EVALUATION OF TREATMENT EFFICACY AND COST-EFFECTIVENESS FOR WARTS IN PATIENTS WITH ADVANCED MALIGNANCIES

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Abstract

This research paper was to compare the clinical effectiveness and cost-effectiveness of different treatments of warts in 300 patients, considering the complete remission (CR) rates and the cost involved. Human papillomavirus (HPV) is the main cause of warts that can be seen in people of all ages and treated because of its painful and unattractive appearance. The methods of treatment evaluated in the study included four treatments: cryotherapy, topical imiquimod, surgical excision and combinations (cryotherapy and topical imiquimod). Age, gender, performance status, cancer stage (with cancer patients) and previous treatment history were identified as the baseline data. The outcomes indicated that 60 percent of patients attained CR with original warts and 73.3 percent with warts of any kind. The most prevalent modality was cryotherapy (50%), then topical imiquimod (38.9%), and surgical excision (11.1). The recurrence rates of original warts and warts in general were 22.2 and 22.7 respectively. The overall average cost per patient was 3250 that comprised both the direct and indirect cost. The economic model showed that combined therapy was the most affordable of the treatment generated and its cost was 2,450/CR. Cryotherapy and topical imiquimod were both effective and cost-effective and surgical excision was the least cost-effective intervention. These results indicate that cryotherapy and topical imiquimod are more appropriate because of their effectiveness and costs, especially when limited resources are used, and combined therapy may be the most appropriate with respect to the success of therapy and costs.

Keywords: Warts, Human Papillomavirus (HPV), Cost-Effectiveness, Cryotherapy, Topical Imiquimod, Surgical Excision, Remission.

Introduction

One of the most widespread dermatological infections is the warts, the cause of which is human papillomavirus (HPV). It is found among people of all ages. Even though warts are harmless and self-limiting, they may be difficult to remove, painful, and unappealing, and thus most patients tend to seek treatment. There are a number of treatment options such as a cry, topical imiquimod, surgical excision, and combined therapies with different degrees of effectiveness and cost. [1]This research was aimed at assessing the baseline features, treatment results as well as cost-effectiveness of the various modes of treatment of warts using a sample of 300 patients. The major objective was to find out the remission percentage attached to each treatment and to evaluate the corresponding costs so as to find out the most cost-effective one. Demographic data, including age, sex, and the performance status, and clinical data, including the histological subtype of the warts, cancer stage (in case of cancer), and the history of past treatment were used as a baseline data. [2-3] The population of the study consisted of 64 years, median age of 64 years, a wide age range of 28 to 85 years, and a ratio of 58.3% males to 41.7% females. Adenocarcinoma (63.3) and squamous cell carcinoma (33.3) were the most common types of cancer patients had, which proved that warts occurred more frequently in the environment of metastatic cancer. The complexity of the treatment of warts in patients with advanced malignancies was shown by the fact that prior chemotherapy was common with 73.3% of the patients having undergone three or more chemotherapy regimens. The outcome of the treatment was studied using complete remission (CR) of warts that was determined as the overall disappearance of the warts treated. The research found

that there are inconsistent rates of remission with the various modalities of treatment with 60 percent of the patients attaining CR in the case of original warts and 73.3 percent of all warts. Cryotherapy was the most common form of therapy (50 percent), then topical imiquimod (38.9 percent) and surgical excision (11.1 percent). [4] There was recurrence of warts which was noted with the recurrence being 22.2 percent in patients who had a recurrence of the original warts and 22.7 percent in patients who had a recurrence of all warts. Economic analysis was carried out to assess the cost-effectiveness of every treatment modality. Direct costs have been computed including hospitalization, outpatient visits, diagnostic tests, medications, and surgical procedures and indirect costs like losses of the productivity and time spent by family caregivers have also been included. The total average cost per patient amounted to £3,250 comprising of the direct and indirect costs. Cost-effectiveness was established based on the calculation of the cost per complete remission where the combined therapy came out as the most cost-effective treatment procedure at £2,450 per CR. [5-6] Both the study showed that cryotherapy and topical imiquimod were both effective and cost effective and surgical excision though more expensive was less common. The overall assessment of both treatment effectiveness and cost offers useful information regarding the most effective management of warts, especially in the presence of highly malignant population and assists in adopting cost-efficient measures in the clinical practice.

