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Literature Review: Effect of Exposure to Weapon Tear Gases CN, CS, and OC on Toxicity

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Abstract: Tear gas is a mixture of chemicals used for crowd control without the use of lethal weapons. Tear gas or also called lacrimator was first used during World War I which was categorised as a chemical weapon. The chemicals contained in tear gas include CS gas (o-chlorobenzylidene malonitrile), CN gas (2-chloroacetophenone), and pepper spray (OC gas, oleoresin capsicum). This research is a literature review. The use of databases in searching for articles using Google Scholar, DOAJ, and Science Direct with the keywords "Tear gas, CN, CS, OC, and Toxicity" conducted by previous studies both at home and abroad. The results of the literature review obtained some toxicity data caused by tear gas exposure which has an impact on toxicity and health. CN, CS and OC are effective lacrimating agents, the evidence of toxicity as measured by threshold time for irritation, is greatest for CN, followed by CS and OC. Typically, eye and respiratory tract irritation occurs within 20-60 seconds of exposure. Tear gas works by irritating the mucous membranes of the eyes, nose, mouth, skin and lungs. This compound causes tears (crying), and hence the gas is called tear gas. Exposure to tear gas causes short-term and long-term effects, including respiratory illness, eye disease, skin inflammation, and damage to the circulatory and digestive systems. The gas also causes sneezing, coughing, breathing difficulties, eye pain, temporary blindness, and fatality.

Keywords: Tear Gas, CN, CS, OC, Toxicity.

Introduction

The rapid development of the world creates complexity, where with a very large population it is not uncommon to cause friction between individuals and groups that lead to acts of rioting that cause security and public order to be disrupted. Law enforcement officers are needed, with a fast and precise role in handling it through measured steps according to humanitarian standards, one of which is by using tear gas weapons. Tear gas, despite its name, does not just make tears. Tear gas is a special chemical with the purpose of riot control agents, tear gas, Mace, lachrymator, and crowd dispersal gas [1].

The chemicals 2-chloroacetophenone (CN), o-chlorobenzylidene malonitrile (CS) and oleoresin capsicum (OC) are materials considered effective by law enforcement as non-lethal options for riot control, for crowd control purposes in chaotic conditions [2]. Products containing CN and CS can also be used as self-defence and protection. In recent years, OC pepper spray has become popular among law enforcement officials, having replaced CN and CS for civilian use. These tear gas chemicals are usually dispersed through aerosols, and upon exposure, they cause rapid and intense irritating effects on the eyes, nose, mouth, skin, and respiratory tract that can cause temporary incapacitation in exposed individuals [3]. Therefore, the impact of long-term exposure to these compounds, especially on human health, has been questioned by the public. The purpose of this review is to summarise and reinforce the existing scientific literature on riot control chemical agent tear gas CN, CS, and OC by highlighting tear gas content, mechanisms, dispersion, and toxicity studies.

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Materials and Methods

Study area

The literature review was conducted by searching and collecting data according to the keywords: Chemical Riot Control Agents, CN, CS, OC Tear gas, and Toxicity. The sources used were articles published in Google Scholar, DOAJ, Science Direct within 75 year (1 October 1948-1 October 2023). The bibliography of articles obtained was then screened to find additional relevant studies including reputable articles and book sources.

Procedures

This literature review uses a systematic literature review (SLR) approach. This involved identifying, assessing and interpreting all findings relating to the topic of discussion from a variety of sources. Systematic review is a term used to refer to a particular research methodology, the development of which is carried out to search, collect, and then evaluate research related to a particular topic focus [4].

The stages of the SLR method are outlined into 3 stages, namely: 1) Planning, in writing refers to the problem formulation described in the introduction, the data used in this research is secondary data, secondary data can be obtained through literature studies, related scientific articles; 2) Implementation, the application of the SLR method can help find sources. At the stage of searching for reference sources or relevant literature by using keywords, searching for journals that use English for international journals, while using Indonesian for national journals; 3) Reporting, the final stage in the SLR method where writing or analysing the results that have been sought will be made in the form of writing which is then continued in the discussion of this literature review [5].

Data analysis

This literature review analysed and identified 100 articles, excluding duplications. Furthermore, articles related to CN, CS, and OC toxicity in humans were screened and summarised to describe the mechanism of action of tear gas and the clinical features of toxicity. Articles used in this review included case reports, theoretical studies, and reviews deemed relevant. A total of 48 articles were considered relevant for review.

