

Use of fentanyl, butyrfentanyl and furanylfentanyl as discussed on Polish online forums devoted to ‘designer drugs’

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Summary

Aim. The study was aimed to analyze information posted by users of synthetic opioids on Polish online drug discussion forums. Special emphasis was given to sources of drugs and their availability, routes of administration, dosages, expected and toxic effects.

Material and methods. 6,143 reports related to synthetic opioids, posted between 2005 and mid 2019 on three widely available popular Polish online forums devoted to psychoactive substances, i.e., <https://hyperreal.info/talk>, <https://dopek.info> and <https://forum.dopalamy>, were collected and analyzed. The article presents data on three most popular opioids, i.e., fentanyl, butyrfentanyl and furanylfentanyl.

Results. Fentanyl was the most widely used and relatively easily accessible synthetic opioid in Poland. Butyrfentanyl and furanylfentanyl were far less popular. The main source of fentanyl was diversion of medicines, notably transdermal patches. Fentanyl, butyrfentanyl and furanylfentanyl are administered orally, buccally, sublingually, intranasally, by inhalation and intravenously. Concomitant use of fentanyl and its derivatives with other psychoactive compounds increases the risk of severe adverse effects.

Conclusions. Our study contributed to a more comprehensive understanding of problems related to abuse of fentanyl, butyrfentanyl and furanylfentanyl in Poland. In the light of the relatively high popularity of pharmaceutical fentanyl used for non-medical purposes, there is an urgent need for more strict control over illegal sales of fentanyl transdermal preparations via the Internet, as well as disposal of used patches. Furthermore, patients using fentanyl should be warned that giving it to another person is against the law, and may lead to development of addiction and other serious health consequences. It is important to educate the society in order to increase awareness of the problem of opioid use, especially by young people, and to pay attention to signals which may indicate addiction among family members.

Key words: fentanyl, butyrfentanyl, furanylfentanyl

Introduction

Recent years have seen a rapid and continuous growth in the availability and use of new psychoactive substances (NPS), in Poland called ‘*dopalacze*’ (‘boosters’). According to the United Nations Office on Drugs and Crime (UNODC) NPS is defined as “a new narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the United Nations drug conventions, but which may pose a public health threat comparable to that posed by substances listed in these conventions” [1]. As a result of the latest amendment to the Act on counteracting drug addiction [2], the term of new psychoactive substances applicable in Poland has been updated and it is now complementary to the cited above. Between 2009 and 2018 a total of 899 NPS were reported to the United Nations Office for Drugs and Crime [3]. In line with these data, in the years 2005–2018, the European Union Early Warning System notified the appearance of 687 NPS, of which 55 were observed in 2018 [4].

NPS is a heterogeneous group of natural, semi-synthetic and synthetic compounds. Based on psychopharmacological activity, six major categories of NPS may be distinguished:

1. Synthetic cannabinomimetics (synthetic cannabinoids) that mimic effects of cannabis.
2. Psychostimulants and empathogens, whose effects are similar to those of amphetamine, cocaine and 3,4-methylenedioxymethamphetamine (MDMA, ecstasy).
3. Hallucinogenic/psychedelic compounds acting in a way similar to LSD or phenylclidine.
4. Synthetic opioids mimicking effects of morphine and heroin.
5. New benzodiazepine derivatives (so-called designer benzodiazepines) with sedative and hypnotic effects.
6. Other, not classified into any of the above groups.

The most popular and also the largest groups of NPS are cannabinomimetics and synthetic derivatives of cathinone, a natural alkaloid found in the leaves and young shoots of *Catha edulis* with psychostimulatory effects [3, 4].

Between the years 2009–2018, 49 new synthetic opioids were identified in Europe, out of which 11 were detected for the first time in 2018 [4]. This group includes primarily fentanyl – non-medical use – and its derivatives, and to a lesser extent compounds with different chemical structures (e.g., desomorphine, MT-45, AH-7921 and its analogues: U-47700 and U-49900) [5–10]. Despite the fact that synthetic opioids are currently a relatively small group of NPS, due to their high potency and rapid action, they pose a particularly great threat to health and lives of their users.

