

A Comparative Study on the Efficacy of Carbon Dioxide Laser, Electrocautery and High Frequency Radiosurgery Ablation in the Treatment of Warts - A Prospective Randomized Trial

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ABSTRACT

BACKGROUND

Wart is a common dermatological condition resulting from infection with human papilloma virus. Clinical management of warts is often challenging as no therapy has proven to be 100 % effective. Evidence based literature for treatment of warts based on newer modalities is yet to be subjected to large, rigorous, blinded, randomized-controlled trials. Carbon dioxide laser, electrocautery and high frequency radiosurgery ablation are most commonly used in clinical settings but the available literature on the efficacies of these modalities is mainly retrospective and comparative data is scarce. This prospective blinded randomized controlled clinical trial was aimed at providing the best comparative evidence for treating warts with the above three mentioned modalities in terms of cure rate, side-effects and recurrences.

METHODS

In total 192 patients were enrolled and randomized into carbon dioxide laser, electrocautery and high frequency radiosurgery ablation treatment groups (1 : 1 : 1). Patients were given a maximum of 4 sittings one week apart. The response and complications were documented at 1st, 4th, 8th and 12th week post-procedure.

RESULTS

Complete cure was achieved with high frequency radiosurgery ablation in 98.3 % patients. This was followed by electrocautery and carbon dioxide laser group with cure rates being 87.3 % and 83.6 % respectively. High frequency radiosurgery ablation also had lesser complications compared to the other treatment groups. Electrocautery was associated with highest side effects.

CONCLUSIONS

High frequency radiosurgery ablation was found superior to both carbon dioxide laser and electrocautery in the treatment of warts.

KEYWORDS

Warts, Lasers, Electrocoagulation, Radiosurgery

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BACKGROUND

Warts or Verrucae are benign epithelial neoplasms arising from skin and / or mucosa due to infection with human Papilloma Virus (HPV). The estimated incidence of warts is around 10 % in children and young adults.¹ Treatment modalities available for warts include destructive, anti-mitotic, virucidal therapies, immunotherapy and combinations of these therapies. Among the destructive therapies, carbon dioxide (CO₂) laser, electrocautery (EC) and high frequency radiosurgery (HFR) ablation are commonly used. CO₂ laser with a wavelength of 10600 nm is used for both cutaneous and mucosal warts.²⁻⁴ EC, a crude form of electrosurgery is considered more effective for thick warts.⁵ HFR is a form of electrosurgery that utilizes radiofrequencies in the range of 500 to 4000 KHz.⁶ The reported success rates of CO₂ laser, EC and HFR are 36 - 96 %, 57 - 95 % and 33 - 80 % respectively.⁶⁻¹² Hence, these are considered as the better established approaches. However, most of the studies on the efficacies of these modalities are retrospective and there is insufficient comparative data. Our aim was to prospectively evaluate and compare the therapeutic efficacies of CO₂ laser, EC and HFR ablation in order to establish an ideal treatment option for different types of warts.

METHODS

This prospective single blinded randomized controlled trial was undertaken in the Department of Dermatology and Venereology of B.P. Koirala Institute of Health Sciences in Dharan, Nepal after approval from the Institutional Ethical Committee. The study protocol conformed to the ethical guidelines of 1975 Declaration of Helsinki. Standard protective measures were taken by the health caregivers and patients throughout the treatment sessions. A total of 392 patients with clinically diagnosed verrucae were screened for a period of one year. A detailed history including chief complaints, duration of illness, precipitating factors, progression, previous treatment(s) and history of similar condition in any of the family members or close contacts was documented in a proforma. Clinical data such as socio-demographic profile of patients and characteristics of the wart (s) was documented. A thorough cutaneous and systemic examination was done and recorded. A total of 192 patients were enrolled into the study after using the exclusion criteria. These patients were randomized into three subgroups by simple randomization technique i.e., CO₂ laser, EC and HFR ablation groups with 64 patients in each group. Patients were explained all the aspects of the procedure, possible outcomes and adverse effects. A written informed consent was taken from each patient. In patients with multiple warts, reference lesions were selected arbitrarily. The reference lesions were photographed before starting the procedure. Each lesion site was thoroughly cleaned with povidone iodine solution and anaesthetized

