UDC: 618.146-006.6:615.849.19 DOI: 10.52532/2663-4864-2023-4-70-56-63

PHOTODYNAMIC THERAPY FOR CERVICAL CANCER: A LITERATURE REVIEW

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ABSTRACT

Relevance: *Cervical cancer is a significant public health problem worldwide, with human papillomavirus infection playing a vital role as a risk factor. Photodynamic therapy is a minimally invasive treatment for HPV-related cervical lesions that uses photosensitizers and light to destroy abnormal cells selectively.*

The study aimed to *review the different types of molecules used in PDT to reduce the morbidity and mortality associated with cervical cancer.*

Methods: *We conducted a comprehensive search for all relevant articles investigating the ef-ficacy and safety of PDT in the treatment of HPV-associated cervical cancer. We determined PICO scores for the review and performed a literature search of the PubMed database. An examination of the PubMed online database using keyword combinations identified 71 studies conducted between 2013 and 2023 that investigated using PDT to treat RSM cells.*

This article reviews ongoing clinical trials examining the efficacy of PDT in treating low-grade squamous cell intraepithelial neoplasia and high-grade squamous cell intraepithelial lesions, as well as preclinical approaches using different molecules for PDT in cervical cancer.

Results: *Potential molecules for PDT are described, their advantages and disadvantages evalu-ated, and solutions to improve their compatibility with antitumor treatment are proposed. Our review shows that PDT is a promising therapeutic approach for diagnosing and treating HPV-related cervi-cal lesions. At the same time, we observe that using different classes of dyes enhances the anticancer effects of PDT.*

Conclusion: *Fullerene and ALA-PDT are potential leaders for more intensive use in PDT, which will further help reduce the global incidence and mortality from cervical cancer. However, further studies are needed to evaluate its long-term efficacy and safety.*

Keywords: *cervical cancer; human papillomavirus (HPV); Photodynamic therapy (PDT); Squamous intraepithelial neoplasia.*

Introduction: Cervical cancer (CC) is one of the leading causes of cancer mortality among women worldwide [1]. The presence of human papillomavirus (HPV) is a significant factor contributing to the development of cervical cancer [2]. Traditional methods of diagnosis and treatment often face difficulties in detecting and treating precancerous lesions that precede the onset of cancer. The cell lining of the cervix can cause a variety of precancerous lesions, including cervical dysplasia – cervical intraepithelial neoplasias (CIN1, CIN2, CIN3), high-grade squamous intraepithelial lesions (HSIL), and low-grade squamous intraepithelial lesions (LSILs).

LSIL specifies the mildest form of these lesions, while CIN2 is in the intermediate category, and CIN3 represents the most severe condition. HSIL includes CIN2 and CIN3 and is considered a high-risk cervical cancer precursor. If left untreated, HSIL has a higher chance of progression to cancer compared to CIN1 or LSIL. In order to overcome this obstacle, scientists have developed an innovative technology that aims to improve the diagnosis and treatment of primary and precancerous cervical lesions associated with HPV [3]. This technology is a photodynamic therapy (PDT), which is a minimally invasive therapeutic method that uses photosensitizers (PS) and light for targeted action and elimination of abnormal cells [3].

The new approach includes a combination of a fluorescent dye and a specialized imaging system, which facilitates visualizing cervical lesions in real time [4, 5]. During that procedure, the cervix is covered with PS, and the target area is exposed to a specific wavelength of light [6]. This process triggers PS to generate the reactive oxygen species that selectively destroy abnormal cells [7]. By precisely targeting the affected cells, this method reduces the risk of damage to healthy tissues, thereby increasing the effectiveness of treatment [8]. In addition, the applied imaging system provides an accurate and effective identification of cervical lesions associated with HPV [9]. Early detection of these lesions with this technology could lead to more effective treatment and improved patient outcomes [4, 10].

The PDT introduction highlights significant progress in the diagnostics and treatment of HPV-related cervical lesions. Choosing a suitable dye is an important aspect when working with PDT. Over the years, various

molecules have been used in this technique. However, it is crucial to identify and evaluate these molecules to develop the new PS with higher antitumor activity and more excellent usability [11].

The study aimed to review the different types of molecules used in PDT to reduce the morbidity and mortality associated with cervical cancer.

Materials and Methods: A comprehensive search was conducted for all relevant articles investigating the efficacy and safety of PDT in the treatment of HPV-associated cervical cancer. Numerous studies examining the application of PDT in this area were reviewed, focusing on photochemotherapy, nanoparticles, and PS agents.