Many people use ‘designer drugs’ because they are easily available, relatively cheap, they foster social bonding and belonging, and their actions are similar to effects caused by psychoactive compounds under legal control. Other important factors are

curiosity, search for novel and exciting adventures as well as negligible knowledge on harmfulness of NPS. Moreover, a growing popularity of NPS would not be possible without the Internet. Social networking services, discussion forums and blogs constitute an important platform to share information on reliable online shops, new compounds, effects of drugs and harm reduction actions [11]. Dynamic appearance of new derivatives with unknown biological activity, as well as the fact that they are very difficult to detect by standard toxicological methods, make NPS particularly dangerous drugs.

Monitoring information posted on websites, online discussion forums and blogs plays an important role in tracking not only changes in the narcotic drug market in response to implementation of new legislative acts, but also new areas of interest among NPS users. Therefore, the aim of our study was to analyze information posted by users of synthetic opioids on Polish online discussion forums devoted to psychoactive compounds. Special emphasis was given to sources of drugs and their availability, routes of administration, dosages, expected and toxic effects.

Methods

Posts on the 'recreational' use of synthetic opioids, fentanyl and its derivatives, desomorphine, U-47700 and AH-7921, found on three easily available Polish websites devoted to psychoactive compounds: <https://hyperreal.info/talk>, <https://dopek.info> and <https://forum.dopalamy.com>, were collected and analyzed.

Each of the websites has separate discussion forums for specific groups of drugs. The total number of reviewed posts was 6,143, of which 5,682 were placed on <https://hyperreal.info/talk>, 397 on <https://forum.dopalamy.com>, and 64 on <https://dopek.info>. Posts representing all kinds of discussions not related to the topic of the study, and posts containing potentially unreliable information were excluded. In total, 5,835 posts from the years 2005–2019 were qualified for the analysis. The article presents information on three compounds, which most frequently appeared on the forums, i.e., fentanyl (3,241 entries), butyrfentanyl (992 entries) and furanylfentanyl (748 entries).

Results

Users of Internet drug forums were mainly young adults, aged between 15 and 35 years (with a predominance of men). A part of them declared the status of a student or a short professional internship. Some forum users published content citing their own experience and belief in knowledge in the field of chemistry, pharmacology and pharmacodynamics of psychoactive substances, and possible interactions of these drugs with food and other biologically active compounds.

Entries available on the three popular Polish Internet forums devoted to psychoactive substances indicate that the first synthetic opioid used for non-medical purposes,

around 2005, was fentanyl, while interest in its synthetic derivatives appeared a few years later –butyrfentanyl in 2012 and furanylfentanyl in 2015.

Sources and forms of fentanyl, butyrfentanyl and furanylfentanyl used as drugs of abuse

Fentanyl

Analysis of posts demonstrates that fentanyl was the most widely used and relatively easily accessible synthetic opioid in Poland. Available sources of fentanyl used for non-medical purposes include illicit production by clandestine laboratories and diversion of medicines. There are several formulations of medicinal products containing fentanyl. From the published texts it appears likely that forum users utilized mainly fentanyl derived from transdermal preparations (Fentanyl transdermal patches – FTP). Single posts reported using injectable formulations and sublingual tablets. On the Internet forums, there are numerous posts describing methods of obtaining fentanyl from patches, doses used, routes of administration, effects, as well as attempts to discontinue use of this compound. According to the users, advantages of fentanyl are its relatively easy access and quick action, while disadvantages include short action and a need to extract the substance from the patches.

There are two main types of transdermal patches currently available that differ in their formulations [11]:

- (1) First generation FTP. The patch has a reservoir containing fentanyl in hydroxyethyl cellulose gel. The reservoir is placed between two functional layers – polyester, water impermeable, and semi-permeable polyacrylic adhesive layer.
- (2) Second generation FTP (matrix patches), where fentanyl is suspended in a gel matrix sandwiched between two silicone adhesive layers.

Pharmaceutical fentanyl used for non-medical purposes mainly derives from the first type of patches. Only few posts described use of fentanyl from matrix patches.

The following options of getting fentanyl transdermal patches emerge from the posts:

- (1) From family members who use/used the preparation.
- (2) From relatives of deceased patients who used fentanyl patches.
- (3) Extorted/counterfeit prescriptions – users share symptoms they should report when visiting a medical doctor in order to obtain a prescription for a desired preparation.
- (4) Used patches, the source of which may be, for example, improperly sealed containers for medical waste in hospital departments.
- (5) Purchase from individuals via the Internet; expired patches are often bought.