with intra-cutaneous Xylocaine (2 %) solution with or without adrenaline (1 : 200000) depending upon the site being treated. Hyperkeratotic skin if present was pared before the procedure. The reference wart (s) were allowed a maximum of 4 sittings with the allocated modality in the following manner; Group A: CO₂ laser 10600 nm (Visco co. Ltd, Seoul, South Korea) was used in focus vaporization method in continuous mode using power depending on the type of the wart. The following settings were recommended : verruca plana, 3 - 4 Watt (W); filiform warts and verruca vulgaris (small / less thick lesions), 5 - 9 W; for verruca vulgaris (large / thick lesions) and periungual lesions, 10 - 14 W was used. Group B: Mini electrosurgical unit, Healocatar, [Indian Healosurg (P) Ltd, New Delhi, India] was used in low or high mode depending on the type of wart. For verruca plana, filiform warts and verruca vulgaris (small) low power setting was used and for verruca vulgaris (thick lesions), palmar and planter warts high power setting was used. Group C: Mega surg-II high frequency radiosurgery unit, Derma India, Chennai, India) was used in electrode cutting mode using power depending on the type of the wart. The following were the recommended settings: verruca plana, 2 - 3 Kilohertz (KHz); filiform warts, verruca vulgaris (small) and periungual lesions, 3 - 4 KHz, and for verruca vulgaris (large), palmar and planter warts: 4 - 5 KHz was used.

Following the procedure, a course of oral amoxicillin or fusidic acid ointment for 5 to 7 days was given to the patients to prevent post-operative secondary infection along with analgesic. Other lesions were also treated simultaneously by the same modality. Following treatment, the lesions were assessed by a blinded observer. The response was documented at 1st, 4th, 8th and 12th week post procedure on the basis of reduction of the total surface area of the reference lesion (s), pigmentation, scarring, pain, secondary infection, skin markings, patient satisfaction, need for further sittings or any other complications. Criteria followed for assessing the reference lesion(s) was as follows

- Complete cure: complete resolution with or without reappearance of skin markings or dermatoglyphics over palm and soles at the 12th week.
- Treatment failure: persistence of one or more reference lesion even after maximum of 4 sittings.
- Recurrence / Relapse: Partial or complete reappearance of the lesion(s) at the same site after complete resolution.
- Defaulter: Those patients who did not come for more than 4 weeks between 2 sittings were excluded from the study.

The data was analysed by using SPSS version 20.0 (IBM, United States) & MS Excel of version 7.0. The categorical data was expressed as frequencies & percentage. The analysis was done as per protocol. Chi-square test and Fisher's exact test were performed to compare proportions of cure or not cure in all three treatment groups and the p-value < 0.05 was considered to be statistically significant.

RESULTS

Baseline Characteristics

Among the 192 patients, 62 % (n = 119) were male and 38 % (n = 73) were female. The mean age of patients was 23.08 ± 9.48 years (range 12 - 75 years). Nearly 76 % (n = 147) patients were between 12 to 25 years age group and majority of them were students. The duration of the disease varied from one month to more than 15 years with approximately 35 % (n = 67) patients presenting within 6 months of its onset. Family members of 21 % (n = 40) patients were also affected.

Multiple lesions were seen in 74 % (n = 142) patients and remaining 26 % (50) patients had solitary lesion. Single body site involvement was seen in 76 % (n = 146) patients whereas 24 % (n = 46) patients had 2 or more body site involvement. The upper limb (excluding palms) was the most common site of involvement in 33 % (n = 64) patients, followed by palms in 26 % (50) patients, lower limb (excluding soles) in 25.5 % (n = 49) patients, soles in 25 % (n = 48) patients, face in 11 % (n = 21) patients, scalp in 3 % (n = 6) patients, neck in 2 % (n = 4) patients and only 1 % (n = 2) patients on the trunk.

Amongst the clinical type of warts, verruca vulgaris was seen in 59 % (n = 113) patients followed by palmar wart, plantar wart, verruca plana, filiform wart and periungual warts in 26 % (n = 50), 24 % (n = 46), 4.7 % (n = 9), 4 % (n = 8) and 2 % (n = 4) patients respectively.

Treatment Outcome

Eighteen patients were lost to follow up and only 174 patients completed the study. Complete clearance after 1 to 4 sittings with no recurrence at week 12 was seen highest in the HFR group followed by EC group and CO₂ laser respectively. Treatment failure was highest in the CO₂ laser group (Figure 1). Statistically significant difference was seen amongst the groups [$\chi^2 = 7.390$; DF = 2; p = 0.025].

