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An Italian survey of opioids misuse: Epidemiological and psychopathological aspects

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ABSTRACT

Objective: Opioid abuse is a worrying reality especially in the US. The increase in the prescription of opioids in Europe poses the risk of a possible increase in the number of abusers also in Italy. The aim of the study is to evaluate the abuse of opioids in the youth population and to evaluate possible correlations with some psychopathological aspects.

Methods: A survey, conducted from July 2019 to March 2020, about the use of opioids was spread to a group of subjects aged between 18 and 40 years. A socio-demographical investigation and psychometric scales evaluating internet game addiction, gaming online, quality of life and general psychometric features were administrated.

Results: Nine-hundred and thirteen subjects completed the survey. Seventeen-five subjects (8.21%) have used one opioid at least once in their lifetime. Weak correlations were found between codeine and morphine intensity of use and sleep disturbance, cigarette smoked per day, while codeine correlates with the number of coffees taken per day and somatization.

Conclusion: Although the data of this survey do not show high percentages of use in Italy (8.21% of the sample have used one of the listed opioids at least once in their lifetime), the correlations founded confirm the literature data already present highlighting the need for constant monitoring of this phenomenon.

Introduction

The biological background of opioids use disorder

Use of opioids (including heroin and prescription opioids) is an emerging epidemiological problem involving between 28.6 and 38 million people globally (Bolshakova et al., 2019). These substances act on the endogenous opioid system which includes the mu, delta, kappa and nociceptin receptors, to which they bind with different affinities and peptides (β -endorphin, enkefaline, dinorphins and nociceptin / orphanin FQ) (Corder et al., 2018). The mechanism underlying the developing of Opioids Use Disorder (OUD) has been explained in several ways. In particular, the individual susceptibility to developing OUD was hypothesized to be related with genetic polymorphisms in several pathways of neurotransmission (dopaminergic, opioidergic and serotonergic) (Saxon et al., 2005). In particular the chronic opioid mis-

use produces a dysregulation in the reward system and in the locus caeruleus, and this leads to the typical behavioural disorders of OUD (i.e., craving) and in the difficult abstinence from the substance intake (Scherbaum and Bonnet, 2018).

Epidemiological data

The misuse of opioid is widespread especially in the US due to the increase in the prescriptions of opioid drugs for the treatment of chronic pain and various other pathologies (Armenian et al., 2018; Schifano et al., 2019). In addition to prescribed medications, the misuse of cough syrups containing codeine and used for recreational purposes should be considered (Schifano et al., 2021; Miuli et al., 2020). The US alone consumes 99% of the world total hydrocodone, the 81% of oxycodone and the 60% of hydromorphone (Board INC. REPORT 2016). Although the phenomenon is smaller in Europe, there has been a signif-

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icant increase in the prescription of opioids in several European countries. A recent study of 400 enrolled elderly inpatients hospitalized for at least 6 months in Germany showed that 10.8% of these had symptoms of opioid dependence (Chiappini et al., 2021). The most recent European Drug Report of 2021 shows how the kidnappings of fentanyl derivatives in 2019 amounted at 15 kgs (1 kilogram for Netherlands alone) and that the prevalence of opioids misuse in Europe ranged from 1% to 7% for 1000 inhabitants aged between 15 and 64 years old (European Monitoring Centre for Drugs and Drug Addiction 2021). As in the U.S. also in Europe the market of Novel Synthetic Opioids (NSOs) has caused an increase in the abuse of opioids in general resulting in an increased risk of overdose: in particular, in Italy there was the first ascertained case of overdose by NSO in 2017 caused by U-47,700. The EMCDDA report shows that in certain European countries the percentage of abuse of opioids other than heroin also exceeds 50%, while in Italy this percentage is less than 10%, confirming heroin as the main opioid used in Italy. It is also estimated that in Italy the percentage of subjects with a high risk of developing an opioid addiction is greater than 5/1000 inhabitants, constituting one of the highest rates in Europe (EMCDDA. Italy Country Drug Report 2019 [Internet] 2019).

Aim of the study

The purpose of this survey is to evaluate the use of opioids above the youngest. A further objective of this study is to correlate the use of these substances with some psychopathological variables assessed by means of a self-administered questionnaire.