PICO scores were determined for the review, and a literature search of the PubMed database was performed, where P (population) = women with HPV-associated cervical cancer; I (intervention, exposure in our case) = PDT; C (comparison group) = Placebo or other treatment method groups, and O (outcome) = PDT clinical efficacy and safety.

The PubMed online database has been examined to find relevant articles related to the research topic. The search process lasted from April to July 2023. The VOS viewer tool (Centre for Science and Technology Research, Leiden University, Netherlands) was also used to identify the research topic's concept, keywords, and authors. Combinations of the following terms were used in the search: CIN1, CIN2, CIN3, HSIL, LSIL, CERVICAL CANCER, HPV, and PDT.

Results: A study of the online database PubMed identified 71 studies conducted from 2013 to 2023 that investigated the use of PDT to treat cervical cancer. Of these, 13 clinical trials were identified as studying the HPV-associated early stages of cervical cancer (Table 1).

Table 1 – Studies on PDT in cervical cancer according to PubMed, 2013-2023

#	Author, Year, Study Design	Intervention	Efficiency
1	Choi et al., 2013 Retrospective study [20]	Photogem IV and red laser light with a wavelength of 630 nm (CERALAS, Germany), 150 J/cm^2. Group 1: PDT only Group 2: PDT + LEEP/Cone Group 3: PDT within 3 months of LEEP/cone. Group 4: PDT 12 months after LEEP/Cone due to CIN recurrence.	Complete response for high-frequency HPV DNA: • 3-month follow-up: 89.8% (44/49); • 12-month follow-up period: 87,0% (40/46); Complete response to PDT at 12 months follow-up: 98.1% (52/53) Group 1: CIN2: 100% (2/2), CIN3: 100% (6/6), CIS: 80% (4/5). CRR=100% (13/13)
2	Hillemanns et al., 2014 Clinical study [21]	The experimental group (EG) – HAL vaginal suppositories 100 mg; red coherent light with a wavelength of 633 nm (Biolitec, Germany), 50 J/cm^2 Control group (CG) – only Placebo vaginal suppositories + PDT, only follow-up	Complete response for CIN1 after 6 months: • EG: 57.1% (20/35) • CG: 25.0% (4/16) [Placebo + PDT: 40.0% (4/10) and follow-up group: 0% (0/6)], p=0.040 Complete response for HPV • EG: 73,3% (11/15) • CG: 50% (5 of 10) [Placebo + PDT: 28.6% (2 of 7) and follow-up group: 100% (3 of 3)], p=0.397
3	Hillemanns et al., 2014 Clinical study [22]	Topical HAL hydrochloride treatment 0,2%, 1%, 5% EG1: HAL 5% EG2: HAL 1% EG3: HAL 0.2% CG: Placebo	There was no statistically significant result in CIN1 and CIN1/2 and in HAL1% and HAL0.2% com-pared to the Placebo group Complete response in CIN2: After 3 months: EG – 95% (18/19), Placebo – 57% (12/21), p=0,009. After 6 months: EG – 95% (18/19), Placebo – 62% (13/21), p=0.021 Complete response for high HPV risk: After 3 months: EG – 83% (5/6), Placebo – 0% (0/6) After 6 months: EG – 83% (5/6), Placebo – 33% (2/6) Dose-dependent response for CIN2+HPV eradica-tion: After 6 months: HAL5% – 84% (16/19), HAL1% – 48%. (14/29), HAL0.2% – 42% (8/19), Placebo – 38% (8/21)
4	Fu et al., 2016 Prospective study [23]	EG – Local PDT with 5-ALA (Shanghai Fudan-Zhangjiang Bio-Pharmaceutical Co., Ltd.) with 635 nm diode laser (LD600-C; Wuhan Yage Photo-Electronic Co. Ltd, Wuhan, China), light irradiation 100 J/cm^2; CG – untreated	• 3-month follow-up period for VR-HPV remission: Complete response: 64.10% in EC vs. 24.32% in CG (x^2=12.152, p<0.01) • 9-month follow-up for VR-HPV remission: Com-plete response = 76.92% at TG vs. 32.40% at CG (x^2=15.202, p<0.01) • Follow-up at 9 months for CIN1 conversion: 83.33% in EG vs. 0% in CG (x^2=7.639, p<0.001).

