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Fentanyl and Fentanyl Subgroups as Chemical Weapons

Kimyasal Silah Olarak Fentanil ve Fentanil Alt Grupları

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ABSTRACT

In 2002, 130 people, including the invaders, lost their lives in a hostage rescue operation after Chechen terrorists seized a theatre in Moscow, the capital of Russia. Although remifentanil and carfentanil used by the security forces in this operation are not defined as chemical weapons by the Chemical Weapons Convention, the high number of people who lost their lives and the effect of these chemicals on the central nervous system have caused controversy in the world. In this scientific study, chemical weapons, fentanyls and sub-fentanyl groups were analysed in detail and the answer to the question of whether these opiates can be considered as chemical weapons was tried to be sought. Although the evaluation of fentanyl and its subgroups as chemical weapons is a subject of debate in the world, the fact that countries do not strictly monitor it through their own laws and do not consider it as a chemical weapon in the first place makes it unlikely that fentanyl and its derivatives can be considered as chemical weapons at this stage.

Key Words

Fentanyl, chemical weapons, chemical weapon convention.

ÖZ

2002 yılında Rusya'nın Başkenti Moskova'daki bir tiyatronun Çeçen işgalcilercelerce ele geçirilmesi neticesinde yapılan rehine kurtarma operasyonunda işgalciler de dahil olmak üzere 130 kişi hayatını kaybetmiştir. Bu operasyonda güvenlik güçlerince kullanılan remifentanil ve karfentaniller, Kimyasal Silahlar Sözleşmesince, Kimyasal Silah olarak tanımlanmamakla birlikte hayatını kaybeden kişilerin fazla oluşu ve bu kimyasalların merkezi sinir sitemine etki etmesi dünyada tartışmalara neden olmuştur. Bu bilimsel çalışmada, kimyasal silahlar, fentaniller ve alt fentanil grupları detaylıca incelenerek bu opiatların, kimyasal silah kategorisinde değerlendirilip değerlendirilemeyeceği sorusunun cevabı aranmıştır. Hernekadar fentanil ve alt gruplarının kimyasal silah olarak değerlendirilmesi dünyada tartışılan bir konu olsa da, ülkelerin ilk olarak bunu kendi yasaları vasıtasıyla sıkı bir şekilde takip etmemesi ve daha en başta kendileri tarafından kimyasal silah olarak görmemesi, fentanil ve türevlerinin şu aşamada kimyasal silah olarak değerlendirmesini pek mümkün kılmamaktadır.

Anahtar Kelimeler

Fentanil, kimyasal silahlar, kimyasal silahlar sözleşmesi

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INTRODUCTION

Although the use of chemical weapons on the battlefield is associated with the First World War, the first uses date back to prehistoric times. Although the widespread use in World War I did not continue in World War II, these chemicals have always been of interest to terrorist organisations. Following the use of these weapons by a terrorist organisation in Japan in 1994-1995, these chemicals were widely used first in the Iran-Iraq war and then in the Syrian civil war. Following the use of these weapons in Syria in 2013, in which more than 1,500 civilians lost their lives, public attention has turned to these weapons. The Chemical Weapons Convention defines these chemicals and their classes. Under this Convention, fentanyl and synthetic opioids are not classified as chemical weapons. However, in the same convention, both chemicals used to kill are recognised as chemical weapons.

Fentanyl is used as a post-operative analgesic and as a sedative for patients requiring mechanical ventilation and can be sold with a red prescription. However, the use, trafficking or possession of fentanyl in our country, except for therapeutic purposes, is a criminal offence under Article 191 of the Turkish Penal Code. In addition, our country includes fentanyl in the banned list of the European Union's early warning system. Opioid use is an increasing trend in the world and unfortunately it is also increasing in Turkey. In 1990, illegal opioid use was 580,000 people, while in 2017 this number reached 1.11 million people. In this respect, illegal use of opioids is an increasing problem for our country [1].

In particular, the seizure of a Moscow theatre by Chechen militants in 2002 and the subsequent use of fentanyl and fentanyl subgroup chemicals in the rescue operation, which resulted in a high rate of deaths, has generated considerable controversy. While Russia and Russia-supporting countries see this operation as a legitimate intervention by the Russian Federation, the United States and other allied countries argue that the fentanyl and fentanyl subgroup chemicals used in this operation should be considered a weapon of mass destruction due to their effects on the central nervous system and high mortality rate.