Transdermal patches differ in contents of fentanyl (dose release: 25 µg/hr, 50 µg/hr, 75 µg/hr or 100 µg/hr). Users, assuming a homogeneous distribution of

the substance in the preparation, freeze a patch, and then divide it into a required number of pieces to take a desired dose of fentanyl once. They spend a lot of time learning how to increase the bioavailability or efficiency of fentanyl extraction from the patch. They share information on physicochemical properties of the preparation. Few posts reported that in transdermal patches fentanyl is present as a free base bound to the matrix by either ionic or covalent bonds; only ionically bound fentanyl is released from the patch.

Butyrfentanyl and furanylfentanyl

Another compound that has gained a relatively high popularity among synthetic opioid users is butyrfentanyl, commonly known as BF or B-F. Unlike fentanyl, butyrfentanyl is available from illegal sources only. It comes in the form of colorless, crystalline substance with a smell of butyric acid. The drug is also available as a water soluble hydrochloride salt. According to the users, butyrfentanyl can also be purchased in a form of a triturate (1:10 or 1:100) with lactose or glucose, a triturate with codeine or caffeine, a triturate with cyclodextrin (an excipient used in a drug formulation technology in order to increase the solubility of an active substance), blotters, crushed dried coltsfoot leaves presoaked with opioid solution in organic solvents and used for smoking (so-called *maczanka*), as well as solutions in propylene glycol and glycerine that are used as liquids for e-cigarettes.

According to reports, furanylfentanyl, abbreviated to Fu-F, is available on the drug market as a white powder, collectable tablets (so-called triangles), solutions, a triturate with dextromaltose, nasal sprays, and in a form of '*maczanka*'. Furanylfentanyl-containing products are illegally sold as *China breath* (used intranasally or sublingually), *China Vapor liquid* (for e-cigarettes) and *FufBrownie*, which according to users '*treats well*' symptoms of withdrawal (jargonly referred to as '*skret*', 'roll-up'). Some forum users shared the composition of hand-made '*maczanka*', for example, dried coltsfoot leaves, 200 ml of spirit, 300 ml of water and 500 mg of furanylfentanyl, powder or triturate.

Routes of administration

Fentanyl

For non-medical purposes fentanyl is taken orally, sublingually, intranasally, intravenously, by inhalation, and on chills mucosa. Sporadically patches were applied directly on the skin. Forum users compared among themselves properties of various preparations, in particular effectiveness with which they can extract the active substance from patches. A subjective assessment of the potency of fentanyl is used as a measure of extraction's efficiency.

Analysis of the posts revealed the following ways of oral administration of fentanyl present in patches:

- (1) Placing a removable protective layer of a patch on the cheek mucosa, so both the outer layer and the layer containing fentanyl are directed to the inside of the mouth. The applied patch is being held for about 20 minutes. After that one can chew the patch. Several users pointed to a bad taste of patches, due to presence of different excipients that were added during the patch formulation process, and potential toxic effects of these compounds. However, the above-mentioned disadvantages did not discourage them from this route of fentanyl administration.
- (2) Squeezing out the content of a patch onto the tongue. This is usually done after drinking warm water in order to dilate blood vessels in the mouth and subsequently increase the absorption of the active substance. It is recommended to not swallow saliva or chew the patch during application.
- (3) Another way of oral administration of fentanyl is to soak a piece of paper with gel from the inside of the patch system. The blotter obtained this way is applied under the tongue; after 10 min it should be chewed.

To increase bioavailability of orally applied fentanyl, use of lozenges containing choline salicylas was often recommended.

Fentanyl can also be taken by inhalation. Users called this method 'vaporization'. A frozen patch is cut into pieces, placed on an aluminum foil and heated. Effects of inhaled vapors appear rapidly but are short-lasting. The inhalation route was the least frequent method of administration of fentanyl. Many users claimed that they had not obtained the full expected activity of fentanyl, and a valuable substance was wasted.

Fentanyl can also be used intravenously. To prepare injectable solutions of the drug transdermal patches are used. Some users injected fentanyl up to 12 times a day.

For extraction of fentanyl contained in patches the following solvents, each containing citric acid, are used:

- (1) sterile water for injection;
- (2) methanol or ethanol;
- (3) dichloromethane;
- (4) hot acetone.