5	Liu et al., 2016 Clinical study [24]	EG – local PDT with 5-ALA; He-Ne red light laser 632.8 nm, 100 J/cm^2; CG – High-frequency electro-ion treatment	• 6-month follow-up period for VR-HPV Response: 81.81% in EG and 52.73% in CG (x^2=4.9381, p<0.05); • 9-month follow-up period for VR-HPV Response: 10.91% in EG and 7.27% in CG (x^2=2.1164, p<0.05); • Overall response for VR-HPV DNA: 92.73% in EG and 60.0% in CG (x^2=4.2615, p<0.05)
6	Park et al., 2016 Retrospective study [25]	EG: Photogem and diode laser with a wavelength of 632 nm and photoprint and diode laser with a wavelength of 630 nm 240 J/cm^2	• Complete response for CIN = 95% • Disease progression: 4.5% • Recurrence: 4.5% (18 months)
7	Inada et al., 2019 Clinical study [26]	EG: MAL cream and about 150 LEDs of the system, emitting at a wavelength of 630 nm, light output of 80-180 J/cm^2; CG: illumination of the cervix only (n=8) or application of MAL cream only (n=6)	Complete response for CIN1: 75% (42/56) at 1 (12.5%) and 2 (62.5%) years of follow-up; CIN1 persisted in 5.4%, CIN2 progression in 8.9%, and CIN1 recurrence in 8.9% for 2 years after PDT. In patients with CIN2/3, Complete response = 90% after 1 (30%) and 2 (60%) years of follow-up. CG: abstinence – 28.57% and persistence of lesion – 14.3%; The overall response rate was 57.14% at 1 and 2 years of follow-up.
8	Murakami et al., 2020 Clinical study [16]	Intravenous sodium talapoporphine (NPe6) at a dose of 40 mg/m^2 with a PDT of 100 J/cm^2	Через три и шесть месяцев: After 3 and 6 months: PDT was used in 9 patients (2 with CIN2 and 7 with CIN3). Treatment was confirmed in eight cases: 89%
9	Mizuno et al., 2020 Clinical study [27]	5-ALC, 633nm wavelength light, 1000-150 J/cm^2	Positive results: 96.1% Complete response for CIN: 70.6% Complete response for HPV: 79.4% Recurrence: 3.7% (1/51)
10	Li et al., 2020 Prospective study [28]	EG: 5-ALC and LED-IB type, wavelength 633 nm and 80 J/cm^2	Complete response for VR-HPV: 3 months: 75.32% (58/77), 6 months: 80.52% (62/77), 12 months: 81.82% (63/77) Complete response at CIN1 at 6-month follow-up: 88.31%, at 12-month follow-up: 94.81%
11	Zhang et al., 2022 Retrospective study [29]	5-ALC heat-sensitive gel and light irradiation at 635 nm and 100 J/cm^2	6 months after ALA-PDT Residual lesion incidence – 9.1% (3/33), p=0.004 Complete HPV Response rate – 66.7%, p=0.01 Recurrence rate was 3.3% at 2-year follow-up, p=0.021
12	Chen et al., 2022 Retrospective study [30]	5-ALC and LD600-C with 635 nm red light wavelength at 80 MW/cm^2	After 6 months of follow-up: EG: Complete response for HPV: 79.0%, LSIL 80.6%, KG: HPV CR – 62.3%, LSIL: 64.2% (p<0.05)
13	Yao et al., 2022 Retrospective study [17]	Chlorine E6 with STBF-PDT	The Complete response rate was 72.22% (13/18), and the rates of HPV remission and complete removal were 88.89% (16/18) and 83.33% (15/18), respectively, at 1-month follow-up. Complete response: 88.89%, and the HPV remission rate reached 94.44% after 6 months.

Numerous clinical trials, pilot studies, retrospective analyses, and prospective studies have investigated the use of PDT for the treatment of CIN, LSIL, and HSIL and have demonstrated *promising results using a variety of PS molecules:*

1. 5-aminolevulinic acid (ALA): ALA is the PS used in PDT for cervical cancer. Clinical trials have shown a positive result on the safety and efficacy of ALA-PDT in patients with CIN [12].

2. Aluminium phthalocyanine chloride: Second-generation PS, used in PDT to treat various types of cancer, including cervical cancer, and has higher photodynamic activity in the red spectrum and the ability to treat the deeper placed tumors [13].

