


RESEARCH NOTE

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Unspecified opioids among opioid overdoses in Oslo, Norway

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Abstract

Objective: Since 2017, an increasing number of opioid overdoses in Oslo, Norway, has been categorized as involving unspecified opioids, as noted in the patient records by the doctor treating the patient. In this study we compare the characteristics of overdoses involving unspecified opioids, long-acting opioids, and heroin. Data on patients presenting with opioid overdose was retrospectively collected from 1 October 2013 to 31 December 2019 at the Oslo Accident and Emergency Outpatient Clinic.

Results: Among 2381 included cases, 459 (19.3%) involved unspecified opioids, 134 (5.6%) long-acting opioids, and 1788 (75.1%) heroin. Overdoses involving unspecified opioids needed longer observation, median 5 h 29 min vs. 4 h 54 min (long-acting opioids) and 4 h 49 min (heroin) ($p < 0.001$), and had a lower Glasgow coma scale score, median 10 vs. 13 in both the other groups ($p < 0.001$). Naloxone was given in 23.3% of cases involving unspecified opioids, vs. 12.7% involving long-acting opioids and 30.2% involving heroin ($p < 0.001$). A larger proportion of patients were transferred to hospital care when unspecified or long-acting opioids were involved compared to heroin, 16.3% and 18.7% respectively vs. 10.1% ($p < 0.001$). Our results indicate that the category “unspecified opioids” encompasses a substantial proportion of opioids acting longer than heroin.

Keywords: Opioids, Opiates, Heroin, Buprenorphine, Methadone, Overdose, Poisoning, Naloxone

Introduction

In Europe there were 1.3 million high-risk opioid users in 2018, and opioids were involved in 82% of drug overdose deaths [1]. The ongoing opioid epidemic in the USA, responsible for about half a million deaths since 1999, has so far come in three waves: first increased prescribing of opioids in the 1990s and overdose deaths from prescription opioids, then an increase in heroin deaths from 2010 following stricter regulation of opioid prescription, finally an increase in overdose deaths related to synthetic opioids from 2013, mainly illegal fentanyl [2, 3].

The main danger of opioid overdose is respiratory depression [4, 5]. Naloxone, an opioid receptor

antagonist, is a highly efficient antidote, but has a shorter half-life even than short-acting opioids like heroin [6]. Still, nearly all patients treated with naloxone for a heroin overdose survive without subsequent observation [7, 8]. However, it is not possible to distinguish between different opioids based on the clinical presentation. Accordingly, observation is recommended for two hours after naloxone treatment, to catch any recurring respiratory depression resulting from opioids with longer half-lives [6].

Opioids were involved in 83% of the 275 registered drug overdose deaths in Norway in 2019 [9]. While heroin used to predominate, the last decade has seen an increasing proportion of deaths related to other opioids [9]. In Oslo, the capital city of Norway, most drug overdoses are treated at a primary care emergency outpatient clinic, the Oslo Accident and Emergency Outpatient Clinic (OAEOC). Since 2017, a large proportion

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of the opioid overdoses treated in this setting have been categorized as involving unspecified opioids, constituting a marked change from previous years [10]. If this category of unspecified opioids to any notable extent were to encompass longer acting opioids than heroin, adhering to the recommended two-hour observation following naloxone administration would be even more important. Hence, in this study we compare the characteristics of overdoses involving unspecified opioids, long-acting opioids, and heroin at the OAEOC.

Main text

Methods

Data on patients presenting with opioid overdose at the OAEOC was retrospectively collected from 1 October 2013 to 31 December 2019, using the case definition and data registration tool developed by the European Drug Emergencies Network (Euro-DEN) [11]. We included all cases of overdose related to the recreational use of opioids. Opioid overdoses also involving other drugs or ethanol were excluded.

The diagnosis of drugs taken was based on the clinical assessment noted in the patient records by the doctor treating the patient, in its turn based on the clinical presentation and all available information from the patient and the patient’s companions. The category “unspecified opioid” is used by OAEOC doctors when the patient has an obvious opioid toxidrome (miosis and reduced level of consciousness) and there is no specific information

on which opioids have been taken. The OAEOC has limited diagnostic and treatment resources available, and patients needing more intensive treatment are transferred to hospital care [12]. Arterial blood gas and toxicological laboratory analyses are not available. Naloxone is available for intramuscular (main use) and intravenous injection. Naloxone infusion is not given.

