of the urine sample was transferred to a 2 mL snap top polypropylene microcentrifuge tube. A total of 100 µL of internal standard solution and 300 µL methanol were added; vortex was mixed for 30 s and centrifuged for 10 min at 10,000 rpm. An aliquot of 200 µL of the supernatant was transferred to an LC vial and diluted with 500 µL of deionized water. A 5-µL aliquot of the diluted supernatant was injected and analyzed by LC–MS-MS. Since the focus of this study was GBP and PRG prevalence among prisoners, no urine hydrolysis was applied as more than 81% of GBP and PRG are excreted unchanged in urine.

Instrumentation

An Agilent LC–MS-MS triple quadruple G6430A mass spectrometer equipped with Agilent 1200 series auto sampler, quaternary pump SL with degasser and thermostatted column compartment was used. Electrospray ionization was used, and the MS operated in multiple reaction monitoring mode with ion mode switching. The optimal conditions were achieved using a nebulizer pressure at 15 psi, capillary voltage of 4,000 V, nitrogen gas heated to 300°C and delivered at 10 mL/min. The column used was a Phenomenex Gemini C18 (150 × 2.1 mm, 5 µm) coupled with a C18 guard column (4 × 2.0 mm). The column temperature was maintained at 40°C. Gradient elution was employed using a mobile phase consisting of A (2 mM ammonium acetate in water) and B (2 mM ammonium acetate in methanol) at a flow rate of 0.3 mL/min. The total run time was 17 min. The gradient mobile phase system started at 80:20 A/B increasing to 60:40 A/B within 2 min. This percentage was maintained for 6 min before being increased to 10:90 A/B for 2 min. The percentage was finally decreased to 80:20 A/B for 7 min in order to condition the column before the next injection. Data analysis was performed using Agilent Mass-Hunter Workstation (version: B.01.05).

Qualitative method validation

Before screening the urine samples, the method was qualitatively validated, initially for 21 AEDs, to determine cut-offs. According to standard practices for method validation in forensic toxicology (20), qualitative method validation parameters are as follows: selectivity and specificity, carryover, matrix effect and limits of detections.

Selectivity was assessed using negative case samples. Specificity was assessed by spiking drug-free matrix with each AED individually. Interferences were examined visually.

Assay LODs and LOQs were determined for urine using three different sources of blank urine samples spiked with decreasing

concentrations of AEDs and analyzed in duplicate for three separate runs.

Carryover was tested by injecting three blank controls after two injections of 300 mg/L of AEDs mix. It was evaluated by dividing the blank peak area at the expected retention time by the mean peak area of the ULOQ and multiplying by 100. No carryover is considered if the value is <10%.

Recovery and matrix effect were evaluated using the post-extraction addition approach for all 21 AEDs in urine (21).

Quantitative method validation of PRG and GBP

Due to the considerable number of GBP- and PRG-positive samples detected during the qualitative analysis, a linearity, precision and accuracy check for these two drugs was carried out before re-analyzing the positive samples quantitatively.

Linearity was assessed by analyzing five separate calibration curves prepared by spiking blank urine with GBP and PRG at eight concentrations ranging from 0.5 to 50 mg/L. A linear regression equation weighted 1/*X* was applied.

Precision and accuracy were assessed by analyzing triplicates of spiked controls at two different concentrations (low and high). Intra-day precision was calculated from three replicates per QC in one batch. Inter-day precision was determined over five different runs. Accuracy was expressed as percentage of the nominal concentration, and precision was established by the percentage of the co-efficient of variation (CV %).

Results and Discussion

A total of 904 urine samples were collected from the eight prisons over a 1 month period (November 2013). The sample number represents all admitted and released prisoners during this month. Samples were analyzed using a simple and accurate method for the simultaneous analysis of 21 AEDs.

Qualitative method validation

No endogenous or exogenous interference was observed, and none of the AEDs or their internal standards showed any interference at the retention time of the other drugs included in the method. LODs, LLOQs and LOQs results are presented in Table I.