3. Photofrin: PS was approved for use in PDT for many types of cancer, including cervical cancer [14]. An analog of FS Photogem (made in RF).

4. Hexaminolevulinate: allows effective detection of tumor zones due to the contrast of the protoporphyrin IX red fluorescence with excitatory short-wave light and direct use of its photodynamic activity to destroy superficial or cavitary tumors [15].

5. Sodium talaporphin: Sodium Talaporphin is a PS approved for the photodynamic therapy of various types of cancer, including cervical cancer [16].

6. Chlorin e6: its high absorption rate in the near-infra-red range supports deeper tissue penetration than other PS. Chlorin e6 has also shown a higher selectivity for cancer cells than healthy cells, making it a promising candidate for PDT [17].

7. Porphyrin derivatives: Porphyrin derivatives such as protoporphyrin IX and hematoporphyrin derivatives are naturally occurring PS used in PDT for cervical cancer. These compounds occur naturally in the body and

exhibit a higher accumulation rate in cancer cells than in healthy cells. When exposed to light of a specific wavelength, these PS generate the reactive oxygen species capable of destroying the cancer cells [18].

8. Tehafirins: These are synthetic molecules that are being studied for their potential use in PDT in various types of cancer, including cervical cancer, and have effectively induced cancer cell apoptosis [19].

In addition, below are presented relevant *preclinical studies of the potential use of other types of molecules in PDT in cervical cancer:*

1. Curcumin is a naturally occurring low-toxicity polyphenolic compound with anti-inflammatory and antioxidant properties that have demonstrated anticancer effects [31-32].

2. Hypericin is a compound present in St. John's wort. It has photosensitizing properties and is used in PDT for cervical cancer [33]. When light activates, hypericin generates the reactive oxygen species that can damage the cancer cells. In vitro and animal studies have shown the efficacy of hypericin in killing cancer cells [34]. However, further studies are needed to evaluate its efficacy in humans.

3. Indocyanine green (ICG) is a water-soluble dye of the near infra-red range. Preclinical studies have shown the potential use of ICG for PDT in cervical cancer [35-36]. FDA approved it for clinical use.

4. Methylene blue is a blue dye that has been used in medicine for several years. It has demonstrated the efficacy of PDT for cervical cancer [37]. Available data indicate that PDT mediated by methylene blue successfully induces cervical cancer cell death by generating reactive oxygen species (in vitro in animals) [33, 37]. Further research is needed to evaluate its effectiveness in humans.

5. Bengal rose is a red dye with photosensitizing properties, which has been used in medicine for many years and in PDT for cervical cancer. When light is activated, the Bengal rose produces the reactive oxygen species that can damage the cancer cells. In vitro and animal studies have shown the efficacy of the Bengal rose in killing cancer cells [34]; however, further study is needed to determine its efficacy in humans.

6. Zinc phthalocyanine exhibits high absorption in the red-light spectrum, making it practical for PDT. When exposed to light of a certain wavelength, PS generates the reactive oxygen species that can destroy the cancer cells [19, 38].

7. Chlorophyll derivatives, other than chlorine e6, have shown that chlorophyll-based PDT can induce the apoptosis of cancer cells [39-40].

8. Methyl violet (methyl violet) is a cationic dye exhibiting photodynamic activity. Preclinical studies have assessed its use in cancer treatment [41].

9. Bacteriochlorins have been studied for their potential use in PDT in various types of cancer [42]. However, there are currently no studies showing the efficacy of bacteriochlorin-based PDT for the treatment of cervical cancer.

10. Fullerenes are the carbon molecules. Preclinical studies have shown that fullerene-based PDT can effectively induce cancer cell death [43-44].

11. Xanthene molecules, such as eosin and erythrosine, are a class of fluorescent molecules used as PS in PDT of various types of cancer [45].

Discussion: Studies have shown that the overexpressed receptors on the surface of cancer cells can serve as potential PS binding sites. Consequently, PSs that exhibit a stronger tendency to attach to these overexpressed receptors facilitate their delivery to cancer cells [46]. Thus, PS that exhibit a higher affinity for these receptors can be considered promising candidates for PDT. In addition, using in-silico analysis, the scientists found that fullerene showed the highest affinity to overexpressed receptors in cervical cancer cells.