Cure Rate According to Size of the Lesion(s) in cm²

Of the 174 patients, 89 % patients had total surface area of reference lesions 5 cm² or less. In these patients the HFR group showed highest cure. In the remaining 11 % patients the total surface area of reference lesions was more than 5 cm², here also the HFR group showed 100 % cure whereas CO₂ laser and EC groups showed significantly lesser cure rates [$\chi^2 = 7.26$; df = 2; p < 0.05] (Figure 2)

Cure According to Clinical Type of Lesion(s)

All three modalities showed complete cure in cases of verruca plana and filiform wart. In patients with verruca vulgaris, the best cure was achieved with HFR ablation while CO₂ laser and EC groups showed comparatively lesser response. This was statistically significantly [$\chi^2 = 6.462$; DF = 2; p = 0.01]. Percentage cure rates for palmar and plantar warts are shown in Table 1.

Cure According to Site of Lesion(s)

On the upper limbs, clearance of reference lesion(s) was seen in all 24 patients who underwent HFR ablation while both EC and CO₂ laser ablation showed lesser cure rates [$\chi^2 = 5.061$; df = 2; p = 0.015]. On the palms, all three modalities showed more or less similar results. On the thighs and lower legs, HFR and EC ablation showed near perfect results while CO₂ laser was seen successful in less than 60 % patients and this was statistically significant [$\chi^2 = 5.702$; df = 2; p = 0.016]. On the soles, all patients in HFR and CO₂ laser groups showed complete cure while patients in EC group showed relatively lesser cure [$\chi^2 = 12.212$; df = 2; p < 0.01]. The face, scalp, neck and trunk all showed 100 % resolution of lesion(s) in all 3 groups (Figure 3).

Cure According to Number of Lesions

All patients across the 3 modalities with solitary lesion (except 1 in CO₂ group) showed complete cure. In patients with multiple lesions, HFR ablation showed cure in 97 % while EC showed cure in 83 % and CO₂ laser showed the least cure in 79 % patients. This was found to be statistically significant [$\chi^2 = 5.418$; df = 2; p = 0.01].

Skin Markings / Dermatoglyphics

At the 12th week, 80 % (139 / 174) patients had either complete or partial reappearance of skin marking or dermatoglyphics among which 90 % (52 / 58) patients were in the HFR group, followed by 77 % (47 / 61) in CO₂ laser group and least in EC group with 73 % (40 / 55) patients [$\chi^2 = 5.5$; df = 2; p = 0.064].

Patient Satisfaction

At week 12, 96.55 % (56 / 58) patients in the HFR group found the result excellent and the remaining 3.45 % (2 / 58) patients found it to be acceptable. In the EC group 90.9 % (50 / 55) patients found the results excellent, 7.3 % (4 / 55) said it was acceptable and 1.8 % (1 / 55) found it unacceptable. Least patient satisfaction was seen in the CO₂ laser group. Overall 86.88 % (53 / 61) patients said that the results were excellent, 11.47 % (7 / 61) found it acceptable while 1.6 % (1 / 61) was not satisfied. (Fisher's exact test, p value = 0.126).

Recurrence

Of the 174 patients, 24 (13.8 %) patients had recurrence. The overall recurrence rate for CO₂ laser group was 24.6 %, for EC group was 14.5 % and for HFR group was 1.7 % [$\chi^2 = 12.976$; df = 2; p < 0.001].

Adverse Effects

Out of the 174 patients, 18.4 % (32) showed pigmentary changes at the end of the 12th week. Maximum patients with pigmentary changes were seen in the EC group and least in the HFR group. Hyper-pigmentation was the predominant change with 28 patients followed by hypo-pigmentation in

2 patients and de-pigmentation in 2 patients. Hyper-pigmentation was present in 13 patients treated with electrocautery followed by 9 patients in CO₂ laser group and 6 in HFR group.

type was seen in 6 patients each of CO₂ laser and EC group and 2 in HFR ablation group. Least scarring was seen in patients who had received HFR ablation.

In 29.7 % (57 / 174) patients, pain was a major complaint on follow up. Maximum patients i.e., 24 / 55 (43.6 %) with pain were in the EC group followed by 32.8 % (20 / 61) patients in CO₂ laser group and least i.e., 13 / 58 (22.4 %) in the HFR ablation group. However this was not found to be statistically significant [$\chi^2 = 5.77$; DF = 2; p = 0.056].

Six out of 174 patients (3 each in EC and HFR group) developed secondary infection in lesions that were treated. No patients in CO₂ laser group developed secondary infection. [Fisher's exact test p value = 0.219]. Among the 174 patients, 13 (6 in EC, 4 in CO₂ laser and 3 in HFR group) showed excessive bleeding from the lesion(s) during or following the procedure [Fisher's exact test p value = 0.512].