Matrix factor and recovery results of two QCs (low and high) using six different sources of matrix are detailed in Table II. Matrix factor values were acceptable for all the drugs (within ±1.25) and ranged between 0.81 and 1.13. Recovery was >80% for all the AEDs.

No carryover was observed for all 21 AEDs in urine. Carryover percentage after the first blank injection was 0% for all drugs except LEV, VPA and LEV, which was 0.06%, 0.03% and 0.35%, respectively. However, these percentages are acceptable (<10%) and very low compared to the high concentrations used (6 X ULOQ).

Quantitative method validation of PRG and GBP

The calibration curves were linear with an R^2 >0.998. Accuracy and precision were assessed by analyzing replicates of spiked controls at two different concentrations (7 and 45 mg/L). The accuracy values were within the acceptable range of ±15% of the nominal concentrations. The intra- and inter-day accuracies ranged from 93.8 to 104.4% for GBP and from 96.2 to 105.3% for PRG. Both intra- and inter-day precision values were acceptable and <15%. The intra- and inter-day precision values were <10.4% for GBP and <7.4% for PRG (Table III).

Table I. Assay LOD, LLOQ and LOQ of 21 AEDs in Urine

AEDs	LOD	LLOQ	LOQ
CBZ	0.25	0.5	0.5
CBZO	0.05	0.25	0.5
ESL	0.25	0.5	0.5
GBP	0.1	0.25	0.5
LAC	0.05	0.25	0.5
LEV	0.1	0.5	5.0
S-LC	0.1	0.25	0.5
LTG	0.25	0.5	0.5
OXC	0.05	0.1	0.05
PBT	1.0	2.5	2.5
PGR	0.5	1.0	0.5
PHT	0.5	1.0	1.0
p-HPPH	0.5	1.0	1.0
RFM	0.1	0.25	0.5
RTG	0.025	0.05	0.05
STP	0.25	0.5	0.5
TIG	0.01	0.025	0.05
TPR	0.25	0.5	0.5
VIG	0.5	1.0	5.0
VPA	2.5	5.0	5.0
ZNS	0.5	1.0	1.0

Admission v's liberation

Samples were collected from prisoners who had just been admitted to or were about to be released from prison in November 2013. Demographic data on selected prisons at the time of the study are presented in Table IV.

Table V shows the number of admission and liberation samples received from each prison. In general, the total AED prevalence was slightly higher among admitted prisoners (19%) compared to their prevalence among released prisoners (16%). Out of 164 positive samples, 115 were admission samples (70%) compared to 49 liberation samples (30%). Interestingly, AED prevalence at HMP Edinburgh was increased in the liberation samples. However, out of the total 85 samples collected from HMP Edinburgh, 60 samples were liberation samples, which may have skewed the results.

AED prevalence per prison

The results of the analysis found 164 of the 904 samples to be positive for at least one AED (18%). Four of the prisons had combined admission and liberation prevalence >20% (Table V).

Cornton Vale is the only all-female prison in Scotland and had the highest AED prevalence at 28%, followed by Perth (27%), Addiewell (25%), Edinburgh (25%) and Low Moss (19%). Barlinnie is the largest prison establishment in Scotland and holds all categories of prisoners. It is known to be overcrowded with prisoners sharing cells that are meant for individual use; however, AED prevalence was only 9% at this prison.

Polmont is the national holding facility in Scotland for young offenders aged 16–21 years. It showed a very low prevalence of AEDs (5%) among this age group. This can either be seen as a sign of

Table II. Recovery and Matrix Factor Values for 21 AEDs Using Low and High QCs and Six Different Urine Sources ($n = 6$ per QC per Matrix)

