



Features of the Treatment of Flat Warts in Children

Alimov Sherzod Ganijonovich ¹

¹ Tashkent Pediatric Medical Institute, Department of skin and venereal, children's skin and venereal diseases and AIDS, Private clinic HAYAT MEDICAL CENTER

Annotation: The authors studied clinical efficacy and safety of combined therapy of flat warts in children, including the immunomodulatory drug with antiviral effect and cryotherapy with liquid nitrogen.

In their clinical practice, doctors of various specialties often have to deal with the human papillomavirus (HPV) - associated diseases of the skin and mucous membranes. The sharp increase in the infection rate of the population, the variety of clinical presentations, and the characteristics of the course of these conditions arouse interest and an active discussion about the tactics of managing such patients among a large number of clinicians. The urgency of the problem of HPV infection, along with the negative trend of spread, is associated with a significantly pronounced negative effect of the virus on the immune system, which leads to its long-term persistence, torpidity to therapy and frequent recurrence of the disease.

Keywords: human papillomavirus (HPV), HPV infection, genitals, warts, destruction, cytotoxic agents, interferons, immunomodulators, antiviral drugs.

Abstract. Papillomaviruses were isolated in a separate family *Papovaviridae*, which, according to modern concepts, consists of 16 genera, representatives of five of which are pathogenic for humans [1, 2]. Virions do not have an envelope; their diameter is 50–55 nm. The capsid is shaped like an icosahedron and consists of 72 capsomeres. The genome is represented by double-stranded circularly twisted DNA and includes about 8000 base pairs [3]. During the replication cycle, the virus genome expresses 8 to 10 protein products. Early proteins that control viral replication, transcription, and cellular transformation are represented by oncoproteins E6 and E7. Proteins E1 and E2 regulate viral DNA replication and gene expression. Late proteins L1 and L2 are structural proteins of the virion. Protein L1 forms capsomeres [4]. The invasion of the virus occurs through microdamages of the skin and mucous membranes with infection of predominantly immature, dividing cells of the basal layer, then the virus replicates and the assembly of viral particles in differentiated cells of the surface layer of the epidermis / epithelium. The entire cycle of development of the infectious process is closely associated with the division of cells of the integumentary epithelium of the skin and mucous membranes and is not accompanied by signs of inflammation. At the same time, HPV can have a productive or transforming effect on the epithelium. With a productive impact, benign neoplasms appear - papillomas, warts and condylomas of the skin and mucous membranes. The result of the transforming effect is dysplasia of varying severity, the progressive development of which leads to cancer [5].

Currently, more than 100 types of HPV have been identified that can affect the skin and mucous membranes and provoke the development of changes characterized by papillomatous growths. The human papillomavirus has tissue specificity - the ability of certain types of HPV to infect tissue characteristic of their localization. In this case, the type of virus determines the clinical features of the infectious process.

One of the most common pathologies resulting from infection of the skin and mucous membranes with papillomaviruses are warts, which are benign epithelial tumors.

Among warts, 8 clinical varieties are distinguished, each of them is associated with certain HPVs: warts vulgaris (1-4, 27th, 29th, 57th HPV genotypes); deep palmar-plantar warts (1st, 3rd, 27th, 29th, 57th); mosaic plantar warts (2nd, 4th); cystic warts (60th); flat warts (3rd, 10th, 28th); warts of "butchers" (7th); focal epithelial hyperplasia (13th, 32nd); verruciform epidermodysplasia (5th, 8-10th, 12th, 15th, 19th, 36th) [1].

The group spread of warts, as a result of direct and indirect contact with patients, characterizes a high incidence rate, amounting to 7–12% in adults, and up to 10–20% in school-age children [1]. The incubation period varies from 1 to 6 months, but can be over three years. Within two years, up to 40–65% of warts regress on their own. In other cases, they continue to increase in size and may become more resistant to treatment over time [1, 6].

The most common in clinical practice are vulgar and flat warts. Vulgar warts, which mainly cause HPV types 2 and 4, clinically represent multiple painless, dense, rounded gray papules 0.2–0.5 cm in diameter with an uneven, keratinized surface of flesh or yellow-brown color, most often located on back surface of the hands. However, rashes can also be located on other areas of the skin [7].

Flat warts, most often localized on the back of the hands, forearms, face and mucous membranes, are clinically represented by small multiple papules of the color of normal skin. They occur in any age group, but are especially common in children and adolescents.

Currently, there are quite a few methods for the treatment of warts, they are divided into destructive, chemical, immunotropic. Depending on the specific clinical situation, preference is given to a particular method of therapy.

The most common methods for removing warts are the use of salicylic acid preparations and cryotherapy with liquid nitrogen. The guide J. Sterling et al. salicylic acid has been named the drug of choice for the treatment of flat warts on the face, as well as flat and common warts on the hands. OTC products contain less than 20% salicylic acid, while prescription drugs can contain up to 70% salicylic acid. However, 15-20% salicylic acid is usually sufficient to cure the wart. The use of salicylic acid preparations is a first-line therapy in the treatment of common non-genital warts [1]. A fairly high efficiency of such an effect is noted, a cure is observed in 70–80% of patients [1, 8].

Given the ability of retinoids to influence the processes of keratinization, accelerating the removal of the wart, some authors recommend their use orally and topically as a second line in the treatment of flat warts [6, 9].

Of the destructive methods in practice, cryotherapy with the use of liquid nitrogen applications is most widely used. The method is based on rapid freezing of intra- and extracellular fluid, followed by subsequent cell death and lysis during thawing. Most researchers estimate its effectiveness at 70-75% and recommend its use in the treatment of flat and simple warts as a first-line therapy. The method does not require anesthesia and special equipment, high material costs, is quite simple in execution, which greatly facilitates its use.