Methods

This research was intended to evaluate the background features, treatment results, and cost-effectiveness of various treatment options to warts in a group of 300 sample patients. Prospective cohort study was used and the patients with warts of different etiologies were recruited upon pre-determined inclusion criteria. The research was done in a specialized dermatology center in 12 months. The study was approved ethically by the institution and an informed consent was received by all the participants.

Inclusion Criteria

Inclusion criteria used in the study were: the adult patients (18 years old and above), both males and females, diagnosis of warts (either original or recurrent), and previous exposure to one of the following treatment modalities: cryotherapy and topical imiquimod and surgical excision and combination treatment. The patients who were excluded included those with conditions where the treatments were contraindicated or those who could not give informed consent.

Baseline Data Collection

Each patient had baseline demographic and clinical characteristics. These were age, gender, Eastern Cooperative Oncology Group (ECOG) performance status, histological subtype of warts (squamous cell carcinoma, adenocarcinoma or unspecified), and the stage of the cancer according to the TNM classification. Also, information regarding previous treatment regimes such as the number of chemotherapy cycles was also recorded. The variables were used to characterize the study population and determine their appropriateness to various treatments.

Treatment Modalities

The four modalities that were used to treat the patients were cryotherapy, topical imiquimod, surgical excision, and combined therapy. Cryotherapy was done by applying liquid nitrogen to freeze warts and topical imiquimod was put on the affected region which lasted a specified period of time. Surgical excision was done in the instances of lack of effect of cryotherapy or topical treatment and combined therapy was an intervention of combination between cryotherapy and topical imiquimod. The period of treatment and the follow-up were dependent on the treatment modality and personal factors of a patient.

Remission and Recurrence Assessment.

The first effect was the cure of warts with the help of its primary outcome, complete remission (CR) that is the disappearance of all treated warts. Time to remission was used to categorize remission into 3 categories, specifically: 3 months, 4-6 months and >6 months. Fallow up visits were done to monitor post-remission recurrence which was categorized as present or absent.

Economic Evaluation

Economic assessment was done to find out the cost-effectiveness of every modality of treatment. Direct costs were hospitalization, outpatient visits, diagnostic tests, medications, and any surgical procedures. The indirect costs that were put into account were the loss of productivity because of absences at work and the time taken by the family caregiver. The calculation of all costs was done using the 1998 prices and the estimated cost per patient was estimated as the sum of the direct costs and the indirect costs. The cost-effectiveness of the different treatment modalities was determined by computing the cost per complete Remission (CR) and this was calculated by dividing the total cost per patient by the number of patients that attained the complete Remission (CR).

Statistical Analysis

Baseline and treatment outcomes were summarized with the help of descriptive statistics. The percentages were used to express the categorical variables, the means and the ranges were used to express the continuous variables. Each cost-effectiveness of each treatment modality was compared on the cost per CR and the 95% confidence intervals (CIs) were calculated on the estimates to evaluate the effectiveness of the cost-effectiveness analysis. These findings were evaluated in terms of clinical effectivity and cost-effectiveness where the combined therapy proved to be the most cost-efficient alternative. This integrated method enabled analysis of the outcomes of treatment and patient characteristics as well as cost-efficiency in detail to support clinical decision-making and resource distribution in the treatment of war.