AEDs	QC1		QC2	
	Recovery (%)	Matrix effect	Recovery (%)	Matrix effect
CBZ	107	1.02 ± 0.05	106	1.02 ± 0.12
CBZO	91	1.04 ± 0.05	98	1.02 ± 0.11
ESL	89	0.82 ± 0.29	95	0.84 ± 0.30
LAC	93	1.04 ± 0.04	97	1.00 ± 0.10
LEV	92	1.01 ± 0.05	95	1.00 ± 0.10
LIC/SLE	87	1.01 ± 0.06	89	1.00 ± 0.11
LTG	109	1.03 ± 0.03	102	1.01 ± 0.07
GBP	104	1.13 ± 0.07	105	1.06 ± 0.09
PBT	83	0.87 ± 0.08	86	0.87 ± 0.08
PGR	98	1.03 ± 0.04	98	1.00 ± 0.14
OXC	105	0.89 ± 0.30	110	0.81 ± 0.16
PHT	88	0.99 ± 0.05	90	1.02 ± 0.15
p-HPPH	85	1.00 ± 0.07	81	1.02 ± 0.08
RFM	96	1.00 ± 0.08	93	1.02 ± 0.09
RTG	87	0.90 ± 1.84	81	0.81 ± 1.16
TIG	80	1.00 ± 0.04	85	1.04 ± 0.05
TPR	102	1.00 ± 0.03	105	1.05 ± 0.09
VIG	76	0.90 ± 0.23	84	0.90 ± 0.19
VPA	103	1.03 ± 0.06	108	1.02 ± 0.14
ZNS	92	1.03 ± 0.06	92	1.04 ± 0.12

Table III. Accuracy and Precision Results of GBP and PRG in Urine

AEDs	Precision				Accuracy			
	Intra-day (%) $n = 3$		Inter-day (%) $n = 15$		Intra-day (%) $n = 3$		Inter-day (%) $n = 15$	
	7 mg/L	45 mg/L	7 mg/L	45 mg/L	7 mg/L	45 mg/L	7 mg/L	45 mg/L
GBP	2.0	1.7	10.4	5.9	93.8	104.4	93.8	104.4
PGR	5.3	2.7	6.9	7.4	96.2	105.3	96.2	105.3

Table IV. Demographic Data on Selected Prisons at the Time of This Study (32, 33)

Prison	Capacity	Population[a]	Sex[b]	Age	Security level	Area
Addiewell	700	700	M	>21	Local	Lanarkshire and West Lothian
Barlinnie	1018	1407	M	>21	Medium	West of Scotland
Cornton Vale	375	248	F	>16	Local	Whole of Scotland
Edinburgh	870	891	M and F	>21	Local	Edinburgh, Lothian, Borders, Kirkcaldy and Fife
Greenock[c]	249	237	M and F	>21	Local	West of Scotland
Low Moss	784	753	M	>21	Local	North Strathclyde
Perth	722	635	M	>21	High	Angus, Dundee, Perth, Kinross and Fife
Polmont	760	521	M	16–21	Local	Whole of Scotland

[a]Prison population number was last updated on July 2014.
[b]M = male and F = female.
[c]Greenock is a male prison but it held a number of female prisoners at the time of the study due to Cornton Vale establishment renovation.

Table V. Admission and Liberation Prevalence on Participating Prisons

Prison	Total samples no.	Positive samples	Prevalence (%)	Admission			Liberation		
				Samples no.	Positive	(%)	Samples no.	Positive	(%)
Addiewell	63	16	25	33	12	44	30	4	13
Barlinnie	172	16	9	106	11	10	66	5	8
Cornton Vale	101	28	28	90	25	28	11	3	27
Edinburgh	85	21	25	25	3	12	60	18	30
Greenock	27	1	4	11	1	9	16	0	0
Low Moss	118	23	19	100	21	21	18	2	11
Perth	187	51	27	123	38	31	64	13	20
Polmont	151	8	5	102	4	4	49	4	8
Total	904	164	18	590	115	19	314	49	16