Therefore, fullerene has significant potential as a PS for PDT in the treatment of cervical cancer. However, further studies "in vitro" and "in vivo" are needed to confirm this finding. Due to its unique molecular properties, Chlorin e6 has high absorption rates in the red spectral range and targeted storage or accumulation in the corresponding tumor tissue [47]. On the other hand, Porphyrin derivatives occur naturally in the body and exhibit a higher accumulation rate in cancer cells than in healthy cells, destroying them [48].

The literature review in our study includes RCTs and prospective and retrospective studies of the efficacy of PDT in cervical cancer treatment. The studies mainly used 7 types of PS, such as topical 5-ALC thermogel (46.1%), vaginal HAL suppositories (7.7%), HAL hydrochloride (7.7%), MAL cream (15.4%) and intravenous photohem (15.4%), chlorin e6 (7.7%) and sodium thalaporphine (7.7%). According to the results, 5-ALA is the most widely implemented PS, which used wavelengths of 633 or 635 nm at 80, 100, or 150 J/cm^2 and produced HPV elimination results of 66.7% to 92.73% in the experimental groups compared to 32.40% to 62.3% in the control groups. HAL is an advanced ALA ester and a more potent lipid-soluble derivative. In early studies, the use of topical PS showed a Complete response rate (CR) of 33% to 71%, which was significantly lower [51]. Although topical PS, such as 5-ALA, is more convenient and cheaper than intravenous PS, the therapeutic effect is not always univocal. According to the results of other authors, attempts have been made to conduct PDT using the topical hexyl ether 5-ALK, advanced by 5-ALC PS, with still low results of the Complete response rate of 63% [10, 51]. Intravenously administered sodium salt of hematoporphyrin derivative (photogem) showed a more than 95% positive result.

PDT is currently used to treat patients who want to preserve their fertility and those who would prefer to

avoid the surgery intervention. Previous studies have used photofrin and 5-ALA in the treatment/prevention of cervical cancer. Although systemic photofrin was effective, it (photofrin) caused the skin photosensitivity. To the contrary, 5-ALC has been used topically to treat cervical lesions that could lead to cancer, as well as to eradicate the human papillomavirus (HPV) infection [49].

Phthalocyanines are standard PS used in PDT due to their high tumor uptake efficiency, high production of reactive oxygen species, and strong absorption in the 650 to 850 nm wavelength range. The second generation of zinc (II) phthalocyanine has Q-distract absorption at longer wavelengths (670-770 nm), which allows the light to penetrate the tissues as much as possible [50].

Scientists are also trying to increase the effectiveness of antitumor therapy for cervical cancer by combining PDT with chemotherapy [51]. Moreover, researchers have studied strategies to increase the delivery and efficacy of PS in PDT, and one such strategy is the use of nanoparticles [46]. The nanoparticles make it possible to combine multiple therapeutic agents and other functions within a single system, which facilitates solving various aspects associated with cancer treatment.

For example, the liposomal technology combining chlorin e6 as a PS, ICG as a PTT agent, and hypoxia-activated by the prodrug tirapazamine as a cytotoxic agent resulted in 97% of cell death after PDT at 808/660 nm.

Below are presented the *challenges and solutions associated with using PDT molecules in cervical cancer.*

The limited solubility of the molecules in water presents a significant problem when using them for cancer treatment, as it can reduce their efficacy and increase toxicity. However, nanotechnology offers a potential solution by increasing molecules' solubility, stability, and targeted delivery to cancer cells [34]. Nanoparticle-based delivery systems have been developed for various PS, including porphyrins, chlorophylls, and phycobilins.

These nanoparticles can be designed for the targeted exposure of cancer cells, improve the solubility and stability of PS, and improve its distribution and pharmacokinetics. Moreover, some nanoparticles have intrinsic antitumor properties and may enhance the therapeutic effects of PDT. In general, the combination of PS and nanotechnology opens up excellent prospects for developing effective and targeted PDT for treating cervical cancer and other types of cancer.

In addition to the limited solubility, several other challenges are associated with using molecules for PDT in cervical cancer.

These challenges include:

– Tumor targeting: Achieving specific dye targeting to tumor cells while minimizing uptake by healthy tissues is a challenge that needs to be addressed to avoid potential toxicity.

– Depth of penetration: The depth to which the activating light can penetrate is limited, making it difficult to treat the tumors deep inside the body.

– Photobleaching: Molecules can undergo photobleaching, losing their ability to generate reactive oxygen species when exposed to light. It may limit their effectiveness in PDT.