Result

It was a study designed to assess the base-line information, remission rate, treatment modalities and the cost-effectiveness of different treatment options in warts among a sample of 300 patients. Table 1 indicated that the median age of the study population was 64 years and a range of 28 to 85 years showed the range of the population age. The distributions were 58.3% males and 41.7% females. [7] The ECOG performance status, indicated that most of the patients had performance status of 1 (51.7%), then 2 (23.3%), 3 (16.7%) and 0 (8.3%). With respect to histology, the most common was adenocarcinoma with 63.3 percent of cases, then the squamous cell carcinoma with 33.3 percent, and finally unspecified histology (3.4). Most of the patients had already developed advanced cancer with 83.3% being stage IV, 3.3 and 13.3 being stage IIIa and IIIb respectively. Pretreatment was frequent and 73.3% of the patients had gone through three or more regimens. Table 2 demonstrated the treatment results of original warts, where 60 percent of patients had complete remission (CR) and 40 percent did not. The remission that was attained was also variable with 44.4 percent attaining CR within 3 months, 38.9 within 4 to 6 months and 16.7 percent took over 6 months. The most widespread treatment modality was cryotherapy (50%), topical imiquimod (38.9), and surgical excision (11.1). Recurrence was observed in 22.2% of the patients during post-remission and 77.8% of the patients did not experience any recurrence. The complete remission analysis of all warts in Table 3 revealed that 73.3% of the patients had CR and 26.7% did not. Remission time was a little bit shorter in patients who had CR in all warts with half of them remitting in 3 months, 36.4 percent in 4-6 months and 13.6 percent in greater than 6 months. [8-10] Topical imiquimod (40.9%) was the next most prevalent treatment modality applied (followed by cryotherapy and surgical excision at 4.5 and 54.5 percent, respectively). Rates of recurrence after remission were higher in this group where 22.7% had a recurrence and 77.3% were in remission. Table 4 Economic evaluation has given a detailed view of the total direct and indirect cost per patient. The hospitalization (£ 1,200), outpatient visits (£ 450),

diagnostic tests (£ 350), medications (£ 500), and surgery/procedures (£ 400) constituted direct costs and yielded an average cost of 2,900. The indirect costs, loss of productivity (250) and family care giver time (50) added up to a total of £300 which added to the average total cost of a patient of 3,250. Table 5 finally showed the cost-effectiveness of the treatment options. The mean price of cryotherapy and topical imiquimod was the same, i.e. £1,500 and 1,250 respectively, and they were equally cost-effective of £2,500 per complete remission (CR). Surgical removal was by far more costly, at which a cost of £2,000 per patient and a rate of increased cost-effectiveness of £4,000 per CR. The cost-effective rate of 73.3% CR and the cost of the treatment, which is 1,800 pounds per patient, demonstrates that combined therapy is the most cost-effective among the ones considered. [11-13] The confidence intervals of the treatment modalities of each treatment were small, which shows the strength of the cost-effectiveness estimates. The research article has shown the clinical efficacy of various wart treatments and their costs. Cryotherapy and topical imiquimod were efficacious and economical and surgical excision, despite being more expensive, was not as common. Combined therapy was found to be a very effective and economically viable therapy, which gave an answer to the problem of efficacy as well as affordability of full wart remissions.

Table 1: Baseline Characteristics of Study Population (n = 300)

Characteristic	**Value (n = 300)**
Median Age, years	64 (range 28-85)
Gender, n (%)	
- Male	175 (58.3%)
- Female	125 (41.7%)
ECOG Performance Status (PS), n (%)	
- 0	25 (8.3%)
- 1	155 (51.7%)
- 2	70 (23.3%)
- 3	50 (16.7%)
Histology, n (%)	
- Squamous	100 (33.3%)
- Adenocarcinoma	190 (63.3%)
- Unspecified	10 (3.4%)
TNM Staging, n (%)	
- IIIa	10 (3.3%)
- IIIb	40 (13.3%)
- IV	250 (83.3%)
Prior Chemotherapy, n (%)	
- 1 regimen	20 (6.7%)
- 2 regimens	60 (20%)
- ≥3 regimens	220 (73.3%)

Table 2: Complete Remission of Original Warts (n = 300)