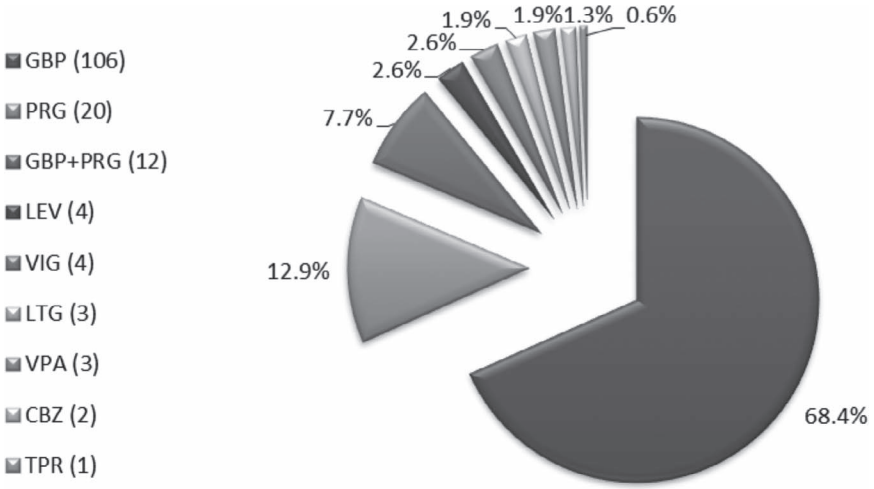

Figure 3. AED prevalence.

their low popularity among adolescents or an indication of their low prescription rate among this group of people.

Finally, Greenock is an establishment that accommodates a wide range of offenders and is considered one of the most diverse in the SPS. They manage adult male and female offenders for those with short-term sentences, long-term sentences and on remand (22). It participated with 27 samples of which one was positive for GBP.

AED prevalence by drug

Among the 22 AEDs investigated in this study, the highest prevalence of AEDs is mainly due to GBP and PRG on their own or in combination (Figure 3). GBP was identified in 118 samples out of the 164 positive samples (72%) and PRG in 32 samples (20%). The percentage of GBP and PGR among Scottish prisons was similar to their prevalence among the prisons in England during the same period of time (2013) (23). Other AEDs detected were LEV and VIG, four samples each. LTG and VPA were positive in three samples each. CBZ and TPR were found in two samples and one sample, respectively.

Out of the 164 samples, only 15 samples were positive for more than one AED (9%). Interestingly, 12 of these specimens contained both GBP and PRG, 8 admission and 4 liberation samples (7%). Other drug combinations found were GBP with LTG (one sample), GBP with TPR (one sample) and LEV with VPA (one sample).

Neuropathic pain treatment guidelines recommend combination therapy using drugs with different mechanisms of action. GBP and PRG could be exchanged to one another based on the patient response to the treatment regimen. Thus, it seems unlikely that practitioners would prescribe both gabapentinoids together (24–26). Hence, the presence of both drugs may represent a change in therapy from one agent to the other. The half-lives of GBP ($t^1/_2 = 5.9$ h) (27) and PRG ($t^1/_2 = 4.6$–6.8 h) (28) are relatively short. However, because sudden termination may trigger withdrawal symptoms, changing therapy would typically require reducing the dose of initial drug while escalating the dose of the replacement one over at least 5–7 days. In such cases, patients could test positive for both drugs. Alternatively, the presence of both drugs may indicate medication dependence or abuse. PRG and GBP concentrations of these 12 samples are presented in Table VI. Sample 10 had high concentrations of GBP and PRG (81.7 and 141.1 mg/L, respectively).

GBP and PRG concentration frequencies

As shown in Figures 44 and 5, urine concentrations of GBP and PRG varied across a broad concentration range, without creatinine correction. The concentrations ranged from 0.5 to 1,100 mg/L (mean, 61.6 mg/L and median, 15 mg/L) for GBP and from 0.5 to 440 mg/L (mean, 59.9 mg/L and median, 7.3 mg/L) for PRG.