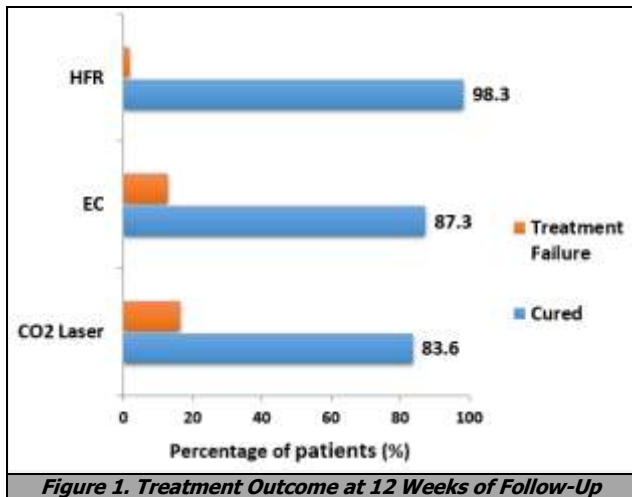


Figure 1. Treatment Outcome at 12 Weeks of Follow-Up

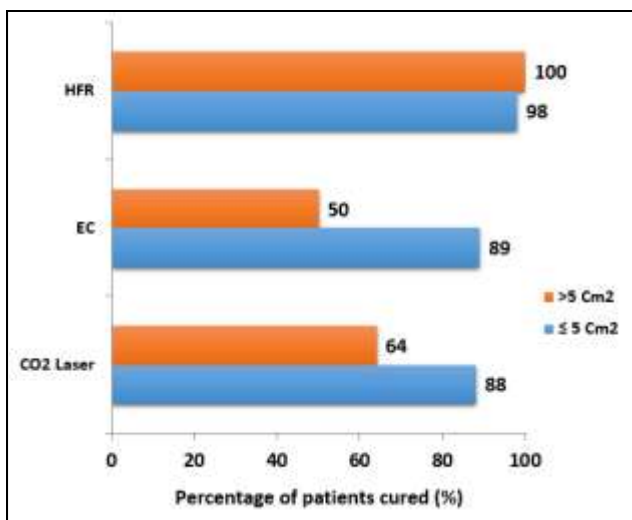


Figure 2. Cure According to the Size of the Verruca Lesion(s) at 12 Weeks of Follow-Up

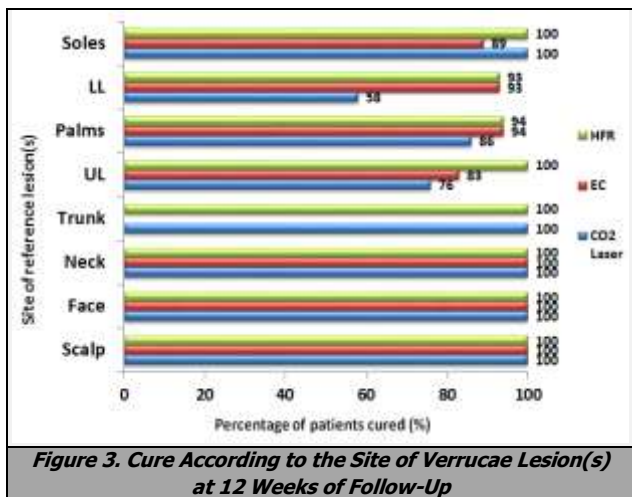


Figure 3. Cure According to the Site of Verruca Lesion(s) at 12 Weeks of Follow-Up

Scarring was seen in 17.24 % (30 / 174) patients. Fourteen of these were of depressed type and 14 were of flat type and 2 patients had raised type of scar. The depressed type was mostly seen with EC (9 / 14) and flat

Clinical Type	CO ₂ Laser			EC			HFR		
	Total Patients	Cured	%	Total Patients	Cured	%	Total Patients	Cured	%
Verruca Vulgaris	38	29	76.3	30	26	86.6	34	33	97
Verruca Plana	5	5	100	2	2	100	2	2	100
Palmar Wart	14	12	85.7	16	15	93.7	19	18	94.7
Plantar Wart	11	11	100	18	16	88.9	14	14	100
Filiform Wart	2	2	100	1	1	100	4	4	100
Periungual Wart	2	1	50	0	-	-	0	-	-

Table 1. Cure According to Type of Verruca at 12 Weeks of Follow-Up

DISCUSSION

Males had more warts than females and maximum number of patients was in the 2nd or 3rd decade which was similar to other studies.^{2,6} Majority of the patients were students and had disease within 6 months period comparable to a previous study.¹²

Similar to other studies most of the patients had multiple lesions.^{2,13} Single body site involvement was seen in majority of the patients. The upper limb including palm was the most common site involved similar to a previous study.¹² In another study done on paediatric patients, the upper limb (including palms) was the most common site.¹⁴