Results and Discussion

Tear Gas

Riot control agents are one of the methods used by law enforcement to alter crowd behaviour commonly referred to as tear gas. Tear gas is an umbrella term that refers to a number of different chemical agents that cause irritation to the eyes, nose, skin, throat, and lungs, as well as lacrimation (watery eyes) [6].

Chloroacetophenone (CN)

A substance found in Mace® products, it was originally developed towards the end of World War I, as a military and law enforcement weapon until before the Geneva convention of 1925 because it subsequently banned the use of CN in war [7]. CN has a molecular weight of 154.59. This compound has a melting point of about 58-59°C, a boiling point of 244-245°C and at 20°C has a low vapour pressure of 5.4×10^{-3} mmHg [8]. CN compounds are insoluble in water, although easily soluble in ethanol, ether, and benzene [9], [10].

Chlorobenzylidene malononitrile (CS)

Is the most commonly used tear gas today. It was synthesised in the laboratory to replace CN as the primary tear gas used by law enforcement due to its higher dispersion and lower toxicity [11]. CS has a molecular weight of 188.6 and is a cyanocarbon structure in the form of a white crystalline solid with a peppery odour with a melting point of about 93°C and a boiling point of 310°C [12]. CS has a low vapour pressure value, is slightly soluble in water and non-volatile, while soluble in acetone, methylene chloride, ethyl acetate and benzene. CS hydrolyses rather slowly in water, producing o-chlorobenzaldehyde and malononitrile [7].

Oleoresin capsicum (OC)

Is an extract from hot chillies of the genus capsicum, and is the active ingredient in pepper spray, commonly used by law enforcement. On the Scoville scale, which is used to assess the

concentration of capsaicin in chillies and spicy foods, tear gas measures about 500,000-2,000,000 Scoville units, which is 400 times greater than jalapeno chillies [13]. OC has been found to contain more than 100 different compounds, including capsaicin, which is the source of OC's irritating properties [7]. OC contains a waxy, oily substance that is combined with an emulsifier such as propylene glycol to suspend it in water. It is then pressurised to create an aerosol pepper spray [14]. OC, capsaicin (N-(4-hydroxy-3-methoxybenzyl)-8-methylnontrans-6-enamide), naturally occurring in the capsicum group of plants and bushes, with a molecular weight of 305.41. OC is an odourless, pungent white solid with a melting point of about 65°C and a boiling point of 210-220°C. CS has a low vapour pressure, is practically insoluble in water but freely soluble in alcohol, ether, chloroform and benzene [15].

Exposure Tear Gas

Tear gas is used in various ways, such as personal defence sprays or grenades or canisters. In addition, it can also be sprayed using liquid formulations released from pressurised dispensers, for powder formulations mixed with pyrotechnics used in the form of grenades and canisters [7]. A common solvent for tear gas sprays is methyl isobutyl ketone (hexone), which is also considered a hazardous material. Tear gas agents are generally dispersed as fine powder particles, e.g. in the form of smoke, through fogging systems, and in the form of water vapour generated from pressurised liquid systems (aerosolisation) [16]. According to the literature review, the terms spray and aerosol can be used interchangeably. However, there are differences between the various forms of lacrimators. Aerosols refer to materials that are airborne dispersions used to cause impact on a large number of people in an area such as crowd control, whereas sprays are usually handheld canisters that contain an active substance in solution that is then sprayed directly to immobilise a small scope of rioters [7]. There are also liquid materials that can be dispersed directly to a large number of people by adding them to water for example through water cannons or others. Devices typically used to fire tear gas are bombs, large spray tanks, grenades or canisters that can be thrown or fired as projectiles, or more flexible handheld spray devices [17].

Mechanism

The general mechanism of tear gas weapons is through the process of activating fibres in the nociceptive nerves, which function to sense damage and harmful stimuli to the body. Activation of exposed nociceptive neurons will cause a sensation of pain and itching that quickly spreads, especially in the eyes, nose, mouth, skin, and respiratory tract [16]. This activates autonomic reflex loops that cause swelling and tissue-specific responses, leading to watery eyes and coughing. In response to activation, nociceptors also locally release neuropeptides that increase inflammation at the site of activation which will exacerbate and prolong the pain and cough [18].