Methods

A survey, conducted from July 2019 to March 2020, about the use of opioids (Oxycodone, Fentanyl, Tramadol, Codeine, Morphine, Buprenorphine, Hydromorphone and Methadone) was distributed, using the "snowball technique", to a group of subjects aged between 18 and 40 years. This age range was chosen to selective include the younger part of the population.

The questionnaire was made up of a socio-demographic and habit questionnaire (including gender, age, education, employment, marital status, N cigarettes/day, N coffees/day, alcohol intake, type of opioids used and the way to obtain opioids) and a battery of psychometric scale including:

- Symptom Checklist-90 (SCL-90) and its subscales (Prinz et al., 2013), a self-administered questionnaire of 90 items that evaluates both internalizing symptoms (depression, somatization, anxiety) and externalizing ones (aggression, hostility, impulsivity) in psychiatric patients/healthy subjects;
- Overall Quality of Life and General Health Brief version (WHOQOL-BREF) and its subscale (Krägeloh et al., 2011) that evaluates subjective perception of the individual health status, (social relationships, work activity, socioeconomic conditions, as they are perceived by the subject).;
- Internet Gaming Disorder scale (IGD) (Monacis et al., 2016); that is a short psychometric tool based on the nine core criteria defining IGD as suggested by the DSM-5
- Online Gaming Scale (OG) (Pápay et al., 2013); that is a 12 items problematic on-line gaming questionnaire-short form.
- Use of Opioids: to evaluate the intensity of use a scale with four values was created (0=never used; 1=one time; 2=rarely; 3=often; 4=every day).

We used "Google Forms" to create this survey, the link generated was spread via mail. The values were collected in an Excel database automatically generated.

This survey was delivered in accordance to the Declaration of Helsinki (2013) (WMA 2013) for research. The data collected were treated anonymously and confidentially.

Statistical analysis

The statistical analysis was made using Statistic IBM SPSS v 25.0. Results are reported as absolute number and frequencies as percentage. The values of continuous variables are reported as mean \pm standard deviation (SD). All tests were two-sided, with a statistical significance set up to p value<0.05. Relationship between dichotomous variables (intensity of opioid users and psychometric scales) has been evaluated through the Pearson's χ^2 analysis, considering the values as "weak" from 0,1 to 0,3, "moderate" from 0,4 to 0,6 and strong from 0,7 to 0,9 (Akoglu, 2018).

Results

Nine hundred and twenty questionnaires were completed. Seven questionnaires do not report sociodemographic data and were excluded from the analysis. Of the remaining 913 tests, males were 36.2%, females were 62.8%, and average age was 25.75 ± 5.87 . The majority of the subjects were students (67,7%) and of these the majority attended university (25,7%). Six hundred and eight subjects (66.1%) used to drink alcohol (mean alcoholic units/day 7.3 ± 6.8), 723 (78.6%) used to drink coffee (mean n coffee/day 2.5 ± 1.3) and 390 (42.4%) is a smoker (mean n cigarettes/day 8.5 ± 6.0).

Seventeen-five subjects (8.21%) have used one of the listed opioids (Oxycodone, Fentanyl, Tramadol, Codeine, Morphine, Buprenorphine, Hydromorphone and Methadone) at least once in their lifetime. The single substance use and the severity of misuse are described in Table 1.

Of these, 34 (45.3%) bought it with a prescription (one of these from the hospital emergency room) and 22 (29.3%) without (10 received it from a friend, three bought it in an online pharmacy and nine had the

Table 1
Use and Severity of misuse (percentage of the whole sample).

Substances Used	N (%)	Severity of misuse	SD
Oxycodone	15 (1.64)	1.80	0.3
Fentanyl	15 (1.64)	1.45	0.2
Tramadol	11 (1.20)	1.82	0.2
Codeine	54 (5.91)	1.65	0.4
Morphine	20 (2.19)	1.52	0.2
Buprenorphine	7 (0.77)	2.14	0.2
Hydromorphone	4 (0.44)	2.75	0.2
Methadone	7 (0.77)	2.29	0.2

SD: Standard Deviation.

Table 2
Psychometric assessment.