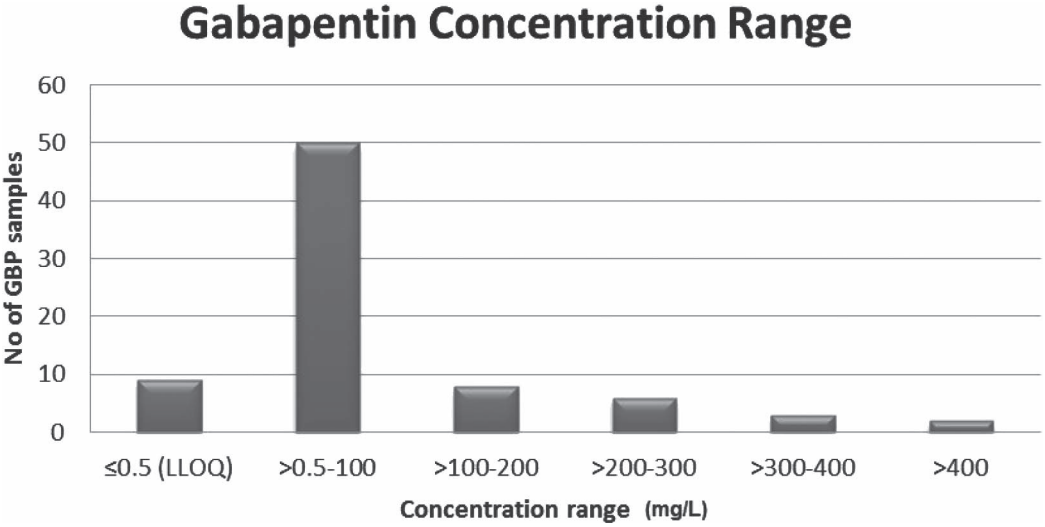

Figure 4. GBP concentration ranges in 118 positive samples.

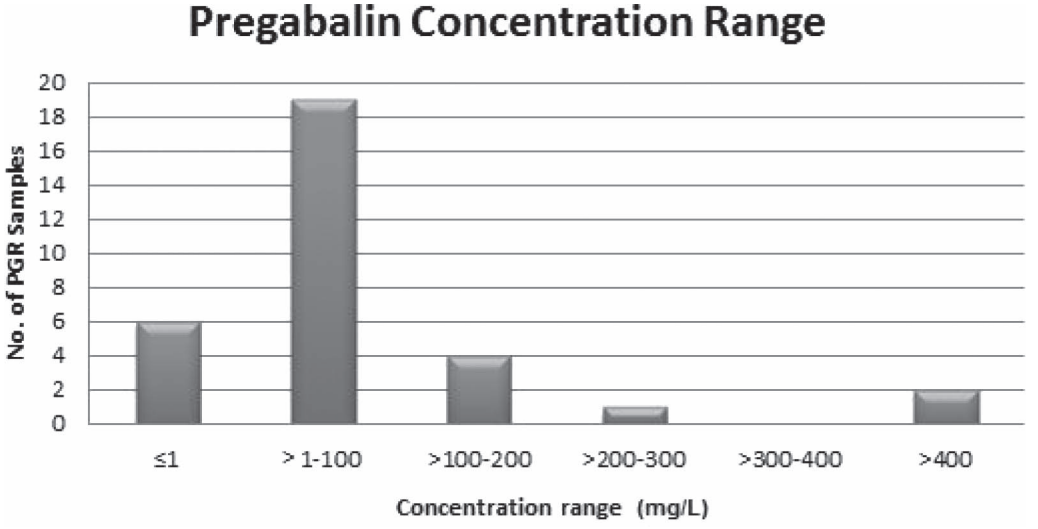

Figure 5. PRG concentration ranges in 32 positive samples.

