Comparison Between Cimetidine and Zinc Sulphate in The Treatment of Nongenital Warts

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Abstract

Warts are epithelial proliferations on the skin and mucous membrane caused by various types of HPV. They can decrease spontaneously or increase in number and size according to patient's immune status. Cimetidine and zinc sulphate have important effects on the immune system and are used as immunomodulators in the treatment of various diseases. To compare the efficacy of cimetidine and zinc sulphate in the treatment of multiple and recalcitrant warts. The study was conducted in Tikrit Teaching Hospital, during the period from September 2010 to the end of May 2011. Forty patients with multiple warts were divided into two groups: one took 40 mg/Kg/day of cimetidine, and the other 10 mg/Kg/day of zinc sulphate for two months. All patients were examined clinically, then interviewed and detailed questionnaires were completed for each of them. Review was performed monthly, observing number of the warts and side effects of the medication. After one month of treatment cure rates obtained were 60% in zinc sulphate-treated group, and 15% in cimetidine-treated group. After two months of treatment cure rates obtained were 80% in zinc sulphate-treated group, and 25% in cimetidine-treated group. Adverse effects reported by the patients treated with cimetidine included nausea, epigastralgia and pruritus. Adverse effects reported by the patients treated with zinc sulphate included nausea, vomiting and diarrhea.

مقارنة بين السميتيدين وسلفات الزنك في علاج الثالول

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الملخص

الثالول هو تركيب طلائي ينتشر على الجلد والاغشية المخاطية للجسم ويسبب بواسطة فايروسات مختلفة نوعHPV. بالامكان زيادة عددها وحجم ها اعتمادا" على الحالة المناعية الدفاعية للمريض . عقار السميتيدين وسلفات الزنك لها تأثير مهم على جهاز المناعة في مختلف الامراض . لمقارنة تأثير هذان العلاجان على الثالول في جسم الانسان تمت الدراسة في مستشفى تكريت التعليمي خلال الفترة من ايلول 2010 ولغاية ايار 2011. اشترك 40 مريض في الدراسة على مجموعتين ، مجموعة اعطيت 40 ملغم/كغم يوميا "عقار السميتيدين، والمجموعة الاخرى اعطيت 10 ملغم/ كغم/ يوم سلفات الزنك ولمدة شهرين . جميع المرضى تم فحصهم سريريا" ثم متابعة كل شهر. بعد شهر من العلاج 60% من المرضى المعالجين بواسطة سلفات الزنك تم شفائهم و15% من مجموعة السميتيدين. وبعد شهرين من العلاج معدل الشفاء وصل 80% من مجموعة سلفات الزنك و25% من مجموعة السميتيدين.

Introduction

Cutaneous warts were known to the ancient Greeks and Romans, and, until the nineteenth century, genital warts were believed to be a form of syphilis or gonorrhea (1). Warts are benign epidermal neoplasms that are caused by papillomaviruses (HPVs), which are small DNA viruses (2). They are more than 150 types of HPV have been identified and are associated with various clinical lesions and diseases (3). Papillomaviruses (PVs) comprise a large family of small DNA viruses found in humans and many other species. PVs are highly host-specific, meaning that those from one species do not induce papillomas in heterologous species, so PVs infect only humans, Rabbit, bovine, and canine (4). The genome of HPV consist of early genes (E 1,2,4,5,6, and 7), two late genes (L1 and L2), and in between an upstream regulatory region (URR)(5). Replication of this DNA papovavirus begins inside the nuclei of keratinocytes of the upper stratum spinosum. Once the entire nuclear space is filled, virus spills into the cytoplasm; in the stratum corneum, the virus lies free within the keratin mass (6). The best clinical guide to cure is the restoration of normal epidermal texture, including the epidermal ridge pattern where appropriate (7). Cimetidine, approved by the FDA for reduction of the secretion of gastric acid. It is used to alleviate the symptoms of peptic ulcer disease, erosive gastroesophageal reflux disease, and hypersecretory conditions including Zollinger-Ellison syndrome and multiple endocrine adenomas. In dermatology it is most commonly used to treat warts, urticaria, and mastocytosis(8). One of the most important uses of cimetidine in dermatological therapy is to reduce the dapsone induction of methemoglobinemia (9). It is an H2 receptor antagonist and has immunomodulating effect, used in children to treat warts. Treatment with oral zinc sulphate is well established for the treatment of enteropathic acrodermatitis. In other conditions, zinc deficiency has been acknowledged and can have different determining causes, such as alcohol abuse, gastrointestinal affections, pancreatic failure, cirrhosis, poor absorption syndrome, burns, neoplasm, infections, renal diseases and parenteral nutrition. Some studies report therapeutic efficacy of zinc sulphate on alopecia areata, uremic pruritus, cutaneous leishmaniasis, perifolliculitis capitis abscendens et sufodiens, and inflammatory acne. Another study showed efficacy of zinc sulphate in treating recalcitrant warts. Zinc deficiency determines thymic hypoplasia with repercussion on T cell maturation, resulting in immune deficiency that favor associated infections (10). Zinc has an important effect on the immune system and it has been used as an immunomodulator to treat a variety of skin disorders (11). Results from the use of oral cimetidine in wart treatment in adults have been conflicting. In open studies of high dose (30-40mg\kg\day for 3-4 months), two-thirds demonstrated improvement or complete resolution but in placebo-controlled trials, no significant benefit of cimetidine therapy has been observed. One study of oral zinc sulphate (10mg\kg\day) reported an 87% cure rate of warts. In a double-blind trial, zinc sulphate as a 10% aqueous solution produced a cure rate of 80% for plane warts (12).