After evaporation of the organic solvent extracts are dissolved in water. Sodium bicarbonate is used to adjust pH of the resulting solution to 5. Because of easy and cheap access to reagents, extractions with sterile water, methanol or ethanol are the most popular methods. In the case of ethanol extraction, several users wrote that as fentanyl dissolves very well in alcohol, there is no need to use citric acid and convert the drug into a soluble fentanyl citrate.

Preferred injection sites are deep veins, so a puncture site is not visible. Long-term (8–10 years) users of fentanyl often inject it into veins located on feet. Syringes for injection of insulin are often used. Fentanyl administered intravenously acts rapidly. “I hit what I had from yesterday’s extraction [a minute ago] and there is a kick, but it is different, these are not pin heights, but just a little shallower with slight dizziness”. Users of fentanyl warned others not to inject the next dose of the drug and calmly wait for the onset of the first one, which appears after 2–3 minutes. For those who plan to start using fentanyl, forums users recommended an initial dose of 1/200 patch, which corresponds to 50 µg of fentanyl. Moreover, they shared information about the usual single doses of 50–100 µg, and the maximum doses – 150–200 µg, warning each other that one should be very careful when taking such doses.

To increase effects of fentanyl users sought how to decrease its metabolism. One option is to ingest an extract from grapefruit seeds, which contain naringin, a flavonoid glycoside – inhibitor of CYP3A4.

Butyrfentanyl

Analysis of the posts indicates that inhalation was the most common route of butyrfentanyl administration. For inhalation, a glass pipe (so-called methpipe) is used, or one may smoke homemade cigarettes. Vapors accumulated above the heated aluminum foil were rarely inhaled because they often cause a severe irritation of the throat. For vaporization, e-cigarette heaters and hot electric bulbs were also used. Potent effects were reported after inhalation of vapors formed during heating of a pure substance or triturate with caffeine or levamisole. Use of triturates with sugars was discouraged because “... they caramelize and char too quickly for bf to sublime from them at an appropriate concentration.”

Other reported routes of administration of butyrfentanyl are as follows:

- (1) Oral administration. According to the users, butyrfentanyl should be taken orally under fasting conditions, as the presence of food in the gastrointestinal tract reduces its bioavailability.
- (2) Intranasal administration (sniffing). The users noted that butyrfentanyl is a strong irritant. In the case of dry mucosa, it was recommended to moisten it with a saline or sea salt solution.
- (3) Buccal administration (butyrfentanyl free base). To reduce dilution of the drug by saliva, forums users recommended use of 1–2 tablets of a medicine containing hyoscine butylbromide, an antagonist of muscarinic cholinergic receptors, one hour before the planned consumption of butyrfentanyl. They mixed ethanol and a triturate of butyrfentanyl with lactose (the sugar does not dissolve in alcohol), filtered the suspension, and finally soaked a paper with obtained clear solution and administered it sublingually.

- (4) Per rectum administration, before which an enema is recommended. For this route, butyrfentanyl in the form of a triturate with cyclodextrin was commonly used.
- (5) Intravenous administration. This route is very rarely used. Solutions of butyrfentanyl have acidic properties, therefore they cause pain at the injection site.

Table 1. **Applied doses of butyrfentanyl depending on the route of administration**

| Route of administration | Doses used |
|--------------------------------------------|------------|
| Orally | 10 mg |
| On nasal mucosa | 6 mg |
| On oral mucosa | 4.5–5.1 mg |
| Inhalation (smoking of prepared cigarette) | 4 mg |
| Rectally | 7 mg |
| Intravenously | 3 mg |

The given values are based on the analysis of information included in posts.

Furanylfentanyl

Routes of administration of furanylfentanyl are the same as for butyrfentanyl, with an additional possibility of smoking, using an e-cigarette (after adding the drug to oil), or heating an alcoholic solution at a concentration of 25 mg/5 ml over an electric bulb. According to users, the effects of furanylfentanyl appear most quickly after inhalation: “feeling like I got hit in the head with a light hammer”. Coughing up a brown-gray mucus is characteristic for this route.