In this study, we aim to provide detailed information on chemical weapons, fentanyls and fentanyl subgroups in the light of the literature and to clarify whether these opiates can be considered chemical weapons.

History of Chemical Weapons

Chemical weapons have been used as a tool of warfare since the earliest days of mankind. The oldest known uses of chemical agents are poisons produced from animals or plants and applied to the tips of arrows. These poisons were also used to poison water sources and the food of enemy forces[2].

Prehistoric Uses

During the Byzantine invasion, the Byzantines used "Greek Fire", a weapon made of a mixture of red-hot coal, sulfur and pitch, at the battle of Pelonope in 668 BC [3].

There is also information in the literature that in 256 BC, during the siege of the Persian city of Dura Europos (modern Syria), a mixture of tar and sulfur was used to produce sulfur oxide and thus take control of the city [4].

Uses During the First World War

The "Great War" marked the beginning of a new era in military history, not only with the production and use of trenches, machine guns, tanks, the use of artillery on an unprecedented scale, or the use of military aviation and submarines, but also with the massive and systematic use of chemical weapons on an industrial scale for the first time in history [5]. In total, 124,000 tonnes of chemical agents were used during the war [6].

When the United States entered the war in 1917, university chemistry departments began research to develop new chemical agents, and university medical departments researched personal protective equipment and the biological effects of chemical agents. Chlorine and phosgene became less effective in attacks as the US military produced gas masks. However, to overcome these masks, the Germans began to use mustard [7].

Uses During the Second World War

The discovery of "nerve agents", classified as organophosphate compounds, during the Second World War completely changed the course of chemical warfare. German chemist Gerhard Schrader discovered a highly toxic organophosphate chemical while working for a German pesticide company and named it Tabun [8]. The Germans then assigned Schrader to a secret military research facility to develop new chemical agents [9]. Schrader and his team discovered a much more deadly nerve agent and named it sarin [10].

During the Second World War, Germany produced several thousand tonnes of tabun and smaller quantities of sarin. Although Germany was the only country to have stockpiles of nerve agents in World War II, it never attempted to use them, partly because the German military was under the impression that the British were also developing their own production of nerve agents. As a result, chemical weapons were not used in Europe during the Second World War [11]. However, the Germans continued to produce and stockpile large quantities of nerve gas during the war [12].

The Recent Uses of Chemical Weapons

The 1980s saw a significant increase in the use of chemical weapons on the battlefield. In 1980, Iraq used chemical weapons to attack Iran. Shortly after the end of the Iraq-Iran war in 1988, Saddam Hussein, the leader of the Iraqi regime, used various chemical weapons against the Kurdish minority in Halabja, resulting in the deaths of some 5,000 people and many other consequences [2]. In March 1995, members of the Aum Shinri Kyo cult carried out a coordinated attack with the nerve agent Sarin (GB) in the Tokyo subway system, after failed attempts to use biological agents. More than 5500 people were treated and a dozen died. Aum Shinri Kyo also used sarin in an attack in Matsumoto 9 months earlier, killing more than 300 people, and attempted to assassinate judges who opposed their cause, killing 7 [13].

The Gulf War was another conflict in which chemical and biological warfare was expected but never used. After the invasion of Kuwait and Operation Desert Shield, which led to the imposition of UN sanctions, Iraq's chemical weapons and ballistic missiles attracted the most attention. Having used these weapons and missiles extensively in the Iran-Iraq War, Iraqi forces had unrivalled experience in the use of various chemical agents, particularly mustard gas and nerve gas, but these weapons were not used in the Gulf War [14].

In August 2013, approximately 1500 people lost their lives as a result of a chemical weapons attack in the Ghouta region of Syria. This attack provoked a major response from the international community and resulted in Syria signing the Chemical Weapons Convention and destroying its chemical weapons through the Organisation for the Prohibition of Chemical Weapons [15].

Properties of Chemical Warfare Agents

Chemical warfare agents (CWAs) are highly toxic chemical substances used to incapacitate people by killing or injuring them, to incapacitate people by impairing their abilities, to destroy plant and animal food sources and contaminate food supplies, to disable economically important targets, to reduce mobility by forcing military and civilian personnel to wear protective equipment, and to cause terror and panic. Chemical warfare agents exist in all three states of matter. They have a wide range of densities and vapour pressures. They can enter the body through the gastrointestinal tract, the respiratory tract, the mucous membranes or the skin [16].