Scales and subscales	Whole sample (n = 913)		Opioid users (n = 75)	
	MEAN	SD	MEAN	SD
IDG	10.10	6.6	11.60	6.9
OG	1.94	3.1	2.63	3.4
TOT SCL90	61.80	56.8	83.87	64.9
Somatization	8.27	8.5	11.41	10.29
obsessivness	8.84	7.8	11.24	8.3
sensitivity	6.17	6.4	8.56	7.4
depression	10.9	10.1	13.93	11.2
anxia	7.20	7.0	9.23	8.6
aggressivity	3.75	4.3	5.36	5.4
phobia	2.17	3.9	3.28	4.6
paranoia	4.55	4.8	6.43	5.7
psychoticism	4.46	5.7	6.95	7.2
sleep disturbance	2.71	2.8	3.61	3.1
neuroticism	14.87	13.2	19.60	14.6
discomfort	15.69	12.4	19.61	13.1
cognitive alteration	10.53	9.7	13.65	10.5
TOT WHOQOL-BREF	91.77	13.6	87.97	14.5

SD: Standard Deviation; IGD =Internet Gaming Disorder scale; OG=Online Gaming Scale; SCL-90=Symptom Checklist-90; WHOQOL-BREF =Overall Quality of Life and General Health Brief version.

opioid at home because a family member used it), 19 (25.3%) did not answer.

The results of the psychometric scales in the sample interior and opioid users are shown in Table 2. Some weak correlations were found, especially in codeine and morphine users. For both codeine and morphine there is a correlation with the number of cigarettes/day (Pearson's χ^2 codeine: 0,144, $p = 0,005$; Pearson's χ^2 morphine: 0,121, $p = 0,018$)

while codeine correlates with the number of coffees taken per day (Pearson's χ^2 : 0,115, $p = 0,002$). The use of codeine correlated also with somatization (Pearson's χ^2 : 0,111, $p = 0,001$), aggressivity (Pearson's χ^2 : 0,106, $p = 0,001$) and sleep disturbance (Pearson's χ^2 : 0,105, $p = 0,002$) domains of SCL90, while morphine correlated only with sleep disturbance (Pearson's χ^2 : 0,141, $p < 0,001$) domain. All these results are described in Table 3.

Table 3
Psychometric correlation with use of Opiods.