Table 2. **Comparison of time of furanylfentanyl action after oral and rectal administration based on information posted on the Internet forums**

| Specification | Orally | Rectally |
|-----------------|---------|-----------|
| Onset | 10 min | 3 min |
| Maximum effects | 30 min | 10 min |
| Total duration | 2 hours | 1.5 hours |

Other compounds co-used with fentanyl, butyrfentanyl and furanylfentanyl

According to reports from the drug forums, fentanyl and its two synthetic derivatives were used in combination with several other psychoactive compounds, namely:

- (1) Opioids: morphine, codeine, dihydrocodeine (DHC), 3-desmethylprodynone (MPPP), buprenorphine, methadone.
- (2) Synthetic cannabinoids, e.g., AM2201, NM2201, AB-CHMINACA.

- (3) Psychostimulatory compounds: (a) synthetic derivatives of cathinone – α -pyrrolidinopentiophenone (α -PVP), 4-fluoro- α -pyrrolidinopentiophenone (4-F-PVP), 3-fluoromethcathinone (3-FMC), 3-ethylmethcathinone (3-EMC), 3-methylethcathinone (3-MEC), α -pyrrolidinoisohexanophenone (α -PIHP), 3,4-methylenedioxy- α -pyrrolidinoisohexanophenone (3,4-MDPHP), 3-methylmethcathinone (3-MMC), 4-methylmethcathinone (4-MMC, mephedrone), pentedrone, ethcathinone, 4-methylmethoxycathinone (4-MMeOC, mexedrone); (b) amphetamine and its derivatives: 2-fluoroamphetamine (2-FA) and 3-fluoroamphetamine (3-FA); (c) ethylphenidate; (d) caffeine.
- (4) Psychedelics: 3-methoxyphencyclidine (3-MeO-PCP), 5-(2-methylaminopropyl)benzofuran (5-MAPB).
- (5) γ -Butyrolactone (GBL), a precursor of γ -hydroxybutyric acid (GHB).
- (6) Benzodiazepines – alprazolam, diazepam, midazolam, etizolam, flubromazolam, clonazepam.
- (7) Dextromethorphan (DXM).
- (8) Moclobemide – an inhibitor of MAO-A.

“I smoked a huge pipe of BF and a line 4-CMC”; “I mixed it with small amounts of gamma [GBL], sometimes with small doses of etizolam and a candy of 150 mg of 5-MAPB. B-F inhaled together with 5-MABP – brilliance”; “with ethylphenidate – pure sweetness, perfect synergy, with benzo, you know, nodding.”

Effects of fentanyl, butyrfentanyl and furanylfentanyl

Expected/desired effects of fentanyl and its two synthetic analogs were euphoria, bliss, relaxation, feeling of heat spreading through the body. “I have never experienced such euphoria as that after fent. In one moment I was wrapped in an opiate shawl. [...]. I felt that I had been waiting all my life for this day. Compared to fentanyl codeine acts like placebo, not worthwhile”; “I do prefer F, that’s the fact. Most of all the opios I know. I do not know why. Maybe because it calms me down. I have a nice ride on it, and the most important thing is that when I’m under its influence I’m not afraid, I don’t feel pain inside, something undefined, something that is monstrous, unbearable, I can’t define my feelings. I love this state, when I am on the verge of waking and sleeping after F. I have not experienced this state after any other opios.” People who often use fentanyl for non-medical purposes reported an increased need to smoke cigarettes and decreased appetite. They neglected personal hygiene and daily duties, and isolated themselves from the society. “If someone wants to cut off all stimuli from both physical and emotional realities at all costs, then fent is created for him”.

Unlike fentanyl, furanylfentanyl is characterized by “a hard entry”. Its actions were summarized by one user: “As for me, this is a kind of code 2.0 with a probability of getting the short end of the stick 200 times greater”; “For me [furanylfentanyl]

it is generally capricious, sometimes I'm satisfied after a poke, sometimes I want to smoke more..." Another user had felt down after taking furanylfentanyl and later on reported "I was laying on this soil, it was very good, nice and warm, I couldn't move at all or I didn't feel like it. My eyes were open and ghosts were flying in this forest. Of course, happiness all the time."