Among 5236 opioid overdoses in the inclusion period, 2808 were excluded as other drugs or ethanol also had been taken. The included cases were categorized as involving unspecified opioids (only), long-acting opioids (buprenorphine and/or methadone, including combinations with other opioids except unspecified opioids), and heroin (only). Another 47 overdoses with opioids or combinations of opioids not categorizable into these three groups were excluded.

The three opioid groups were compared on observation time, Glasgow Coma Scale (GCS), vital signs, naloxone administration, and transfer to hospital. Statistical analyses were done using SPSS 27. Continuous variables were compared using Kruskal–Wallis test. Categorical variables were compared using chi-square test, or Fisher’s exact test when >20% of the cells had an expected count <5.

Results

In total 2381 opioid overdoses were included. Median age among the patients was 38 years (interquartile range 31–46), 1892 (79.5%) were males. There were 459

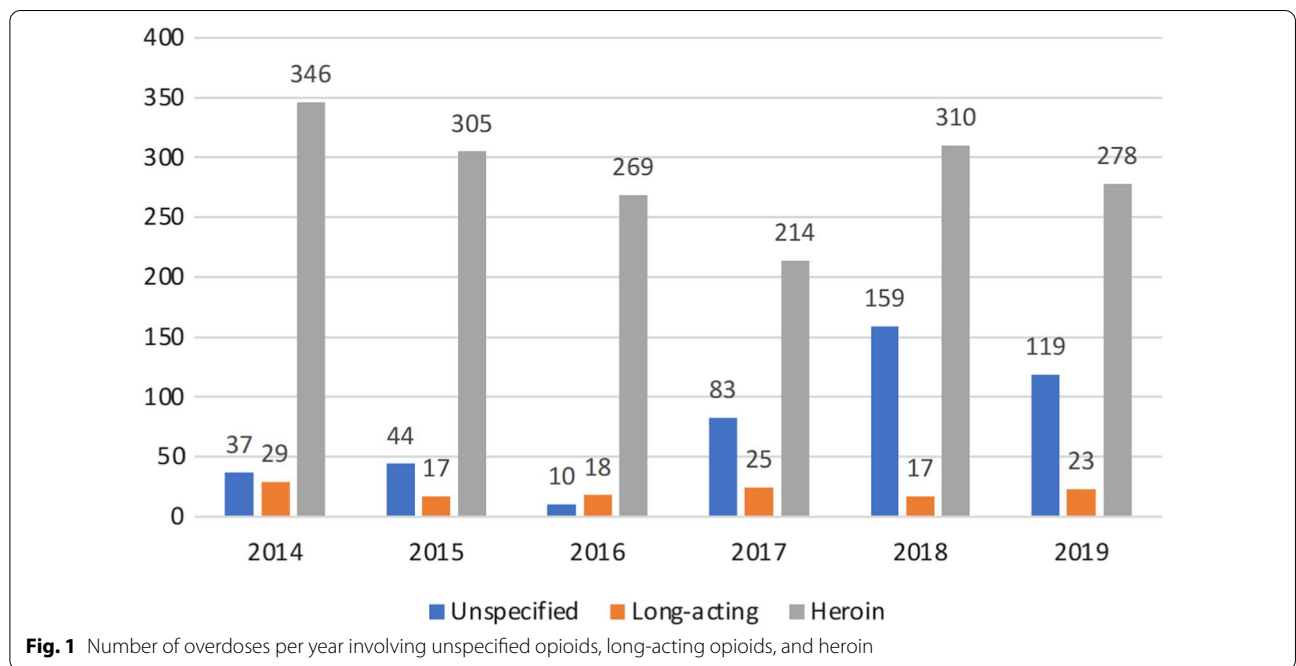


Table 1 Characteristics of overdoses involving unspecified opioids, long-acting opioids, and heroin