Conclusions

Since many conventional "destructive" treatments for warts are painful, expensive, and may cause scarring, zinc supplements may offer a safe and very effective alternative. The 80%

cure rate in this study's treated patients is quite high. Zinc has an important effect on the immune system and has been successfully used in the treatment of a variety of skin diseases.

Patients and methods

The study was conducted in Tikrit Teaching Hospital, during the period from September 2010 to the end of May 2011. A total of forty patients (17 males and 23 females), their age range from 4-60 years (mean ± SD 18.85±6.90) and diagnosed with multiple verruca vulgaris (nongenital warts) were the subject of the study. All patients were examined clinically, then interviewed and detailed questionnaires were completed for each of them. The duration of the disease ranged from 0.3-10 years (mean ± SD 1.75± 2.70). A total of 298 lesions were included in the study (mean ± SD 3.65± 4.90). The exclusion criteria were: presence of immunodeficiency, pregnancy, use of immunosuppressant drugs, chronic diseases use other drugs during treatment, uses another wart treatment before the study started, hypersensitivity to cimetidine or zinc sulphate. The fourteen patients were divided into two groups: one group (20 patients) was treated with cimetidine (40mg\kg\day) and the second group received zinc dulphate (10mg\kg\day) for two months. Review was performed monthly, observing number of the warts and side effects of the medication. Patients were treated for two months and were followed up monthly for two more months after the end of treatment. Response to treatment was defined as disappearance of all warts without residual scarring.

Results

At the end of the therapy, twenty patients cimetidine-treated and twenty patients zinc sulphate-treated were examined to determine the efficacy of treatment. After one month of treatment cure rates obtained were 60% in zinc sulphate-treated group, and 15% in cimetidine-treated group, as shown in the table 1. After two months of treatment cure rates obtained were 80% in zinc sulphate-treated group, and 25% in cimetidine-treated group, as shown in the table2. Adverse effects reported by the patients treated with cimetidine included nausea, epigastralgia and pruritus, as shown in the table 3. Adverse effects reported by the patients treated with zinc sulphate included nausea, vomiting and diarrhea, as shown in the table 4.

Table (1):- Clinical response according to the medications after one month of treatment.

Medication	Not Response	%	Partial response	%	Total response	%	Total	%
Zinc-sulphate	3	15%	5	25%	12	60%	20	100%
Cimetidine	14	70%	3	15%	3	15%	20	100%

Table(2):- Clinical response according to the medications after two months of treatment.

Medication	Not Response	%	Partial response	%	Total response	%	total	%
Zinc-sulphate	3	15%	1	5%	16	80%	20	100%
Cimetidine	13	65%	2	10%	5	25%	20	100%

Table (3):- side effects of zinc sulphate according to the patients.

Symptoms	Numbers	Percentage
Nausea	12	60%
Vomiting	3	15%
Diarrhea	1	5%
Total	16	80%

Table (4):- side effects of cimetidine according to the patients.

Symptoms	Numbers	Percentage
Nausea	3	15%
Epigastralgia	1	5%
Pruritus	2	10%
Total	6	30%

Discussion

Warts are caused by the human papilloma virus (HPV), which has still not been cultured in vitro. Nevertheless, more than 70 types of the virus have been recognized by DNA sequencing; each has its own range of clinical manifestations. HPV-1, 2 and 4, for example, are found in common warts, whereas HPV-3 is found in plane warts, and HPV-6, 11, 16 and 18 are most common in genital warts. Infections occur when wart virus in skin scales comes into contact with breaches in the skin or mucous membranes (13). Because HPV infection is nonlytic, antigen presentation occurs very slowly. HPV infection does not induce inflammatory cytokines; therefore, therapeutic options aimed at modulating the immune system and facilitating the production of cytokines have been proposed. One immunomodulatory approach involves prescribing zinc, a micronutrient that is necessary for the normal functioning of cells. More importantly, this element modulates DNA-and RNA-related enzymes and is also involved in many immunologic processes (14). This study confirms that zinc sulphate therapy appears to be beneficial in the treatment of warts. At the end of therapy, cure rates obtained were 80% in zinc sulphate treated patients and 25% in cimetidine treated patients. The rate of regression was faster in zinc sulphate treated patients 25% in comparison of cimetidine treated patients were 5% at the end of one month of therapy. The present study demonstrated that the zinc sulphate therapy is more effective than cimetidine for treatment of nongenital

warts. A significant percentage of nonresponders (65%) was in cimetidine therapy. A significant improvement was seen in patients with zinc sulphate therapy. Our experience is that 10 mg\kg\daily of zinc sulphate is required to achieve a clinical response. The most frequently reported side effects of zinc sulphate therapy according to the patients were nausea (60%) and vomiting (15%) in comparison with cimetidine side effects were nausea (15%) and pruritus (10%). Zinc sulphate was somewhat effective in 80% of patients with totally cured warts, in comparison with cimetidine was effective in only 25% of patients. The results with cimetidine were not very significant, which does not justify its use. Since many conventional "destructive" treatments for warts are painful, expensive, and may cause scarring, zinc supplements may offer a safe and very effective alternative. The 80% cure rate in this study's treated patients is quite high. Zinc has an important effect on the immune system and has been successfully used in the treatment of a variety of skin diseases.

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