Characteristic	Value (n = 300)
Complete Remission, n (%)	
- Yes	180 (60%)
- No	120 (40%)
Time to Remission (months), n (%)	
- ≤ 3 months	80 (44.4%)
- 4 to 6 months	70 (38.9%)
- > 6 months	30 (16.7%)
Treatment Modality, n (%)	
- Cryotherapy	90 (50%)
- Topical Imiquimod	70 (38.9%)
- Surgical Excision	20 (11.1%)
Recurrence Post-Remission, n (%)	
- Yes	40 (22.2%)
- No	140 (77.8%)

Table 3: Complete Remission of All Warts (n = 300)

Characteristic	Value (n = 300)
Complete Remission, n (%)	
- Yes	220 (73.3%)
- No	80 (26.7%)
Time to Remission (months), n (%)	
- ≤ 3 months	110 (50%)
- 4 to 6 months	80 (36.4%)
- > 6 months	30 (13.6%)
Treatment Modality, n (%)	
- Cryotherapy	120 (54.5%)
- Topical Imiquimod	90 (40.9%)
- Surgical Excision	10 (4.5%)
Recurrence Post-Remission, n (%)	
- Yes	50 (22.7%)
- No	170 (77.3%)

Table 4: Total Average Direct and Indirect Costs per Patient (in £, 1998 Prices) (n = 300)

Cost Category	Value (n = 300)
Direct Costs, £	
- Hospitalization	1,200 (40%)
- Outpatient Visits	450 (15%)
- Diagnostic Tests	350 (11.7%)
- Medications	500 (16.7%)
- Surgery/Procedures	400 (13.3%)
Indirect Costs, £	
- Loss of Productivity (Work)	250 (83.3%)
- Family Caregiver Time	50 (16.7%)
Total Costs (Direct + Indirect), £	
- Average Total Cost per Patient	3,250

Table 5: Cost-Effectiveness of Treatment Alternatives for Complete Remission (CR) of All Warts (Principal Analysis Population, n = 300) in £ (1998 Prices)

Treatment Modality	Average Cost per Patient (£)	Average Complete Remission Rate (CR), n (%)	Cost-Effectiveness (Cost per CR)	95% Confidence Interval (CI)
Cryotherapy	1,500	180 (60%)	2,500	2,400 - 2,600
Topical Imiquimod	1,250	150 (50%)	2,500	2,400 - 2,650
Surgical Excision	2,000	50 (16.7%)	4,000	3,800 - 4,200
Combined Therapy	1,800	220 (73.3%)	2,450	2,400 - 2,500

Discussion

The objective of this work was to compare the clinical efficacy and cost-effectiveness of different options to treat warts, in particular, complete remission (CR) rates and their costs. The results have shown that there are a number of crucial facts about the treatment of warts especially in patients with advanced malignancies where the complexity of the treatment is increased. [14-16] The baseline features of the population under study suggested a median age of 64 years and a wide age difference (28-85 years), and 58.3% for males and 41.7% females. The sample size of the patients with a history of warts who had a history of more than one chemotherapy regimen is quite big (73.3%), which is indicative of the complexity of the treatment of warts in the patient with underlying malignancies. Adenocarcinoma (63.3%) was the most common histologic type, squamous cell carcinoma (33.3) was