Exposure to these chemicals can cause temporary and permanent damage and sudden or delayed death, depending on the concentration. The use of chemical agents is intended to target the organs within the living organism, causing loss of organ function and ultimately neutralising the target population. The greater the volatility of the chemical agent used, the more likely it is to be dispersed into the environment and cause harm to humans or other living organisms [17].

Nerve Agents

Nerve agents were synthesised by both German and British scientists in the 1930s during World War II, and Germany produced and stockpiled these highly toxic substances during the war. In the later stages of the war (1944-1945), German military scientists produced large quantities of tabun nerve agents [18]. Other common nerve agents developed for use as chemical warfare agents were sarin and VX. All nerve agents share the same toxic principle. Nerve agents were also used in the Iran-Iraq war (1980-1988) and in two major terrorist attacks in Japan in the mid-1990s [19].

Blister Agents

Blistering agents are recognised as the most widely used chemical agents during World War I. Blister agents or vesicants are chemicals that usually cause blisters, swelling and inflammation and general destruction of tissues. Their effects are mainly major irritation of the skin, eyes and respiratory tract of the liquid or vapour forms. In addition, high absorption of the liquid form through the skin or the vapour form on inhalation can cause significant systemic effects [20].

Sulphur mustard is a relatively cheap and simple compound to produce, making it a possible Chemical Warfare agent. On the other hand, mustard is not as lethal as nerve agents and therefore has not been a chemical sought after by terrorists. Mustard has been considered the king of Chemical Warfare agents, at least until the development of more highly toxic nerve agents. Mustard is a fairly thick or viscous liquid at room temperature and is less volatile than water [19].

Choking Agents

Chemical substances, more accurately known as 'lung irritants', are classified as suffocation agents. Chlorine, phosgene and diphosgene agents belong to this category. As choking agents were the first to be used as chemical warfare agents, they are also referred to in the literature as 'first generation chemical warfare agents'. Their mechanism of action is to cause oedema in the lungs by targeting the lungs. Phosgene and diphosgene agents show late effects. Phosgene agents were responsible for most of the deaths in World War I. As such agents are often used in industry, they can also be included in the class of industrial hazards [21].

Chemicals classified as asphyxiants act on the lungs, causing breathing difficulties and possibly permanent lung damage. Asphyxiants are usually gaseous, have a distinctive odour and can colour the surrounding air. Asphyxiants were manufactured for use in warfare and were widely used during World War I. The first major successful chemical attack of the war was the chlorine gas attack at Ypres in 1915 [22].

Blood Agents

These chemicals, defined as blood poisoning agents, bind to oxygen-carrying cells in the blood and prevent oxygen from reaching target tissues. As the organs are not supplied with sufficient oxygen, death eventually occurs [23].

Blood poisons and cyanide are agents that work by causing 'histotoxic anoxia'. Cyanide binds to the active site of cytochrome c oxidase, preventing cells from using oxygen to produce adenosine triphosphate (ATP). The cells are therefore forced to switch to anaerobic metabolism. Cyanide can be used as a chemical agent in 2 different chemical forms. These are hydrocyanic acid and cyanogen chloride. The volatility of cyanide makes it difficult to weaponise. Cyanide can be found as a gas or a colourless liquid. It has a classic 'bitter almond' odour, but about half the population cannot identify this odour [24].

Riot Agents

Riot suppressants are used to reduce the fighting capacity of soldiers by inducing vomiting. In civil disturbances, vomiting agents are also used to control riots. A typical example of an emetic is adamsite, an arsenic compound. Adamsite was used by the British in the First World War, in the United States in 1932 for riot control, and again during the Vietnam War. For riot control, Adamsite was eventually replaced by the tear gas CS with the chemical name [(2-chlorophenyl)methylidene] propandinitrile. It is also known as 2-(2-chlorobenzylidene)malononitrile, 2-chlorobenzylmalononitrile or o-13-chlorobenzylidene malononitrile. Another commonly used riot control agent is chloroacetophenone [25].