Many users have experienced adverse effects after using fentanyl, butyrfentanyl and furanylfentanyl, e.g., miosis, dizziness, drowsiness, somnolence ["I don't even know when those nightmarish and scary nods started (I guess that's the name of constantly waking up and falling asleep, which lasted for about an hour for me)], nausea, confusion, tachyarrhythmia, breathing problems (shortness of breath with a reduction in the number of breaths or short-term apnea), and allergic reactions in the form of urticaria and itching, which did not disappear after application of commonly available H₁-histamine receptor antagonists. It should be emphasized that respiratory depression is particularly dangerous. It develops rapidly and can be fatal within a few minutes: "After fent – you die much faster [than after heroin]". Some posts warned about a high risk of respiratory depression from combining fentanyls with GBL and benzodiazepine derivatives: "But when I think bf + benzo it reminds me when ... got off the bed and lost his breath after such a mix (bf + flubromazolam iv)." Posts also highlighted a rapid development of tolerance, especially after intravenous administration. One user reported that he initially had used 5 g of furanylfentanyl within 4 or 5 days but after some time he used 20 g within 3 days. The strong addictive potential of fentanyls was emphasized: "I don't know, but I will never free myself from f. My sick head loves it too much. Toxic, destructive love [...], it is like a mad, obsessed dance over the abyss. The bottom of this abyss is death." Another user summarized the addictive effects of butyrfentanyl with the following words: "You will become mentally addicted after just a few times. Physical addiction comes after days of continuous use and is terrible." Many users wrote that the first three days after stopping fentanyl were the most difficult. The commonly described symptoms of withdrawal syndrome were hallucinations, anxiety, vomiting, diarrhea, excessive sweating ("I've smoked 3 G [furanylfentanyl]... I have to go buy electrolytes. Sweating is terrible"), headache, abdominal pain, osteoarticular pain, and memory impairment ("Pain. Heat and cold alternately. Pain, pain and more pain, delirium, nightmares... I think I'm dying"). In order to stop the addiction, users used methadone, heroin, morphine, buprenorphine, drugs containing codeine, dextromethorphan and benzodiazepine derivatives ("a week without bf, I'm helping myself with Acodin and thiocodin...").

Discussion

The current study provides information on the 'recreational' use of three synthetic opioids: fentanyl, butyrfentanyl and furanylfentanyl, available on Polish Internet forums related to drugs. Special emphasis is given to sources of drugs under discussion, their

availability, routes of administration, anticipated and toxic effects. To our knowledge, this is the first study of this type in Poland. It is noteworthy that the three discussed opioids are under legal control [2, 13, 14].

According to analyzed posts, fentanyl was the most prevalent opioid. The drug was synthesized for the first time in 1950s by Janssen Pharmaceutica (Belgium) in a search of potent and fast acting analgesics [15]. Fentanyl is a potent agonist of μ -opioid receptors with affinity 50–100 times higher than morphine [15]. Stimulation of μ_1 receptors mediates analgesic and anesthetic properties, while stimulation of μ_2 receptors may result in respiratory depression [16]. Fentanyl formulations are used as analgesics during anesthesia and premedication, neuroleptoanalgesia (in combination with droperidol) and in the treatment of chronic pain that requires constant opioid administration during prolonged period of time and does not respond to other pain relievers [15].

The first data on the use of fentanyl for non-medical purposes dates from 1980s (California, USA) [9], while first lethal overdoses in Europe were reported in Sweden in 1990s [17]. In the following years, an interest in fentanyl and its availability gradually increased in other European countries. Due to fentanyl overdose, 1,100 people died in Estonia in 2005–2013, 180 in Sweden in 2006–2013, 160 in Germany in 2007–2011, 40 in Finland in 2008–2010, and 70 in the United Kingdom in 2007–2012 [10]. It is considered that fentanyl is responsible for the recent opioid crisis in the USA and Canada [18, 19]. The drug is also abused in Poland [20].