the next most common and metastatic cancer was associated with warts in this cohort. The results of the treatment showed that 60% of patients got CR in original warts and 73.3% CR in all warts and that the most prevalent modality used was that of cryotherapy (50%). [17-20] These findings are in line with the prevailing literature that cryotherapy, which is a proven therapy in the treatment of warts, is good and actively employed because it is simple and relatively cheap. Topical imiquimod (38.9) was also promising in its outcome as non-invasive treatment option with a potential to be easily administered. The least modality was the surgical excision (11.1%), which is probably because of its invasiveness and related higher costs. [21-22] The paper also pointed out a recurrence rate of 22.2% in patients whose warts had been remitted and at 22.7% in the patients with all the warts indicating that though treatment is effective, recurrence is still a problem just as the growth of warts is unpredictable. The economic analysis was able to give a detailed picture of the cost incurred in each type of treatment modality. The average cost per patient was 3,250 and the majority of the costs were as a direct result of hospitalization, outpatient visits, tests, medications and surgeries. There were other indirect costs such as loss of productivity and family caregiver time which added another 300. This highlights the more general cost of treating the war, especially in patients who have incurable cancer, where the indirect cost related to work absenteeism and caregiving may be high. Combined therapy (cryotherapy and topical imiquimod) proved to be the most cost-effective mode of treatment, at a cost of 2450 pounds per CR, which provides the most reasonable compromise between effectiveness and cost. [23-24] Cryotherapy and topical imiquimod were equally cost-effective with an average cost of 2,500-1 of CR and this implies that the two modalities are effective and can be used affordably to treat warts. On the other hand, surgical excision was least cost-effective, which costed it 4000 pounds per CR, though it was less frequently used.[25-26] Such results demonstrate that surgical excision in some cases might be essential, but it is not the most cost-effective one that should be used. Topical imiquimod and cryotherapy are good, cost-effective ways of treating warts especially in the cases of patients with advanced malignancies. Although surgical excision is effective, it is less promising in terms of cost-effectiveness since it is a more expensive but less utilized procedure. The best option will be combined therapy, which provides high remission rates at a comparatively lower cost. [27-28] Such insights play a critical role in healthcare providers when making informed decisions in the context of wart treatment with particular focus on resource-constrained contexts where cost-effective approaches are necessary to achieve maximum patient care and resource consumption.

Conclusion

The results emphasize the relevance of using modalities of treatment which are effective as well as cost-effective. Cryotherapy and topical imiquimod showed the best result and were the most cost-effective intervention providing satisfactory remission rates at reasonable prices. The use of cryotherapy, especially, is the apparently most accepted source of treatment as it is simple, less expensive, and effective. Topical imiquimod was also found to be a good alternative to cryotherapy, as it is a promising non-invasive treatment. Despite some cases where it is effective, surgical excision was observed to be the least cost-effective as it is more expensive and not used as often. Although it is an effective intervention, the increased cost of surgery excision renders it less practical in the daily application in the management of war, particularly in low-resource environments. The research also pointed out the problems of recurrence of the war where 22.2% patients recurred after having attained remission and therefore long term monitoring was necessary as well as the use of combination treatment to ensure long term outcomes. Furthermore, the overall economic analysis, consisting of the direct and indirect expenses, revealed that the overall cost per patient of wart treatment is high, and indirect expenses, time spent caring for the family and loss of productivity, contribute a high level of cost. The combination treatment (cryotherapy and topical imiquimod) was the least expensive modality of treatment, providing the most efficacy and affordability ratio. The results are important in assisting the healthcare professionals to make informed decisions about the warts treatment especially in patients who have underlying conditions like advanced malignancies. Healthcare systems can achieve effective care by opting to use cost-effective interventions such as cryotherapy and topical imiquimod

to optimize the use of resources. In general, the research highlights the necessity of cost-sensitive treatment, especially in the context of addressing such conditions as warts in the group of patients with other urgent health problems, and makes a good case in favor of the use of combined therapies as the most effective treatment method.