		Oxycodone	Fentanyl	Tramadol	Codeine	Morphine	Buprenorphine	Hydromorphone	Methadone
alcoholic units /die	χ^2	-0,007	-0,008	-0,010	-0,001	-0,003	-0,007	-0,006	-0,005
	p	0,876	0,866	0,822	0,983	0,943	0,876	0,896	0,906
	N	495	495	495	495	495	495	495	495
N cigarettes/die	χ^2	0,011	-0,034	-0,085	,144**	,121*	-0,039	-0,069	-0,013
	p	0,824	0,506	0,098	0,005	0,018	0,442	0,179	0,795
	N	382	382	382	382	382	382	382	382
N coffee/die	χ^2	-0,009	0,031	-0,001	,115**	,089*	-0,016	-0,014	-0,012
	p	0,805	0,408	0,971	0,002	0,017	0,661	0,699	0,747
	N	716	716	716	716	716	716	716	716
IGD	χ^2	0,020	-0,001	-0,014	0,052	-0,025	-0,034	-0,026	-0,037
	p	0,541	0,971	0,676	0,118	0,446	0,309	0,436	0,263
	N	911	911	911	911	911	911	911	911
OG	χ^2	0,015	-0,003	-0,021	0,055	0,006	-0,015	-0,017	-0,026
	p	0,650	0,931	0,523	0,095	0,846	0,642	0,607	0,441
	N	911	911	911	911	911	911	911	911
TOT SCL90	χ^2	0,043	0,046	0,005	,098**	,082*	0,002	0,002	-0,001
	p	0,197	0,165	0,880	0,003	0,013	0,952	0,958	0,988
	N	911	911	911	911	911	911	911	911
somatization	χ^2	,072*	0,033	0,018	,111**	,071*	0,014	0,010	0,012
	p	0,029	0,315	0,591	0,001	0,033	0,664	0,753	0,724
	N	911	911	911	911	911	911	911	911
obsessivness	χ^2	0,019	0,027	-0,017	0,062	0,045	-0,018	-0,022	-0,027
	p	0,568	0,419	0,599	0,062	0,171	0,580	0,514	0,412
	N	911	911	911	911	911	911	911	911
sensivity	χ^2	0,011	0,043	-0,010	,084*	,078*	-0,014	-0,013	-0,015
	p	0,746	0,199	0,764	0,011	0,019	0,667	0,694	0,648
	N	911	911	911	911	911	911	911	911
depression	χ^2	0,023	0,050	-0,002	,068*	,074*	-0,005	-0,005	-0,010
	p	0,480	0,134	0,962	0,039	0,025	0,877	0,873	0,772
	N	911	911	911	911	911	911	911	911
anxia	χ^2	0,062	0,058	0,028	,086**	,091**	0,017	0,030	0,020
	p	0,061	0,083	0,405	0,009	0,006	0,610	0,369	0,549
	N	911	911	911	911	911	911	911	911
aggressivity	χ^2	,087**	0,041	0,035	,106**	,076*	0,032	0,032	0,032
	p	0,009	0,217	0,285	0,001	0,023	0,339	0,338	0,328
	N	911	911	911	911	911	911	911	911
phobia	χ^2	0,013	0,047	0,001	,081*	0,050	-0,001	0,003	0,000
	p	0,703	0,156	0,983	0,015	0,135	0,983	0,928	0,992
	N	911	911	911	911	911	911	911	911
paranoia	χ^2	-0,011	0,009	-0,005	,080*	,068*	-0,019	-0,020	-0,016
	p	0,740	0,789	0,880	0,016	0,040	0,574	0,549	0,626
	N	911	911	911	911	911	911	911	911
psychoticism	χ^2	0,032	0,040	-0,007	,090**	0,056	-0,005	-0,008	-0,009
	p	0,331	0,227	0,836	0,006	0,089	0,891	0,810	0,787
	N	911	911	911	911	911	911	911	911
sleep disturbance	χ^2	,072*	0,051	0,018	,105**	,141**	0,035	0,028	0,034
	p	0,031	0,125	0,591	0,002	0,000	0,286	0,398	0,307
	N	911	911	911	911	911	911	911	911
neuroticism	χ^2	0,045	0,054	0,013	,092**	,088**	0,009	0,011	0,009
	p	0,179	0,104	0,692	0,006	0,008	0,790	0,739	0,775
	N	911	911	911	911	911	911	911	911
discomfort	χ^2	0,036	0,045	0,003	,075*	,070*	0,000	-0,002	-0,003
	p	0,277	0,179	0,923	0,024	0,035	0,991	0,946	0,928
	N	911	911	911	911	911	911	911	911
cognitive alteration	χ^2	0,009	0,029	-0,023	0,064	0,044	-0,023	-0,026	-0,034
	p	0,781	0,388	0,492	0,053	0,180	0,496	0,433	0,310
	N	911	911	911	911	911	911	911	911
TOT WHOQOL-BREF	χ^2	0,004	-0,042	-0,007	-,094**	-,086**	-0,005	0,004	0,009
	p	0,896	0,206	0,840	0,005	0,010	0,870	0,893	0,797
	N	911	911	911	911	911	911	911	911

** $p < 0,01$ (two tail); * $p < 0,05$ (two tail). In bold significative values.

χ^2 = Pearson's χ^2 ; IGD =Internet Gaming Disorder scale; OG=Online Gaming Scale; SCL-90=Symptom Checklist-90; WHOQOL-BREF =Overall Quality of Life and General Health Brief version.

Discussion

General considerations

From the analysis of the survey data, it is clear that subjects who abuse opioids are a small part of the population. It is also evident that, within the general population, opioid abusers do not have a prescription for purchase. Our result showed also that codeine, morphine, oxycodone and fentanyl were the most used opioids. These results can exemplify the "switch" of the choice of opioid used (from heroin to "pharmaceutical" ones) both in US and Europe already hypothesized by the UNODC (*World Drug Report 2021*). This change in type of opioid use may find its roots in the greater ease in the production and cost-effectiveness of "pharmaceutical opioids" as well as in the illusory feeling of greater control over withdrawal or collateral symptoms. The phenomenon of opioid abuse in subjects who take these substances in order to treat pathologies, is a numerically important phenomenon. These results are in line with the literature data, in which the abuse by patients with a prescription stands at around 40% in U.S. (*van Amsterdam and van den Brink, 2015*): in fact, in our case the 45.3% of the subject had a prescription. The data collected, testifying to a rather low opioid abuse in the general population, appear in line with those already known although there is evidence of an increase in the prescription of opioids in Europe, the phenomenon of opioid abuse does not affect many people (*Rosner et al., 2019*).