OC, commonly used in pepper sprays, is extracted from chillies and contains a number of other different compounds in varying amounts [7]. Capsaicin is the most abundant bioactive component in OC. In the process of work, exposure to compounds is responded to by Transient Receptor Potential (TRP) which is an ion channel involved in the detection of physical and chemical stimuli in various cell types, including sensory nerve cells, one of which activates the nonselective cation channel Transient Receptor Potential Vanilloid 1 (TRPV1) [19]. TRPV1 is a response by nociceptive nerve fibres and is sensitive to activation of TRPV1 by capsaicin which activates the same nerves at high temperatures (43°C) [20]. Thus, fibre as heat and acid, produces a burning sensation [21].

CS and CN, although both are different compounds. In their system of action, both will activate the TRPA1 receptor. TRPA1 is a cation channel similar to TRPV1 on the same sensory neurons. However, TRPA1 is activated by dangerously cold temperatures, as well as a number of environmental irritants, including chemicals in toxic air pollution, cigarette smoke, and mustard gas [22]. Activation of these receptors produces a painful burning sensation associated with touching something very cold, such as dry ice, or very cold metal. Activation of TRPV1 or TRPA1

by tear gas exposure causes ion channels in nerve fibres to open, allowing Na and Ca cations to flow into the cell. This depolarises the neuron, which transmits an electrical signal to the brain that is perceived as pain [23]. In addition the signal also activates the parasympathetic reflex arc of the nervous system causing increased blood flow and swelling at the contact site. Activation of both TRPV1 and TRPA1 causes tissue-specific responses such that in the respiratory tract, it causes a cough reflex, airway constriction and mucus production. In the eye, activation of these fibres causes lacrimation [3].

In an active TRPV1 or TRPA1 channel, the presence of Ca substance entering it will cause the neuron to release neuropeptides at the site of chemical contact that can act on neuronal and non-neuronal cells in the area. Substance P neuropeptides activate additional nociceptive fibres, which will amplify the pain signal. Substance P and other neuropeptides act on the surrounding non-neuronal cells resulting in the release of inflammatory mediators [24]. This inflammatory cascade causes acute inflammation and tissue damage, which if prolonged will cause damage to surrounding cells [25]. The vagal sensory nerves, which innervate the lungs, respond highly to TRPV1, making the respiratory tract sensitive to pepper spray [20]. Subsequent inflammation of the respiratory tract further aggravates coughing, as does mucus secretion triggered by reflex rotation [26].

Neurogenic inflammation by TRPV1 and TRPA1 plays a role in airway inflammation that will be worse in conditions of congenital respiratory disorders such as asthma [27]. Asthmatics will be highly responsive to the presence of Substance P, meaning they will be sensitive to acute tear gas exposure and subsequent long-term aggravating effects [28]. While the immediate symptoms are complex and fairly well understood, the long-term health consequences are less studied.

Composition and Range of Exposure

Despite using the term "tear gas," its active compound composition is not actually a gas CS tear gas agents are typically sprayed as microparticles encapsulated in aerosols measuring 3 to 10 micrometres in diameter. In the common use of fireworks for CS tear gas dispersal, the constituent composition consists of 45% CS agent, 30% potassium chlorate, 14% epoxyresin, 7% maleic anhydride, 3% methyl nadic anhydride, and 0.03% mixed residue balance [29]. Although the intrinsic toxicity of these ingredients in the composition of fireworks has not been studied in detail, their safety data sheets indicate significant toxicity. The pyrotechnic devices can be hand-thrown or fired from a launcher, can reach distances on targets within 400 metres and can penetrate window glass. The affected dispersal area ranges from 60 to 300 square metres [30]. In addition, the launcher can also be modified by mounting on specialised aircraft and vehicles for deployment. Unmanned aircraft-based dispersal systems have been widely developed, are in the testing phase so that they can be widely adopted. Pepper spray (OC) is usually deployed from a flexible handheld canister. However, it is also available in grenade-like and projectile forms. CN can be dissolved in solvents, used in irritating sprays such as Mace, or dispersed from ready-made grenades [31].