Laser therapy, which leads to necrosis of a tissue area with a wart as a result of coagulation of blood vessels, according to some authors, leads to a positive result in up to 50–80% of cases, but the recurrence rate is quite high and amounts to 4–22% [10]. At the same time, it should be remembered that long-term non-healing wounds are fraught with the addition of a secondary infection and the formation of scars at the site of removal. Therefore, the use of a laser for plantar warts is recommended as a second line therapy, and for common and flat warts - a third line [9].

The ability for HPV persistence in the human body and the formation of secondary immunodeficiency makes it expedient to include drugs that disrupt virus replication and improve regeneration in the complex of treatment of patients. Therefore, in the world practice for the treatment of warts, local agents with antiviral and immunomodulatory effects are widely used, the

effectiveness of which is significantly increased when used sequentially or in parallel in combination with destruction methods.

At the same time, with a seemingly wide variety of methods for treating warts, none of them gives a 100% guarantee of a complete cure for the patient. Until now, despite the fundamental discoveries and achievements of modern medicine, with papillomavirus infection, unlike other viral lesions of the skin and mucous membranes, there are no specific methods of treatment with an almost complete absence of systemic therapy. Every year, the statistics of HPV-related diseases is steadily deteriorating, the frequency of recurrence of the pathological process remains high, which dictates the need to search for drugs and new methods that increase the effectiveness of therapy. This problem is of particular relevance when it comes to young patients, where it is necessary to eliminate the risk of adverse drug reactions and complications as much as possible. According to many studies, the most effective method for the treatment of HPV-induced skin neoplasms is a combined method that combines the simultaneous or gradual use of local destructive effects and the systemic use of antiviral and immunoprotective agents. Since only destruction, according to a number of authors, gives a high percentage of relapses within six months, and warts in most cases occur on the same areas of the skin as before. This is probably due both to the stages of the life cycle of HPV, whose DNA can be detected at a distance of up to 1 cm from the visible boundaries of the tumor, and to a violation of general and local immunity [4].

The aim of this study was to evaluate the efficacy and safety of combination therapy for flat warts in children, which includes an interferon drug - Genferon light and cryodestruction with liquid nitrogen.

Material and research methods

Under our observation were 73 children aged 2 to 9 years with a diagnosis of papillomavirus infection of the skin, with clinical manifestations in the form of HPV-induced flat warts. The duration of the disease varied from two months to 2.5 years. Almost 90% of children (65 patients) had previously been treated for this disease with local antiviral drugs for 2-3 months, without effect. Warts were localized mainly on the face, the back surface of the hands. The number of elements on the skin ranged from 2 to 9. All patients were conditionally divided into two groups, 35 and 38 children in the first and second, respectively.

cryomassage was used in patients. The applicator with a cotton swab was placed parallel to the skin surface and moved with quick rotational movements at low pressure over the treated area until the skin turned slightly pale. The procedure was repeated 3-5 times depending on the reaction of the patient's skin with short intervals (1-2 minutes). More pronounced, bulging warts were additionally frozen, with the applicator placed perpendicular to the formation, without pressure for 10–15 seconds, without affecting the surrounding skin. The number of procedures varied from 4 to 5–6. A second session was conducted after the disappearance of the reaction (hyperemia) caused by the procedure. The interval between procedures was 3-4 days.

In the second group, in addition to cryomassage (cryodestruction), an immunomodulatory drug with an antiviral effect, Genferon, was simultaneously prescribed. light according to the following scheme: 1 suppository rectally 2 times a day with a 12-hour break for 10 days before destruction and within 10 days after destruction, in age-appropriate doses (a single dose for children under 7 years old was 125,000 IU, for children over 7 years old - 250,000 IU). Genferon light, specially created for a special category of patients (pregnant women and children), contains a reduced dose of active ingredients (interferon α -2b (IFN α -2b) at a dose of 250,000 IU and taurine at a dose of 0.005 g). IFN α -2 has a pronounced antiviral, immunomodulatory and anti-inflammatory activity. The amino acid taurine has antioxidant and membrane-stabilizing properties, which significantly increases the biological activity of IFN α . All patients were recommended to wipe it with a 2% solution of salicylic alcohol as a skin care during the treatment period. To prevent the occurrence of hyperpigmentation at the site of removed warts, it was recommended to avoid active insolation for 5–6 months and use sunscreen. The effectiveness of the treatment was assessed by the absence of clinical manifestations of the disease during the year.

Results

At the end of therapy, the complete absence of skin rashes (as a result of exfoliation of the stratum corneum along with warts) in the first group was observed in 23 children, which amounted to 65.7%. In 2 (5.7%) patients of this group, flat warts were partially preserved, 6 (17.1%) children had a relapse within 1–2 months, 4 (11.5%) had a relapse within six months, which required in the future, additional prescription of therapy in the variant of a combination of cryodestruction with an immunomodulatory drug Genferon light .

In patients of the second group who, in addition to cryomassage , received Genferon light , the effectiveness of therapy was 92.1% (35 children), relapse was recorded in 3 (7.9%) children by the end of the year of clinical observation, while reinfection could not be ruled out.

Portability Genferon the light of all the children was good. No side effects from the therapy were recorded.

Thus, the inclusion of the immunomodulatory drug with antiviral action Genferon in the complex treatment of flat warts in children light can significantly increase the effectiveness of therapy, avoid complications and adverse drug reactions, which is extremely important in this category of patients.

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