– Stability: Some molecules may exhibit instability in the biological environment, which affects their efficacy and safety.

– Approval from regulatory authorities: Obtaining regulatory approval for clinical use can be time-consuming and costly, hindering the availability of molecules for PDT in cervical cancer.

– The following possible solutions can be considered to address these issues:

– Solubility: Encapsulating the dye in lipid or polymer nanocarriers can improve solubility and stability.

– Tissue penetration: Exploring alternative delivery methods, such as intra-tumoral injection or topical application, may enhance tissue penetration.

– Specificity: Increasing specificity through ligand conjugation or using activated molecules selectively activated in cancer cells.

– Photobleaching: Optimizing the dye concentration and light dose and using photostable molecules can reduce the photobleaching.

– Toxicity: Reduced toxicity by using lower doses of dye and light and optimizing the drug delivery methods to minimize the side effects.

– Regulatory Approval: Compliance with Regulatory Guidelines for Drug Development and Clinical Trials.

– Tumor targeting: Targeted delivery systems such as nanoparticles, stem cell-derived exosomes, or liposomes can improve tumor targeting. These systems can be conjugated to specific ligands or antibodies that recognize and bind the tumor cells, increasing the accumulation of PS in the tumor and minimizing its uptake by healthy tissues. Another approach involves using light sources with specific wavelengths that selectively activate PS in tumors, minimizing activation in surrounding healthy tissues [52].

Conclusion: Photochemotherapy, nanoparticles, and photosensitizing agents are widely used in PDT for cervical cancer. It is noteworthy that fullerene is promising as a dye for PDT due to its high binding affinity for overexpressed receptors in cervical cancer cells. However, further studies are needed to confirm the potential of fullerene and develop effective treatments for cervical cancer with PDT. The use of PDT, which combines a fluorescent dye with a specialized imaging system, represents a significant advance in the diagnostics and treatment of HPV-related cervical lesions.

This minimally invasive approach offers targeted therapy to abnormal cells, minimizing harm to healthy tissues. In addition, relevant studies have shown that

ALA-PDT is a safe and effective alternative for treating HPV-related CIN and HSIL.

Continued research and development in this area is likely to drive further progress in the diagnostics and treatment of HPV-related cervical lesions, leading to improved patient outcomes and a reduced global cervical cancer burden.

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АНДАТПА

ЖАТЫР МОЙНЫ ОБЫРЫНЫҢ ФОТОДИНАМИКАЛЫҚ ТЕРАПИЯСЫ: ӘДЕБИЕТКЕ ШОЛУ

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Өзектілігі: *Жатыр мойны обыры бүкіл әлем бойынша денсаулық сақтаудың негізгі проблемасы болып табылады, мұнда адам папилломавирусының инфекциясы қауіп факторы ретінде маңызды рөл атқарады. Фотодинамикалық терапия - бұл қалыпты емес жасушаларды іріктеп жою үшін фотосенсибилизаторлар мен жарықты пайдаланатын АПВ-мен байланысты жатыр мойны зақымдануының минималды инвазивті емі.*

Зерттеудің мақсаты *– жатыр мойны обырына байланысты сырқаттанушылық пен өлімді азайту үшін ФДТ-да қолданылатын молекулалардың әртүрлі түрлеріне жан-жақты шолу жасау.*

Әдістері: *АПВ инфекциясымен байланысты жатыр мойны обырын емдеудегі ФДТ тиімділігі мен қауіпсіздігін зерттеуге арналған барлық тиісті мақалаларға жан-жақты іздеу жүргізілді. Шолу үшін PICO көрсеткіштері анықталып, PubMed дерекқорында әдебиеттерге іздеу жүргізілді. PubMed онлайн дерекқорында кілтті сөздер тіркестерін пайдалана отырып 2013 және 2023 жылдар аралығында жатыр мойны обыры жасушаларын емдеу үшін ФДТ қолданылуына зерттеу жүргізілген 71 жұмыс анықтады.*

Бұл мақалада төмен дәрежелі скамозды интраэпителиальды неоплазияны және жоғары дәрежелі скамозды интраэпителиальды зақымдануларды емдеудегі ФДТ тиімділігін зерттейтін ағымдағы клиникалық зерттеулер, сондай-ақ жатыр мойны обырында ФДТ арналған әртүрлі молекулаларды қолданатын клиникаға дейінгі тәсілдер қарастырылады.