A previous study using CO₂ laser for treating warts demonstrated approximately 95 % clearance in 75 plantar warts after only one sitting.¹⁵ While another study using CO₂ laser in 27 patients with recalcitrant warts of hands and feet showed complete response in 81 % patients after one sitting. These patients remained free of lesions at the 6th month follow-up visit. Other patients required up to 3 more treatment with the laser during the first 6 months to remain free of lesions. Overall, all patients had achieved complete cure following at least 4 sittings.¹⁶ In a retrospective study of CO₂ laser ablation done in 68 patients with recalcitrant warts the cure rate was 57.4 % after a single sitting.³

In our study, complete clearance of lesion(s) after a single sitting was seen in 81 % patients with HFR ablation

followed by 52 % & 51 % patients with EC and CO₂ laser ablation respectively. The mean number of sittings was highest for CO₂ laser and least for HFR. A previous study on CO₂ laser showed that the response to therapy increases with increase in the number of sittings.²

Almost all patients who completed the study achieved a response of 75 % or more. A previous study with CO₂ laser on resistant warts reported cure of > 75 % in over half of the patients.¹⁷ Various studies done on recalcitrant or persisting warts using CO₂ laser have reported complete clearance ranging from 30 - 60 percent.^{3,17,18} In an earlier study using CO₂ laser on plantar warts, 74 % patients with solitary and 62 % patients with multiple recalcitrant lesion(s) respectively showed complete clearance.² In our study there were 49 patients with recalcitrant warts and among them 22.5 % (11 / 49) patients had solitary lesions while 77.5 % (38 / 49) patients had multiple lesions. All 11 patients with solitary recalcitrant lesions showed complete cure [3 in CO₂ laser group and 4 each in EC and HFR group]. In multiple lesions, HFR group showed 100 % (12 / 12) response, followed by EC and CO₂ laser with 80 % (8 / 10) and 69 % (11 / 16) patients respectively. Our study showed better efficacy with HFR and EC while response to CO₂ laser was comparable to previous studies done on multiple recalcitrant warts.

In our study, lesion(s) having < 5 cm² or ≥ 5 cm² total surface area, had comparable cure rates among all 3 modalities and was not statistically significant. HFR showed higher cure rate for verruca vulgaris as compared to EC and CO₂ laser. For palmar warts, all 3 modalities had comparable results. Both CO₂ laser and HFR showed 100 % cure rate while EC was relatively less responsive in treating plantar warts. An earlier study using CO₂ laser on plantar warts reported a success rate in between 54 - 89 percent.¹⁹ All three modalities showed 100 % response in cases of verruca plana and filiform wart. A previous study on filiform warts also reported 100 % resolution with electrosurgery.¹²

A retrospective study with CO₂ laser on warts reported that the site of involvement had no influence on the cure rate.²⁰ Our study however showed that site did influence the cure rates among the three groups when lesion(s) were on the upper limb (excluding palms), lower limb and the soles. Rest of the sites had comparable cure rates.

In our study, all patients with solitary lesions except one in CO₂ laser group showed complete clearance. HFR ablation was more effective in treating multiple warts as compared to the other 2 modalities and this was statistically significant. A previous study using EC in the treatment of solitary lesion demonstrated 65 % clearance which was much less than our study.⁹ A previous study using CO₂ laser showed overall cure rates of 83.5 % for solitary and 66 % for multiple lesions. For recalcitrant warts (both solitary and multiple together) cure rate was 68 percent.² A previous CO₂ laser study with 18 patients having persistent warts (solitary plus multiple), showed a 56 % cure rate. This was less than our as well as another study done in the past by Mancuso et al. However there was no significant difference in cure rates between solitary and multiple resistant warts in a different study.²⁰ At the 12th week, reappearance of skin markings or dermatoglyphics was seen maximum in the HFR

group followed by CO₂ laser group and least in EC group. This might have been due to higher incidence of scarring associated with EC. A study done on verruca vulgaris and plantar warts reported reappearance of skin markings in 66% patients who had undergone pulse dye laser treatment.²¹

Recent studies on the use of intralesional bacillus Calmette–Guerin (BCG) vaccine immunotherapy in the treatment of recurrent multiple warts have been used, in which 75.53 % patient showed complete clearance.²² Large, blinded randomized controlled trials are needed for evaluating the treatment of warts using newer modalities.

CONCLUSIONS

HFR ablation had the highest efficacy and minimum complications in treating warts. Assuming that the diagnosis of wart is certain, switching to a new treatment modality is appropriate if there is no response after 4 treatment cycles. Follow up of at least three months is advisable.

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