	Unspecified opioids n (%)	Long-acting opioids n (%)	Heroin n (%)	p-value for comparison across all three groups	p-value for pairwise comparisons		
					Unspecified vs. long-acting	Unspecified vs. heroin	Long-acting vs. heroin
Males	369 (80.4)	99 (73.9)	1424 (79.6)	0.24			
Age (years) ^{a,b}	39 (33–46)	44 (36–51)	38 (30–46)	<0.001	0.001	0.013	<0.001
Observation time (h:min) ^a	5:29 (3:49–7:01)	4:54 (2:45–6:48)	4:49 (2:48–6:16)	<0.001	0.070	<0.001	0.37
GCS at presentation ^{a,c}	13 (10–14)	14 (13–15)	14 (13–15)	<0.001	<0.001	<0.001	0.54
Lowest GCS ^{a,d}	10 (9–13)	13 (11–14)	13 (10–14)	<0.001	<0.001	<0.001	0.46
Bradypnoea (RR < 12/min)	80 (17.4)	26 (19.4)	504 (28.2)	<0.001	0.69	<0.001	0.036
Tachycardia (HR ≥ 100/min)	51 (11.1)	14 (10.4)	277 (15.5)	0.024	0.95	0.022	0.15
Bradycardia (HR < 50/min)	9 (2.0)	3 (2.2)	45 (2.5)	0.78			
Hypertension (BP ≥ 180 mmHg)	2 (0.4)	1 (0.7)	10 (0.6)	0.90			
Hypotension (BP ≤ 90 mmHg)	21 (4.6)	5 (3.7)	72 (4.0)	0.85			
Hyperthermia (temp ≥ 39.0 °C)	5 (1.1)	1 (0.7)	16 (0.9)	0.91			
Hypothermia (temp < 35.0 °C)	66 (14.4)	15 (11.2)	149 (8.3)	<0.001	0.42	<0.001	0.33
Naloxone treatment	107 (23.3)	17 (12.7)	540 (30.2)	<0.001	0.011	0.004	<0.001
Transferred to hospital	75 (16.3)	25 (18.7)	180 (10.1)	<0.001	0.62	<0.001	0.003
Total	459 (100)	134 (100)	1788 (100)				

BP blood pressure, GCS Glasgow coma scale score, HR heart rate, RR respiratory rate, temp temperature

^a Median (interquartile range)

^b Missing data for 89 cases (unspecified 49, long-acting 3, heroin 37)

^c Missing data for 7 cases (unspecified 1, heroin 6)

^d Missing data for 401 cases (unspecified 26, long-acting 26, heroin 349)

(19.3%) cases involving unspecified opioids, 134 (5.6%) involving long-acting opioids, and 1788 (75.1%) involving heroin (Fig. 1).

Cases involving unspecified opioids had longer observation time, median 5 h 29 min vs. 4 h 54 min (long-acting opioids) and 4 h 49 min (heroin) ($p < 0.001$), and lower GCS than both other groups, median 13 vs. 14 at presentation ($p < 0.001$) and 10 vs. 13 at the lowest ($p < 0.001$) (Table 1). In overdoses involving unspecified opioids 23.3% received naloxone compared to 12.7% of cases with long-acting opioids and 30.2% of cases with heroin ($p < 0.001$). Cases involving unspecified opioids and long-acting opioids were similar to each other but differed from heroin in that a smaller proportion presented with bradypnoea, 17.4% and 19.4% vs. 28.2% respectively ($p < 0.001$), and a larger proportion

was transferred to hospital, 16.3% and 18.7% vs. 10.1% ($p < 0.001$).

Discussion

Patients treated for opioid overdose categorized as involving unspecified opioids had a lower level of consciousness and needed longer observation time than other opioid overdose patients, and as many were transferred from outpatient care to hospital admission as when long-acting opioids were involved. This indicates that the category of unspecified opioids among opioid overdoses in Oslo, Norway, encompasses a substantial proportion of opioids acting longer than heroin. The increase in the number of overdoses involving opioids other than heroin is in line with trends seen

both elsewhere in Europe and in the USA [1–3] and also in overdose deaths in Norway [9].

The increase in the number of overdoses involving opioids acting longer than heroin also underscores the importance of the recommended two-hour observation following naloxone administration. Patients overdosing on longer acting opioids have a greater risk of recurrent respiratory depression following naloxone treatment and may become in need of repeated naloxone administration. Hence, they should be observed long enough for this potential need to have manifested itself [6]. To avoid acute opioid withdrawal symptoms, which often will antagonize the patient and lead to self-discharge rather than the recommended observation, naloxone should be given intramuscularly (not intravenously) and titrated carefully until the patient breathes adequately [13].

Limitations

The study was based on clinical diagnosis of toxic agents. Toxicological laboratory analyses could have provided specific information on which opioids constitute the category of unspecified opioids. However, toxicological laboratory analyses are not regularly done at the OAEOC and were not available to us. Though the opioid toxidrome with miosis and reduced level of consciousness is easily recognizable, the lack of laboratory support for the diagnosis of specific opioids is a limitation in our study.

It is possible that some patients were observed longer because they had recurring respiratory depression. However, we did not have information on respiratory function over time. It is highly likely that patients with recurring respiratory depression also had prolonged or recurring reduced level of consciousness, which in itself would lead to longer observation. Hence, we do not think that the lack of this information alters the interpretation of our findings.