Clinical Overview

The effects of tear gas chemical weapons are related to the concentration of the compound and the duration of exposure, such that a high concentration over a short period of time is more harmful than the same dose delivered in a low concentration over a longer period [32]. Evidence of toxicity, as measured by irritation thresholds (Table 1), was greatest for CN (1.0 mg/m^3), followed by CS (0.004 mg/m^3) and OC (0.002 mg/m^3) [33]. In contrast, OC and CS are less toxic than CN (Table 1) [34]. Some reports describe cases of death as a post-exposure effect of CN, which occurs at high concentrations in confined spaces for long periods of time [35]. Although some have questioned the safety of CS and OC, both are considered generally safe when used appropriately. The eyes and respiratory system are the main targets with eye and respiratory tract irritation occurring within a relatively short exposure time of 20-60 seconds [36].

Table 1. A comparison of the estimated human toxicity of CN, CS and OC [37]

Parameter	CN	CS	OC
Threshold for eye irritation (mg/m^3)	**1,0**	**0,004**	**0,002**
Effective concentration—ICt50 (mg/min/m^3)	**20-50**	**4-20**	**-**
Estimated lethal dose—LCt50 (mg/min/m^3)	**8.500-25.000**	**25.000-100.000**	**> 100.000**

Note: CN, 2-chloroacetophenone; CS, o-chlorobenzylidene malonitrile; OC, oleoresin capsicum.

Tear Gas Toxicity

Tear gas exposure will result in a variety of complex health effects, including acute and chronic effects. Articles have shown the mechanism of action of tear gas agents to be mediated by specific receptors [38]. While specific receptors will contribute to its acute pain and irritation effects, the electrophilic reactivity of the agent occurs simultaneously with solvent toxicity and pyrotechnic reaction products, involving several toxicological mechanisms that remain to be studied [39].

Direct Exposure Effect

CS and OC produce similar symptoms. Acute exposure to CS at concentrations commonly used by law enforcement for riot control purposes results in immediate irritation of the eyes, nose, mouth, skin and respiratory tract. The effects on the skin include itching, burning, and redness of the skin with the potential for blistering, and allergic contact dermatitis, especially if there is a history. Exposure to the eyes can cause lacrimation, blepharospasm, itching, and burning sensation [7]. When inhaled, CS exposure often causes coughing, choking, salivation, and tightness in the chest. OC exposure causes pain and tingling in the respiratory tract with coughing. Signs and symptoms of OC contact with the eyes include lacrimation, conjunctival inflammation, blepharospasm, redness, pain, burning, and oedema. Some evidence suggests that OC compounds may also temporarily inhibit the blink reflex of the eye and limit responses to mechanical and chemical stimuli [10]. Like CS, the dermal effects of OC can include pain, tingling, redness, swelling, and blistering [7]. The effects of CN are similar to CS and OC, but will be significantly more severe and potentially life-threatening especially if the procedure is not appropriate. Whereas CN is a more toxic lacrimator than CS and is more likely to cause serious injury to the skin such as causing acute skin infections [40].

Respiratory Effects

Much of the research around the effects of tear gas exposure has come from laboratory animal studies or from small studies of previously healthy individuals under controlled conditions, and although the extent of these studies is questionable for safety assessment [31]. For example, a study that concluded that tear gas exposure was not associated with increased airway resistance was conducted on only seven healthy military volunteers, and those with a history of chronic respiratory disease were excluded [1]. The use of tear gas in riots or large-scale civil unrest events may result in prolonged, repeated or highly concentrated exposure, posing a greater threat to respiratory health in the short and long term [7]. High concentrations of CS or OC can cause severe respiratory symptoms, such as reactive airway dysfunction syndrome, in individuals exposed to CS and OC and haemoptysis [41]. Infiltration of capsaicin compounds in the lower respiratory tract may induce pulmonary oedema, apnoea and respiratory arrest. Several surveys conducted after recent large-scale tear gas use in Turkey reported persistent cough, chest pain, sputum production, haemoptysis, difficulty breathing, and nasal discharge, sometimes lasting for weeks after exposure [31]. Pulmonary function tests observed restriction and obstruction of the middle and small airways which were more severe in females [6]. Restrictive effects were also observed in residents of areas where tear gas was used, indicating that tear gas agents are a persistent environmental health hazard [31].

Eye Effects

Tear gas exposed at close range can cause very severe eye injury, including corneal stromal oedema, conjunctival tears and deep vascularisation of the eye [42]. Other eye complications include vitreous haemorrhage, traumatic optic neuropathy, symblepharon, pseudopterygium, infective keratitis, trophic keratopathy, glaucoma and cataracts. There is one report describing four subjects who developed corneal erosion after exposure to pepper spray, indicating that the OC or solvent in the spray may cause nerve damage.