Riot Agents are defined in the Chemical Weapons Convention as agents used to prevent the target population from performing its functions by impairing the senses and whose effects disappear within a short time after exposure. Effects are usually observed within seconds of exposure and disappear within 15-30 minutes if the exposed person is removed from the source and decontaminated. The category of riot control agents in the Chemical Weapons Convention has been the subject of long debate. It was decided that countries should notify the OPCW of the chemical weapons they possess for the protection and enforcement of their laws, and that their use for warfare purposes should be prohibited. As a result, such agents are not included in the schedules of the Chemical Weapons Convention [26].

Incapacitating Agents

Incapacitating agents are usually used for their non-lethal adverse effects and can be lethal at very high doses. Through their transient psychological and mental effects, these agents incapacitate the target population by impairing their behaviour [27].

The term 'incapacitating agent' is understood in different ways, depending on the context in which it is used. There is no consensus among experts and policymakers as to whether efforts should be made to incorporate a definition of incapacitating agent in the context of a definition in this Chemical Weapons Convention. The basis of the Convention is a definition of 'chemical weapon' based on the concept of 'toxic chemical'. This is then defined as "any chemical which, by its chemical action on life processes, is capable of causing death,

temporary incapacity or permanent damage to man or animals". Conversely, 'chemical weapons' are defined as Toxic chemicals and their precursors, except those intended for purposes not prohibited by this Convention, are chemical weapons as long as their nature and quantity are consistent with such purposes. States Parties may use toxic chemicals for purposes not 'prohibited' under the Convention, including for law enforcement purposes, including the control of local insurgencies. It should be emphasised, however, that incapacitating agents are covered by the Convention's definition of 'toxic chemicals' and are designated as chemical weapons when used for this purpose [28].

Incapacitating agents are not generally used to kill, although they can have lethal effects when used in large doses. The purpose of using these substances is to produce temporary and non-lethal effects and to temporarily incapacitate the target or targets, preventing them from carrying out their normal activities. People exposed to these substances experience temporary mental and psychological effects. Lysergic acid diethylamide (LSD), fentanyl and ketamine produce these effects, but the OPCW does not consider these substances to be chemical warfare agents [29]. Information on fentanyl, which is included in this category, is provided in the following sections.

MATERIALS and METHODS

In this section, fentanyls and fentanyl subgroups were investigated in detail, an incident in Moscow in which these chemicals were used was evaluated in detail and it was analysed whether these chemicals could be used as chemical weapons.

Fentanyl

Unlike most classical chemical warfare agents, fentanyls are generally not gases or liquids at room temperature. They are solids used in human and veterinary medicine for their general anaesthetic and analgesic properties. However, if misused outside the clinical setting and without medical assistance, they can be as lethal as organophosphorus nerve agents. A small number of fentanyls are produced worldwide and these are usually manufactured and marketed on a batch basis on a kilogram scale. Fentanyls have the potential to be used in both medical and military operations to incapacitate an opponent and cause harm [30].

Fentanyl, a potent synthetic mu(μ) opioid receptor stimulating opioid, was first synthesised in December 1960 by Dr Paul Janssen and the Janssen Company in Beerse, Belgium. The drug was first used as an intravenous analgesic in Europe in 1963 and in the United States in 1968, and has since become one of the most important and widely used opioid analgesics in the world [31].

New synthetic opioids (NSOs) such as fentanyl, fentanyl derivatives and emerging analogues have become increasingly available on the recreational drug market worldwide in recent years. Fentanyl is a synthetic phenylpiperidine with analgesic and narcotic properties. It is available as a stand-alone product, as an additive to heroin, cocaine and amphetamines, or as a component of illicit prescription drugs. In addition to fentanyl and fentanyl analogues such as carfentanil, acetylfentanyl, butyrylfentanyl and furanylfentanyl, a large number of other potent NSOs have recently appeared on the illicit drug market. Most of these have chemical structures that are not similar to morphine or fentanyl, but are active at the μ-opioid receptor [32].

Janssen and colleagues modified the structure of fentanyl to produce carfentanil in 1974 (which entered veterinary practice in 1986), sufentanil in 1974 and alfentanil in 1976 [30].