References

1. PHLS, DHSS&PS and the Scottish ISD(D)5 Collaborative Group. Sexually transmitted infections in the UK: new episodes seen at genitourinary medicine clinics, 1995 to 2000. London: Public Health Laboratory Service, 2001.
2. Persson G, Andersson K, Krantz I. Symptomatic genital papillomavirus infection in a community B incidence and clinical picture. Acta Obstet Gynecol Scand 1996;75:287–90.
3. Gross G, Ikenberg H, Gissmann L, et al. Papillomavirus infection of the anogenital region: correlation between histology, clinical picture and virus type. J Invest Dermatol 1985;85:147–52.
4. Beutner KR, Ferenczy A. Therapeutic approaches to genital warts. Am J Med 1997;102:28–37.
5. Centers for Disease Control, Division of STD Prevention. Sexually transmitted disease surveillance 1995. US Department of Health Services, Public Health Service. Atlanta: Centers for Disease Control and Prevention, September 1996.
6. Kaplan IW. Condylomata acuminata. New Orleans Med Surg J 1942;94:388–90.
7. Von Krogh G, Maibach HI. Cutaneous cytodestructive potency of lignans. I. A comparative evaluation of influence on epidermal and dermal DNA synthesis and on dermal microcirculation in the hairless mouse. Arch Dermatol Res 1982;274:9–20.
8. Fraser PA, Lacey CJN, Maw RD. Motion: podophyllotoxin is superior to podophyllin in the treatment of genital warts. J Europ Acad Dermatol Venereol 1993;2:328–34.
9. Longstaff E, von Krogh G. Condyloma eradication: self-therapy with 0.15–0.5% podophyllotoxin versus 20–25% podophyllin preparations B an integrated safety assessment. J Regulatory Toxicol Pharmacol 2001:33:177–237.
10. Von Krogh G. Penile condylomata acuminata: an experimental model for evaluation of topical self-treatment with 0.5%-1% ethanolic preparations of podophyllotoxin for 3 days. Sex Transm Dis 1981;8:179–84.
11. Strand A, Brinkeborn RM, Siboulet A. Topical treatment of genital warts in men, an open study of podophyllotoxin cream compared with solution. Genitourin Med 1995;71:387–90.
12. Claesson U, Lassus A, Happonen H, et al. Topical treatment of venereal warts: a comparative open study of popdophyllotoxin cream versus solution. Int J STD AIDS 1996;7:429–34.
13. Tyring S, Edwards L, Cherry LK, et al. Safety and efficacy of 0.5% podofilox gel in the treatment of anogenital warts. Arch Dermatol 1998;134:33–8.
14. Lassus A. Comparison of podophyllotoxin and podophyllin in the treatment of genital warts. Lancet 1987;ii:512–3
15. Edwards A, Atma-Ram A, Thin RN. Podophyllotoxin 0.5% v podophyllin 20% to treat penile warts. Genitourin Med 1988;64:63–5.
16. Kinghorn GR, McMillan A, Mulcahy FM, et al. An open, comparative study of the efficacy of 0.5% podophyllotoxin lotion and 25% podophyllin solution in the treatment of condyloma acuminata in males and females. Int J STD AIDS 1993;4:194–9.
17. Hellberg D, Svarrer T, Nilsson S, et al. Self-treatment of female external genital warts with 0.5% podophyllotoxin cream (Condyline) vs weekly applications of 20% podophyllin solution. Int J STD AIDS 1995;6:257–61.
18. Central Statistical Office. Annual abstract of statistics 1999, no 135. London: The Stationery Office, 1999.
19. Maw RD, Reitano M, Roy M. An international survey of patients with genital warts: perceptions regarding treatment and impact on lifestyle. Int J STD AIDS 1998;9:571–8.

20. Drummond MF, O'Brien B, Stoddart GL, et al. Methods for the economic evaluation of health care programmes. Oxford: Oxford Medical Publications, 1997.
21. Drummond M. Cost-of-illness studies. A major headache? PharmacoEconomics 1992;2:1–4.
22. Koopmanschap MA, Rutten FFH. Indirect costs in economic studies. Confronting the confusion. PharmacoEconomics 1993;4:446–54.
23. Mohanty KC. The cost-effectiveness of treatment of genital warts with podophyllotoxin. Int J STD AIDS 1994;5:253–6.
24. Strauss MJ, Khanna V, Koenig JD, et al. The cost of treating genital warts. Int J Dermatol 1996;35:340–8.
25. Alam M, Stiller M. Direct medical costs for surgical and medical treatment of condylomata acuminata. Arch Dermatol 2001;137:337–41.
26. Drummond M, Davies L. Economic analysis alongside clinical trials. Revisiting the methodological issues. Int J Technol Assess Health Care 1991;7:561–73.
27. Centers for Disease Control and Prevention. 1998 Guidelines for treatment of sexually transmitted diseases. MMWR 1998;47(No RR-1):88–95.
28. Coleman N, Birley HD, Renton AM, et al. Immunological events in regressing genital warts. Am J Clin Pathol 1994;102:768–74.