Skin Effects

In cases where clinicians have examined patients exposed to CS, skin burns have often been reported, especially when exposed to large amounts, such as in a case involving a riot at a Vietnamese refugee detention centre in Hong Kong [41]. Several cases of very severe skin reactions in response to CS exposure have been reported, including severe facial erythema and swelling that obstructed vision. Physicians from the Department of Dermatology at San Francisco General Hospital observed severe CS-induced erythematous dermatitis of the face, neck, and hands [43]. Cases of allergic contact sensitisation were reported with patches of erythema and multiple vesicular eruptions on the skin after severe exposure to CS. Ninety per cent of workers at a plant producing CS agents reported a history of dermatitis on the arms and neck, with 7% showing positive patch test reactions to CS, suggesting that CS may act as a contact sensitizer [44].

Cardiovascular and Gastrointestinal Effects

In the gastrointestinal tract, irritation due to ingestion of compounds such as CS can cause nausea, vomiting, diarrhoea, and haematemesis [7]. Various cardiovascular effects, including tachycardia and transient hypertension, in some cases occur due to being triggered by sensory-autonomic reflexes or anxiety, pain, or psychological distress.

Severe Injuries and Fatal Effects

There are many case reports of injuries and deaths associated with exposure to high concentrations of tear gas or exposure in confined spaces or over long periods of time. Deaths and respiratory tract injuries were reported following tear gas discharges in prisons [34]. CS and OC are increasingly used in prison systems in anticipation of inmate-on-inmate disturbances, often in enclosed and poorly ventilated spaces. Deaths of inmates with pre-existing respiratory conditions have been attributed to multiple exposures to CS and OC and lack of decontamination [45]. Another study documented cases of death within 1 hour of exposure to OC, although a direct causal relationship has not been found [46]. Severe injuries and deaths have been reported during massive tear gas use in Egypt, Turkey, Bahrain and Brazil. These are often caused by direct or close impact of tear gas munitions causing severe head and eye injuries and burns. A well-documented case is the death of 37 Egyptian prisoners in a prisoner's car who were fired upon with tear gas ammunition. Reports suggest an association between CS exposure and miscarriage [20].

Other targets of tear gas agents

Due to their electrophilic nature, tear gas agents are likely to react with many other biomolecules in the eyes, respiratory tract and skin. The nature of such targets is largely unknown. Similar to acrolein and related electrophiles, tear gas agents can damage and deplete biological redox systems in the epithelial lining fluid and within cells and mitochondria, modify structural proteins and nucleic acids, and inactivate enzymes [47]. There is little research on the endocrine effects, immunological consequences, and histological changes of CS exposure, but several animal studies suggest that potential effects may occur. Studies in rats injected with CS found histological changes in the adrenal and thyroid glands, although it is unclear whether dermal or inhalation exposure to CS in humans would produce the same response [48]. Other studies of CS exposure in mice report suppression of humoral immune responses and increased corticosteroid levels. The mutagenicity and potential carcinogenic effects of tear gas are

also not well understood, with clear research still lacking. Some laboratory studies suggest that CS is not mutagenic or is weakly mutagenic, but the results of carcinogenicity studies have not been confirmed and most studies have been limited to laboratory studies rather than human studies. The mutagenicity and potential carcinogenic effects of tear gas are also not well understood, with clear research still lacking. Some laboratory studies suggest that CS is not mutagenic or is weakly mutagenic, but the results of carcinogenicity studies have not been confirmed [3] and most studies have been limited to laboratory studies rather than human studies. The mutagenicity of capsaicinoids has been extensively tested, but the results are still conflicting. Tear gas dispersal involving mixed fireworks can produce thermal degradation by-products that are potentially harmful to human health [20].

Conclusions

CN, CS and OC are effective lacrimation agent tear gases that are ideal for riot control. Tear gas works through the process of activating nociceptive nerve fibres, which function to sense damage and noxious stimuli. The activation of nociceptive neurons causes a rapidly spreading sensation of pain and itching, especially in the eyes, nose, mouth, skin and respiratory tract. Although there are significant clinical effects, they are not expected to occur after exposure. Tear gas in addition to its ability to cause respiratory distress is dangerous if you have congenital diseases such as asthma, eye irritation that damages the cornea, burns and skin irritation, cardiovascular with symptoms of vomiting and nausea. Other symptoms can also include conjunctivitis and oedema.

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