Table VI. GBP and PRG Concentrations in Samples Containing Both Drugs

Sample no.	Sample type	GBP (mg/L)	PRG (mg/L)
1	A	2.2	25.1
2	L	3.0	1.1
3	L	8.1	14.2
4	A	10.5	128.7
5	L	14.1	2.2
6	L	18.1	2.7
7	A	36.4	438.2
8	A	42.7	0.8
9	A	66.9	0.6
10	A	81.7	141.1
11	A	93.7	2.6
12	A	170.8	15.2

The median concentrations of GBP were 2-fold greater than PRG. This is generally consistent with the relative potency of these drugs. The recommended dose of GBP is 900–1,800 mg/day, and its therapeutic range in blood varies between 2.2 and 6.1 mg/L, whereas the recommended dose of PRG is 150–600 mg/day with a therapeutic range in blood of 1.3–4.9 mg/L. Both drugs are not metabolized, not bound to plasma proteins and are eliminated unchanged by the kidneys, 81% for GBP and 92% for PRG (29). Urine concentrations were reported to range between 2.5 and 35,345 mg/L for GBP and 2.5 and 6,892 mg/L for PRG among pain clinic patients, but it was unknown whether all patients were prescribed these two drugs or not (30). In this study, 20 of the GBP positive samples and 10 of the PRG positive samples had urine concentrations 5–50-folds higher than the median values of both drugs reported in the literature. It was not possible to determine whether these high concentrations were due to prescribed doses of medication or misuse among the prisoner population.

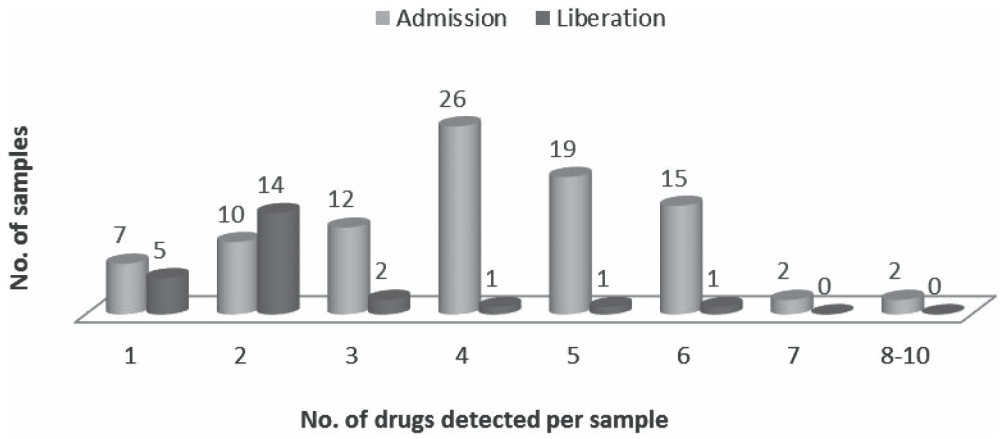

Figure 6. Number of drugs detected in samples among admitted and released prisoners.