Combinations of heroin and undiagnosed benzodiazepines could also be an explanation for the longer observation time seen for unspecified opioids. In a study done at the OAEOC in 2015 with toxicological analysis of saliva samples from patients with recreational drug overdose, benzodiazepines were found in more than half the patients, though not clinically suspected [14]. In the same study, methadone was found in one out of four patients though not clinically suspected [14], confirming that long-acting opioids do occur more frequently than caught by the clinical radar.

Abbreviations

BP: Blood pressure; GCS: Glasgow coma scale score; HR: Heart rate; OAEOC: Oslo Accident and Emergency Outpatient Clinic; RR: Respiratory rate; temp: temperature.

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Not applicable.

Author contributions

ZZI, TMTN, MB and OMV conceived and designed the study. ZZI, TMTN, and OMV collected and collated the data. ZZI, TMTN, and OMV analysed the data with contributions from MB. ZZI, TMTN, and OMV drafted the manuscript. All the authors revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Data are currently not available for sharing. Several manuscripts based on the data set are in preparation. Requests concerning the data may be sent to the corresponding author.

Declarations

Ethics approval and consent to participate

The study was done as part of a quality improvement study, commissioned by the director of the Department of Emergency General Practice at the OAEOC and by the head of the Department of Acute Medicine at the Oslo University Hospital (OUH), as per the Norwegian Law on Health Personnel §26. The OUH Information Security and Privacy Office (ref no 2013/3706) assessed the study to be a quality improvement study. Hence the need for approval by an ethics committee was waived by the Norwegian ethics committee regulations for quality improvement studies. The need for informed consent from the patients was also waived by the Norwegian ethics committee regulations for quality improvement studies. Data were registered anonymously from electronic medical records. The study was performed in accordance with guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). European drug report 2020: trends and developments. Lisbon, Portugal: EMCDDA; 2020.
2. Centers for Disease Control and Prevention (CDC). Understanding the epidemic. CDC. 2020. <https://www.cdc.gov/drugoverdose/epidemic/index.html>. Accessed 2 Feb 2021.
3. Wilson N, Kariisa M, Seth P, Smith H, Davis NL. Drug and opioid-involved overdose deaths: United States, 2017–2018. *MMWR Morb Mortal Wkly Rep.* 2020;69:290–7.
4. Boyer EW. Management of opioid analgesic overdose. *N Engl J Med.* 2012;367:146–55.
5. Sporer KA. Acute heroin overdose. *Ann Intern Med.* 1999;130:584–90.
6. Clarke SF, Dargan PI, Jones AL. Naloxone in opioid poisoning: walking the tightrope. *Emerg Med J.* 2005;22:612–6.
7. Willman MW, Liss DB, Schwarz ES, Mullins ME. Do heroin overdose patients require observation after receiving naloxone? *Clin Toxicol.* 2017;55:81–7.

8. Stam NC, Pilgrim JL, Drummer OH, Smith K, Gerostamoulos D. Catch and release: evaluating the safety of non-fatal heroin overdose management in the out-of-hospital environment. *Clin Toxicol*. 2018;56:1135–42.
9. The Norwegian Institute of Public Health [Folkehelseinstituttet]. Drugs in Norway [Narkotika i Norge]. Folkehelseinstituttet. 2019. <https://www.fhi.no/nettpub/narkotikainorge/>. Accessed 4 Apr 2020.
10. Tran JV, Brekke M, Vallersnes OM. Poisonings by substances of abuse at the Oslo Accident and Emergency Outpatient Clinic 2014–18. *Tidsskr Nor Legeforen*. 2021;141:646–51.
11. Wood DM, Heyerdahl F, Yates CB, Dines AM, Giraudon I, Hovda KE, et al. The European Drug Emergencies Network (Euro-DEN). *Clin Toxicol*. 2014;52:239–41.
12. Vallersnes OM, Jacobsen D, Ekeberg O, Brekke M. Outpatient treatment of acute poisoning by substances of abuse: a prospective observational cohort study. *Scand J Trauma Resusc Emerg Med*. 2016;24:76.
13. Kim HK, Nelson LS. Reducing the harm of opioid overdose with the safe use of naloxone: a pharmacologic review. *Expert Opin Drug Saf*. 2015;14:1137–46.
14. Vallersnes OM, Persett PS, Oiestad EL, Karinen R, Heyerdahl F, Hovda KE. Underestimated impact of novel psychoactive substances: laboratory confirmation of recreational drug toxicity in Oslo, Norway. *Clin Toxicol*. 2017;55:636–44.

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