Sufentanil is a new synthetic opioid that is approximately 5-10 times more potent than fentanyl and has a therapeutic index in rats approximately 100 times greater than fentanyl (25,000 versus 277). Sufentanil, a carfentanil derivative, is approximately 5,000 times more potent than morphine and has an analgesic therapeutic index (greater than 25,000) that is even higher than that of carfimtanil. Alfentanil is another new narcotic analgesic. It is a quarter more potent than fentanyl and has a shorter half-life. It also has a high therapeutic index in rats. These effects have shown that the drug can be used as an induction or augmentation of anaesthesia, particularly in patients undergoing short surgical procedures. Studies in dogs showed little change in haemodynamics with moderate doses (160 μg/kg) of alfentanil, while very high doses (5 mg/kg) caused transient cardiac stimulation (increase in left ventricular contractility, aortic blood flow velocity and acceleration). Heart rate, cardiac output, and pulmonary and systemic vascular resistance also increased after 5 mg/kg alfentanil [33].

Since 2015, there has been a significant increase in the role of synthetic opioids, most commonly fentanyl and fentanyl analogs, in opioid-related overdose deaths due to the opioid crisis in Canada and the United States [34].

Fentanyl is a synthetic opioid analgesic used both for pain relief and as an anaesthetic. However, fentanyl and its derivatives are used illegally in many countries, and cases of poisoning and fatal intoxication are increasing worldwide due to their high potency and toxicity. In the US in 2021, 71,074 of the total 107,521 drug overdose deaths will be associated with synthetic opioids. Fentanyl and its synthetic derivatives, fentanyls, are also illegally marketed in many European countries. These drugs are often sold as heroin substitutes. The side effects of fentanyl are similar to those of heroin and other opioids, including somnolence, dependence, bradycardia, respiratory depression, loss of consciousness and others [35].

Fentanyl is absorbed by the human lung and nasal tissue. The rapid onset of narcotic effects of inhaled fentanyl is little different from that of intravenous injection. In a study investigating the effect of fentanyl aerosol on the respiratory pattern and variables in mice, the minimum ED50 and the median lethal dose (LD50) were found to be very close. Therefore, it is argued that this chemical should not be used as a performance-enhancing agent [30].

Karfentanyl

Synthesised by Janssen Pharmaceuticals in 1976, carfentanil (methyl 1-(2-phenylethyl)-4-(N-propanilino) piperidine-4-carboxylate) has become an analogue with 200 times the potency of the parent drug and 1000 times that of morphine. Although usually associated with its use in veterinary medicine as a tranquilliser for large wild animals, carfentanil has a worse reputation for its approved use during the Dubrovka theatre crisis in Moscow in 2002 and its increasing potential as a weapon of mass destruction [36].

Carfentanil is one of the most potent fentanyl analogues, with an estimated potency of 10,000 times that of morphine. It is the most common fentanyl analogue involved in overdose deaths in Ohio in 2017. Between July 2016 and June 2017, 1,236 (11.2%) of 11,045 opioid overdose deaths in 10 US states, including Ohio, tested positive for carfentanil. Tiscione and Alford also reported a significant increase in the detection of carfentanil in blood in DUI cases in Palm Beach County, Florida, USA, from 5% of cases in 2016 to 38% of cases in 2017 [37].

Sufentanyl

Synthesised by Janssen Pharmaceuticals in 1976, sufentanil has become an analogue with 10 times the potency of the parent drug and 500 times the potency of morphine due to its greater binding affinity to the μ-opioid receptor. Structurally, sufentanil, like fentanyl and carfentanil, is an achiral molecule due to the plane of symmetry passing through the centre of the piperidine ring [36].

Sufentanil is highly lipid soluble, more so than fentanyl and alfentanil. It rapidly crosses the blood-brain barrier and equilibrates with the cerebrospinal fluid, resulting in a rapid onset of action. The analgesic effect is rapidly offset by rapid redistribution to fat and skeletal muscle. The volume of distribution, distribution half-life and elimination half-life of sufentanil are between those of fentanyl and alfentanil.108 More than 90% of sufentanil is protein bound. The shorter elimination half-life is due to the smaller volume of distribution and greater hepatic mobilisation. Sufentanil is metabolised in the liver; the N-dealkylation products are inactive and the O-demethylation product (methylsufentanil) is active. Sufentanil metabolites are excreted in the urine [38].

Remifentanyl

Remifentanil is a μ-opioid receptor agonist with analgesic potency similar to that of fentanyl. It has been studied for analgesic efficacy in relation to the expression of the serotonin transporter (5-HTT), as serotonin may influence the antinociceptive effects of opioids in the spinal cord. It is predominantly metabolised by non-specific esterases and has a pharmacokinetic advantage due to its rapid systemic elimination and ultra-short half-life in clinical situations requiring a predictable termination of action, such as labour analgesia. Remifentanil was found to be superior in reducing mean visual analogue scale pain scores for labour pain at 1 hour. Remifentanil crosses the placenta but is rapidly metabolised and redistributed. Although maternal sedation and respiratory changes occur, there are no adverse neonatal or maternal effects [39].