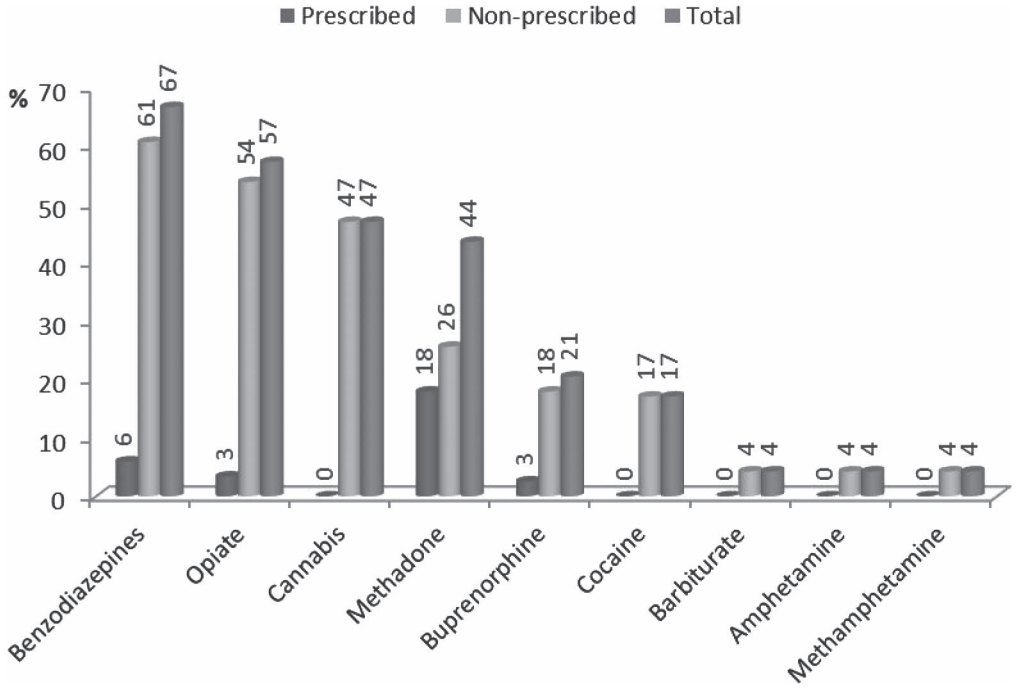

Figure 7. Prescribed and non-prescribed drugs present in AED samples.

Illicit drug prevalence in positive AED samples

The urine samples were initially screened by the SPS for drugs of abuse using urine dipstick analysis. Drugs tested were amphetamines, barbiturates, benzodiazepines, buprenorphine, cannabis, cocaine, methadone, methamphetamines and opiates. AED-positive samples were matched with SPS screening results in order to investigate the presence of illicit drugs in these samples. It should be noted that this comparison was made only to the dipstick screening results and that confirmation testing results are confidential so were not provided to the researcher.

Out of the 164 positive AED samples, 117 samples (71%) were matched at the time of this study. This comparison gives insight into the combination of other drugs that may have been prescribed or used alongside AEDs. A total of 95 of the matched samples (81%) screened positive for at least one common drug of abuse. It was expected that the number of illicit drugs detected among admitted prisoners ($n = 93$; 80%) was higher than the liberated ones ($n = 24$; 20%) as illustrated in Figure 6. The most frequently detected drugs with AEDs were benzodiazepines (67%), opiates (57%) and cannabis (47%), both prescribed and abused drugs as shown in Figure 7. The majority of these samples were positive for non-prescribed drugs. For instance, benzodiazepines were non-prescribed in 71 samples (61%), and opiates were also misused in 63 samples (54%), whereas all 55 cannabis samples were non-prescribed (47%). Methadone was positive in 51 samples (44%) of which 31 samples were non-prescription cases (26%). Cocaine and buprenorphine were also detected in 18% and 17% of the samples, respectively, as non-prescription use, whereas amphetamines, methamphetamines and barbiturates were only found in 4% of the AED samples and were all abuse cases.

Study limitation

This study is limited without information regarding age, sex and medical history for each urine sample. The difficulty in obtaining

further information from medical records was mainly due to the study being anonymous; therefore, it would not have been possible to check medical/prescribing records that would allow differentiation between prescribed and abused AEDs.

Conclusion

The study results were comparable to the survey conducted in Edinburgh but on a larger scale (8). The study shows a high prevalence of AEDs (18%) largely due to GBP and PRG on their own or in combination with other drugs of abuse. The majority of AED positive samples also contained at least one illicit drug, the most frequently encountered being benzodiazepines, opiates and cannabis. In the absence of knowing how many of the participants were prescribed gabapentinoids, it is not possible to conclude if they were being abused or prescribed. The results were discussed with the SPS Health Board Leads who confirmed that there is evidence up to 33% of those in custody are prescribed gabapentinoid with HMP Perth & Edinburgh having the highest prescription number; thus, the results of this study is expected. The greater issue is the over-prescribing of these drugs when there is no evidence that the individual meets the prescribing criteria for such medications. Currently, NHS Boards are actively reviewing all gabapentinoid prescriptions, and these medications are no longer given in possession. Furthermore, the recent re-classification of gabapentinoids as Class C controlled drugs will definitely impact on their possibility to be abused (31).

Ethical Approval

The study was approved by the WoSRES (reference: 12/WS/0312).

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