Codeine and sleep quality

An interesting aspect that emerged from the study concerns the correlations that emerged between opioids and some psychopathological aspects. In particular, a correlation emerged between the use of morphine and codeine and low sleep quality. Again, there is a confirmation of the literature data, in which subjects who use opioids had a worse quality of sleep and the treatment of these addictions leads to an overall improvement in the quality of sleep (*Baykara and Alban, 2019*). Specifically, opioid abuse seems to affect sleep quality in several ways: disrupted sleep architecture and sleep-disordered breathing are often observed during polysomnography, interacting with each other in a complex way (*Cao and Javaheri, 2018*).

Codeine and aggressivity

Certain considerations can be made on the correlation between codeine and aggression, in particular in relation to the consumption of this substance in different settings. Especially in the U.S. some subcultures use codeine especially in relation to listening to rap or hip-hop music in whose lyrics the effects of the substance are often enhanced (*Miuli et al., 2020*; *Agnich et al., 2013*). It would be interesting to investigate whether these subcultures are also present in Italy and if they can somehow cause an increase in the consumption of codeine. The increased aggressiveness in opioid users found in our study could explain the increased risk of self-injurious behavior in young substances users already well documented in the literature (*Martinotti et al., 2021*).

Opioid misuse and smoking habits

Another correlation found was that between morphine, codeine and the use of cigarettes. This correlation can also be explained on a biological basis, since the release of dopamine induced by nicotine is in fact closely related to the endogenous system of opioids; it is not strange, therefore, that nicotine-dependent subjects also tend to abuse other substances, including opioids. In particular the opioid system and the nicotinic-cholinergic system interact in important pathways to modulate the effects of opiates and the effects of nicotine on drug reward, drug tolerance, drug withdrawal and nociception (*Yoon et al., 2015*).

Limitation

The first limitation of this study was the relatively small sample size in order to analyze all the implication of this phenomenon and further investigations are needed to evaluate the actual impact of the use of codeine in young people. A further limitation is the weakness of the correlation founded, making it necessary to enlarge the sample analysed to confirm these hypotheses. The use of self-administered psychometric scale could be also considered a limitation of this work.

Conclusions

The data collected from this survey demonstrate that the phenomenon of opioid abuse does not currently have any worried dimensions although a high level of vigilance on the opioids use should be maintained, especially in the youngest. These data are substantially in agreement with those currently present in the literature even if the "switching" in "pharmaceutical" opioids use may be seen as a new worrying trend. Interesting aspects to be explored in further investigations are the correlations between psychopathological aspects and the abuse of opioids, specifically sleep disturbance, aggressivity and smoking. Furthermore, different and more specific types of populations (e.g., elderly, patients with chronic or psychiatric diseases) should be considered for a more precise description of the use of these substances.

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Declaration of Competing Interest

This study was partially founded by the Just-SO project.

CRediT authorship contribution statement

Gianfranco Stigliano: Conceptualization, Data curation, Writing – original draft. **Andrea Miuli:** Data curation, Formal analysis, Investigation. **Aliseo Lalli:** Data curation, Formal analysis, Investigation. **Maria Chiara Alessi:** Data curation, Formal analysis, Investigation. **Antonella Sociali:** Data curation, Formal analysis, Investigation. **Fabiana Esposito:** Writing – original draft. **Laura D'Angelo:** Writing – original draft. **Giacomo d'Andrea:** Supervision, Writing – review & editing. **Alessio Mosca:** Supervision, Writing – review & editing. **Maria Chiara Santovito:** Supervision, Writing – review & editing. **Giovanni Martinotti:** Funding acquisition, Writing – review & editing. **Massimo di Giannantonio:** Writing – review & editing, Validation.

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