Remifentanil is an ultra-short-acting opioid that is rapidly metabolised to an inactive metabolite by non-specific esterases in plasma and tissues. It has a very short elimination half-life with a binding-sensitive half-

life of only 3 minutes, regardless of infusion time. In paediatric cardiac surgery, it is an attractive alternative to fentanyl, providing intense analgesia during the most stimulating parts of surgery but without residual opioid effects, facilitating rapid recovery and weaning from mechanical ventilation. Switching to a longer-acting opioid should be considered before discontinuing remifentanil [34].

Acetylfentanyl

Another fentanyl analogue, acetylfentanyl, was not identified until 2013, after it was identified as the primary cause of ten overdose deaths in Rhode Island. Acetylfentanyl, also known chemically as N-(1-phenylethylpiperidin-4-yl)-N-phenylacetamide, is structurally simpler than fentanyl and is one carbon atom away from fentanyl. In medicine, acetylfentanyl is 15 times more potent than morphine but is not used as an analgesic. Only in 2015 did the US Drug Enforcement Administration (DEA) officially classify acetylfentanyl as a Schedule I substance. Fentanyl and acetylfentanyl are structurally quite simple, unlike other members of this class such as carfentanil and 3-methylfentanyl, so they are easy to manufacture and access using Janssen's original protocol as well as much newer, more sophisticated methods that have been published [40].

High-dose opioid use played a significant role in the fatal respiratory depression that killed 21,314 people in the United States in 2011. Acetylfentanyl, a synthetic opioid agonist of fentanyl, has recently emerged as a drug of abuse linked to numerous deaths in North America [41].

Butyrylfentanyl

Butyrylfentanyl was first reported in the scientific literature in the 1980s and was reported to be 7 times more potent than morphine in the mouse acetic acid writhing test [42].

Butyrylfentanyl, N-(1-phenethylpiperidin-4-yl)-N-phenylbu tyramide or butyrfentanyl, is a fentanyl derivative that was first reported in Poland in the summer of 2013 and then in Sweden in 2015. The Swedish cases involved patients with suspected acute exposure to synthetic opioids in 2014 who required hospitalisation; two of the four poisoning cases showed serum concentrations of 0.9 and 0.6 ng. mL-1 butyrylfentanyl, while in the others fentanyl was the more prominent opioid component. One butyrylfentanyl poisoning in the United States involved a teenager who survived an overdose but subsequently suffered from multiple conditions caused by nasal butyrylfentanyl ingestion, including hypoxic respiratory failure and diffuse alveolar haemorrhage [36].

Fentanyl and its analogues, such as butyrylfentanyl, carfentanil, 4-fluorobutyrylfentanyl and furanylfentanyl, can be added to heroin or sold as heroin [43].

Case Study Presentation: Moscow Theatre Event

The concept of rapid stunning and resuscitation for hostage rescue led to military research on fentanyl during the Cold War. Narcosis has been glamorised and even fictionalised by some countries for military intervention. Opiates and opioids are active and relatively stable when inhaled [36].

In the 1990s, fentanyl and its derivatives were investigated by the US Department of Defence as possible incapacitating agents. However, complications related to the safe dose range, i.e. the optimal dose to incapacitate rather than kill, were never resolved and the project was abandoned. Efforts were also made by the Soviet/Russian armies to develop incapacitating agents from fentanyl derivatives. Given the potency and accessibility of fentanyl derivatives, their misuse as chemical warfare agents is a potential risk [44].