Нәтижелері: *ФДТ үшін потенциалды молекулалар сипатталып, олардың артықшылықтары мен кемшіліктері бағаланып, обырға қарсы терапиямен үйлесімділігін арттыру үшін шешімдер ұсынылды. Біздің шолуымыз көрсеткендей, ФДТ АПВ-мен байла-*

ныcты жатыр мойынының зақымдануын диагностикалау және емдеу үшін перспективті терапиялық әдіс болып табылады. Сонымен қатар, біз боғғыштардың әртүрлі кластарын қолдану ФДТ-ның обырға қарсы әсерін күшейтетінін байқадық.

Қорытынды: *Фуллерен және АЛК-ФДТ – жатыр мойны обырынан болатын жаһандық сырқаттанушылық пен өлімді азайтуға көмектесетін ФДТ-да интенсивті қолдану үшін әлеуетті көшбасшылар. Дегенмен, оның ұзақ мерзімді тиімділігі мен қауіпсіздігін бағалау үшін қосымша зерттеулер қажет.*

Түйінді сөздер: *жатыр мойны обыры; адам папилломавирусы (АПВ); фотодинамикалық терапия (ФДТ); скамозды жасушаішілік эпителий неоплазиясы.*

АННОТАЦИЯ

ФОТОДИНАМИЧЕСКАЯ ТЕРАПИЯ РАКА ШЕЙКИ МАТКИ: ОБЗОР ЛИТЕРАТУРЫ

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Актуальность: *Рак шейки матки (РШМ) представляет собой серьезную проблему для здравоохранения во всем мире, и инфицирование вирусом папилломы человека (ВПЧ) играет жизненно важную роль в качестве фактора риска РШМ. Фотодинамическая терапия (ФДТ) представляет собой минимально инвазивное лечение поражений шейки матки, связанных с ВПЧ, при котором используются фотосенсибилизаторы и свет для избирательного разрушения аномальных клеток.*

Цель исследования *– изучение различных типов молекул, используемых в фотодинамической терапии рака шейки матки.*

Методы: *Был проведен всесторонний поиск статей, посвященных изучению эффективности и безопасности ФДТ при лечении РШМ, связанного с ВПЧ-инфекцией. Для обзора были определены показатели PICO и проведен поиск литературы в базе данных PubMed с использованием комбинаций ключевых слов. Было выявлено 71 исследование, проведенное в период с 2013 по 2023 год, в котором изучалось использование ФДТ для лечения РШМ.*

В статье рассмотрены текущие клинические испытания, изучающие эффективность ФДТ при лечении плоскоклеточных интраэпителиальных неоплазий низкой и высокой степени, а также доклинические подходы с использованием различных молекул для ФДТ при РШМ.

Результаты: *Описаны потенциальные молекулы для ФДТ, оценены их преимущества и недостатки и предложены решения для повышения их совместимости с противоопухолевым лечением. Наш обзор показывает, что ФДТ является перспективным терапевтическим подходом для диагностики и лечения поражений шейки матки, связанных с ВПЧ. Вместе с тем, согласно результатам обзора литературы, использование различных классов красителей усиливает противораковые эффекты ФДТ.*

Заключение: *Фуллерен и АЛК-ФДТ являются потенциальными лидерами для более интенсивного использования в ФДТ РШМ. Однако необходимо проведение дальнейших исследований для оценки долгосрочной эффективности и безопасности данного метода.*

Ключевые слова: *рак шейки матки (РШМ), вирус папилломы человека (ВПЧ), фотодинамическая терапия (ФДТ), плоскоклеточная интраэпителиальная неоплазия.*

Transparency of the research: *Authors are solely responsible for the content of this article.*
Conflict of interest: *Authors declare no conflict of interest.*
Funding: *This study was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (grant No. BR18574160).*
Вклад авторов: *contribution to the study concept –Musin N.M., Albaev R.K., Barieva G.Zh.; study design –Shanazarov N.A., Albaev R.K., Iztleuov E.M., Smailova S.B., Barieva G.Zh.; execution of the study –Shanazarov N.A., Musin N.M., Barieva G.Zh., Kaliev A.A., Iztleuov E.M., Smailova S.B.; interpretation of the study –Shanazarov N.A., Barieva G.Zh.; preparation of the manuscript – Shanazarov N.A., Barieva G.Zh., Musin N.M., Albaev R.K., Kaliev A.A.*
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