For non-medical use fentanyl is obtained from illegal producers (Illicitly Manufactured Fentanyl – IMF) or from medications (Pharmaceutical Fentanyl – PF) [21–23]. Research conducted in March 2019 by the Australian Institute of Criminology, in which availability of fentanyl on six drug markets in darknet was analyzed, revealed that more than 40% of offered fentanyl was in the form of transdermal systems, 26% as a powder and 24% in the form of tablets, while solutions and intranasal aerosols were offered less frequently [24]. On the drug market fentanyl is often labeled as *Apache*, *China Girl*, *China White*, *Dance Fever*, *Friend*, *Goodfellas*, *Jackpot*, *Murder 8*, and *Tango & Cash* [8, 21]. In Poland, fentanyl is commonly named *China White* or *synthetic heroin*. Fentanyl is also obtained from pharmaceutical preparations, usually transdermal patches, more often first generation ones, which contain the drug reservoir, rather than from matrix systems [21, 25, 26; current results]. It has been documented that after 72 hours of intended use a patch may contain up to 28–84% of an initial fentanyl dose, therefore its use for non-medical purposes can lead to serious toxic effects, including death [27]. It has to be emphasized that all above-mentioned ways to obtain ‘second hand’ fentanyl are illegal in Poland. In Poland, distribution of medicinal products containing narcotic substances is controlled by two legislation acts: Pharmaceutical law of September 6th 2001 [28] and the Act on counteracting drug addiction of July 29th 2005 [29]. Cited laws clearly indicate that medications containing fentanyl can be sold only in pharmacies, based on specific prescriptions. Sale via the Internet, in-

cluding resale of any prescription drug, is illegal. Moreover, according to Article 58 of the Act on counteracting drug addiction, even unpaid share of a narcotic drug is considered a crime [29]. Another essential problem is a resale of expired transdermal systems with fentanyl. The Act Pharmaceutical law does not allow sale of expired medications and, according to the regulation of the Minister of Health of February 27th 2012 [30] on detailed conditions and procedures for dealing with narcotic drugs and psychotropic substances and their category 1 precursors, their mixtures and medicinal products, spoilt, counterfeit or expired containing narcotic, psychotropic substances or their category 1 precursors, medical facility which is in possession of expired narcotic medication must inform provincial pharmaceutical inspector, secure the expired drug and hand it over for inactivation. However, this regulation does not concern expired medications that are in possession of patients and, what is important, patches that were used for the indicated time by patients in healthcare facilities. Therefore, despite of the still high content of the active substance, they constitute an unregistered medical waste.

In the USA and Canada, fentanyl for non-medical use is usually obtained from illicit manufacturers [6, 21, 31]. Some drug dealers mix it with other drugs of abuse: heroin (so-called fake heroin), cocaine, methamphetamine, MDMA as well as with alprazolam – an anxiolytic medication [6, 21, 32–36]. In European countries, fentanyl for non-medical use is obtained both from pharmaceutical preparations and illegal manufacturers [23, 25, 26].

Butyrfentanyl is an agonist of μ -opioid receptors with a potency 7 times higher than morphine [37]. Currently there are no published data on affinity of furanylfentanyl to opioid receptors, however, it is speculated that its potency is lower compared to fentanyl. Both synthetic fentanyl derivatives are not registered for treatment in humans. They are available only on the clandestine market and sold in the form of powder, tablets, capsules, blotters, liquids for e-cigarettes, and solutions for injections [23, 38–40]. In Poland, butyrfentanyl was seized for the first time in 2013 in the form of powder and powder mixed with lactose in a 1:100 ratio [38]. According to the report of the Polish Chief Sanitary Inspectorate, furanylfentanyl was present in products composed of dried plant material in various shades of green (*GUMIŚ Zielony 0.5 g (Green Gummybear 0.5 g)*, *GUMIŚ Zielony 1.0 g (Green Gummybear 1.0 g)*, *Zielony Gumiś (Green Gummybear)*, *Talizman GT 0.5 g – Ziel (Talisman GT 0.5 g – Green)*, *Talizman GT 1.0 g – Ziel (Talisman GT 1.0 g – Green)*, *Talizman Ziel (Talisman Green) imitation, Index, Talizman Motocyklisty (Biker's Talisman)*) and in combination with nicotine in products composed of green dried plant material with cut brown pieces [40, 41].

Routes of administration of fentanyl and its two derivatives listed on the Internet forums include: oral, intravenous, intranasal (application of aerosol or sniffing the powder), sublingual, rectal and transdermal administration (patches) as well as inhalation (smoking cigarettes, e-cigarettes or inhalation of vapors), and are in line with those published in the official reports and scientific journals [e.g., 6, 10, 38–40, 42–49].