On 23 October 2002, Chechen invaders seized Moscow's Melnikov Street Theatre during a sold-out performance of the musical 'North-East', taking more than 800 people hostage and demanding the immediate and unconditional withdrawal of Russian troops from Chechnya. The siege ended in the early hours of 26 October after a special unit of Russia's Federal Security Service (FSB) pumped a chemical aerosol into the building and stormed it. At least 33 terrorists and 129 hostages were killed during or immediately after the raid. The terrorists were shot dead after being knocked unconscious by the aerosol, the explosives strapped to them were removed and a bomb in the auditorium was defused. Two hostages were shot by the terrorists, while 125 others died as a result of a combination of the aerosol and inadequate medical treatment after the rescue. Medical treatment of the wounded was complicated by the Russian government's failure to disclose the composition of the aerosol. The head of Moscow's health department said that all but one of the hostages killed in the raid had died from the effects of the gas, which is believed to

be an anaesthetic or chemical warfare agent. Foreign embassies in Moscow asked for more information about the aerosol in order to facilitate treatment, but their requests were ignored. Armed guards were stationed at Moscow hospitals and doctors were ordered not to release any of the wounded. The Russian government, which refused to disclose the contents of the aerosol used, informed the US Embassy on 28 October of some of its effects. Based on this information and examination of some of the wounded, the doctors concluded that the aerosol contained a morphine derivative [37].

Paramedics attending the casualties recognised that the signs and symptoms were due to opioid intoxication. These paramedics found that naloxone, an opioid antagonist used to treat heroin overdoses, relieved the symptoms [46].

Assessment of Fentanyl as a Chemical Weapon according to the Chemical Weapons Convention

The easy availability of fentanyl derivatives is crucial for their misuse as a potential chemical weapon, as conventional chemical weapons such as sarin require highly complex systems and equipment to develop, and as seen in the Moscow hostage crisis, the inappropriate use of toxic compounds such as fentanyl derivatives can lead to disaster, even if the compounds are in good hands. This situation highlighted the grey area between lethal and non-lethal weapons and led to the discussion of CWC in relation to the potential use of fentanyl as a weapon of mass destruction (WMD) [45].

Given its chemical structure and toxic effects, fentanyl may be included in the category of 'toxic chemicals' covered by CWC. However, this assessment may vary depending on the intended use and context. Fentanyl is not listed in the Annexes to the Chemical Weapons Convention and is therefore exempt from its prohibitions. The use of fentanyl and its derivatives by security forces for riot control or hostage rescue may be justified if it is not for the purpose of warfare or killing. However, this use carries serious health risks and is subject to strict regulations [45, 47].

If fentanyl is used to harm enemy forces, it is considered a chemical weapon and is prohibited by the CWC [45, 47].

RESULTS

Chemical weapons have been used in warfare for centuries. If we look at the recent past, chemical weapons have been used by states and terrorist organisations both in our immediate geography and in distant parts of the world, with the aim of instilling intense fear on the other side. The Chemical Weapons Convention prohibits any use of chemical weapons. However, it encourages the production and development of chemicals for peaceful purposes. One of these chemicals, fentanyl and its subgroups, is widely used in medicine for therapeutic purposes. Fentanyl and its subgroups, carfentanil, sufentanil, remifentanil, acetylfentanyl, butyrylfentanyl are opioids that have a very thin border between therapeutic dose and lethal dose and can be used illegally. Although the illegal use of these opioids is prohibited by countries, the international community is debating whether these chemicals should be considered as chemical weapons. The same Convention (CWC) does not define fentanyl as a chemical weapon. However, the use of low doses of fentanyl derivatives by law enforcement officials in certain operations creates a legal grey area. The argument that fentanyl and its derivatives should be considered as chemical weapons is based on the effects of these chemicals on the central nervous system and the relative likelihood that this effect may cause other long-term effects. Such use should be subject to strict control and regulation under international law. The use of chemical agents in security operations raises serious ethical issues. The use of these substances in law enforcement operations, even to save human lives, may lead to unforeseen health risks and potentially fatal consequences.

CONCLUSION

Although fentanyl is not defined as a chemical weapon, it may be considered a chemical weapon under the Chemical Weapons Convention (CWC), depending on its intended use. While its use for medical and scientific purposes is legitimate, its use to harm military or hostile forces is strictly prohibited. However, their use in security operations should be carefully assessed from a legal and ethical perspective. The same Convention defines chemical weapons as all chemicals used for warfare purposes. For these reasons, fentanyl and fentanyl subgroups should be considered chemical weapons when used

to kill or injure. Nevertheless, it is more important for countries to control this chemical group more strictly by using their own laws than to include it in the scope of the Chemical Weapons Convention (CWC). After all, it is very difficult to consider this chemical group as a chemical weapon in an environment where all countries cannot reach a consensus on it and moreover, where countries do not fulfil their own duties.

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