Toxicological studies document that fentanyl used for non-medical purposes is often combined with ethanol, opioids such as morphine, heroin, prescription drugs (including tramadol, oxycodone, hydrocodone, buprenorphine, and methadone), other synthetic NPS opioids, cocaine, amphetamine and its derivatives, cannabinoids, benzodiazepine derivatives, antidepressant drugs, and dextromethorphan [e.g., 8–10, 17, 21]. According to scientific literature, in the majority of lethal overdoses more than one opioid was involved. In addition to fentanyl, the most frequently detected drugs in post-mortem samples were: morphine, heroin, methadone, oxycodone, hydrocodone. Recently, new drugs, including carfentanyl, acetylfentanyl, furanylfentanyl, acrylfentanyl, MT-45, and U-47700, have also emerged. Additionally, ethanol, cannabinoids, cocaine, benzodiazepines, and antidepressants were frequently detected [e.g., 5, 6, 49–63]. Analysis of entries on Polish Internet drug forums shows that fentanyls have been taken together with other psychoactive compounds: opioids, psychostimulants – mainly synthetic derivatives of β -cathinone, cannabinoids, hallucinogens, sedative-hypnotic drugs (benzodiazepine derivatives). However, the above information should be approached with a dose of skepticism because in the case of purchase from a dealer, in a stationary or online store, the qualitative and quantitative composition of the product usually differs significantly from the declared or expected one.

Toxic effects of fentanyl, butyrfentanyl and furanylfentanyl described on the Internet forums are characteristic of opioids intoxication. These include symptoms of the central nervous system depression: constriction of pupils and their low reactivity to light, dizziness, anxiety, disturbances of consciousness ranging from disorientation and excitation similar to delirium, to psychomotor retardation and coma. In some cases, especially these involving use of high doses of opioids or concomitant use of fentanyl derivatives with other central depressants (benzodiazepines, GBL), rapidly progressing respiratory depression – shortness of breath with a reduction in the number of breaths or short-term apnea – was observed. Other symptoms included cyanosis, disturbances in the function of cardiovascular system, nausea, vomiting, and excessive sweating. Many abusers developed opioid tolerance and strong drug craving. Attempts of dose reduction or cessation often resulted in the development of characteristic withdrawal syndrome in which strong nausea and vomiting, abdominal pain, diarrhea, severe musculoskeletal pain, sleep disorders (mainly insomnia), mood changes with predominant irritability and tantrums were present. Above-mentioned signs indicate a development of opioid addiction [64].

Study limitations

A significant limitation of the current study was the choice of only three Internet forums in Polish related to recreational drug use – <https://hyperreal.info/talk>, <https://dopek.info> and <https://forum.dopalamy> – as a source of information on fentanyl and its two derivatives. These forums were selected based on their popularity among drug

abusers. We acknowledge that the selection of posts for analysis suffers from limited objectivity. Data presented within the current study are based on posts of anonymous users. Therefore, it can be assumed that the personal data provided in the entries, including age, gender and educational/professional status, could not fully reflect actual data. Moreover, described effects of opioids and duration of the effects are subjective. Potency and duration of the effects as well as spectrum of produced effects depend on both a particular compound and a dose used. However, in the case of products obtained from illegal sources, their actual qualitative and quantitative composition often differs from the one declared on the label, while remaining content of fentanyl in used transdermal patches varies over a wide range.

Conclusions

The current study extends the knowledge on problems associated with synthetic opioids abuse in Poland. Fentanyl, butyrfentanyl and furanylfentanyl are used in combination with other psychoactive substances, thus increasing the risk of severe intoxication. Relatively high popularity of fentanyl obtained from transdermal patches draws attention to the necessity to counteract illegal drug distribution via the Internet, education of patients using fentanyl for medical purposes (with emphasis on the fact that the medication is prescribed for the use of a particular patient and sharing it with another person is against the law and may lead to addiction and other severe health consequences). Another issue requiring attention is a need of registered disposal of transdermal patches containing fentanyl after their intended use by patients in healthcare facilities. It is important to educate the society in order to increase awareness of the problem of opioid use, especially by young people. Special emphasis should be given to potential signs that may manifest the opioid abuse by a family member (such as pinpoint pupils, cut transdermal patches, fragments of burnt aluminum foil or plastic sachets with dried plant material or powder).

Supported by the Medical University of Lodz, Poland (503/3-011-01/503-31-002-19).

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