

EFFICACY OF PULSED DYED LASER (585 NM) IN THE TREATMENT OF MOLLUSCUM CONTAGIOSUM SUBTYPE 1

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Abstract. Molluscum contagiosum is a common cutaneous disease that may be difficult to treat when there are multiple lesions; especially in children. This study was conducted to determine the efficacy of pulsed dye laser (585 nm) in the treatment of molluscum contagiosum in 20 children. In the treated group, 70.5% of lesions healed after the first treatment; the remaining 10.6% after the second treatment (2 weeks later). The overall cure rate was significantly different from the control group ($p < 0.01$). The therapy was also well tolerated. Only mild transient hypopigmentation and erythema were observed. None encountered infectious events. In conclusion, pulsed dye laser is a good alternative treatment for molluscum contagiosum due to high efficacy and mild transient side effects.

INTRODUCTION

Molluscum contagiosum (MC), caused by a DNA poxvirus (Gottlieb and Myskowski, 1994; Diven, 2001; Husar and Skerlev, 2002), has a worldwide distribution with an incidence of 2-8% of children (Billstein and Mattaliano, 1990). It is more prevalent in tropical areas (Hanson and Diven, 2003). It mainly affects children, sexually active adults and persons with impaired cellular immunity. Direct contact is presumed to be the method of spread, including autoinoculation (Koebner phenomenon), sharing swimming pools and contact with fomites (Gottlieb and Myskowski, 1994; Husar and Skerlev, 2002; Hanson and Diven, 2003). The severity of disease and number of

lesions may vary from a few to hundred, depending on the individual and their immune status. The severity is increased in atopic dermatitis and immunocompromized persons.

MC virus, indistinguishable by clinical features (Gottlieb and Myskowski, 1994; Diven, 2001; Husar and Skerlev, 2002; Hanson and Diven, 2003), is divided into 4 subtypes (Uemura, 1991) by restrictive endonuclease analysis (Scholz *et al*, 1989) or polymerase chain reaction (PCR) (Nunez *et al*, 1996). The most common subtype is subtype 1 (75-90%) (Gottlieb and Myskowski, 1994; Hanson and Diven, 2003) and the least common is subtype 4 (Nakamura *et al*, 1995). Subtype 2 is more common in human immunodeficiency virus (HIV) infected persons (Yamashita *et al*, 1996).

There are several means to treat this infection, including curettage (Hanson and Diven, 2003), cryotherapy, pulsed dye laser (Hughes, 1998; Hammes *et al*, 2001), topical agents, including cantharidin (Hanson and Diven, 2003), tretinoin, potassium hydroxide

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(KOH) (Romiti *et al*, 1999, 2000) and imiquimod (Skinner, 2002), as well as systemic agents, including cimetidine (Dohil and Prendiville, 1996) and griseofulvin. The decision to treat is based on the severity and recalcitrance of the disease, the likelihood of spreading, the autoinoculation rate, the parent's concern, the patient's fear, compliance, efficacy and the safety of the treatment.

Pulsed dye laser (PDL) is highly effective and has low side effects. We conducted a study to determine PDL's efficacy in MC treatment based on the MC subtype.

MATERIALS AND METHODS

Study population

Twenty children, under 15 years of age, were enrolled in the study. The study was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. The objectives of the studies were stated and written consent was obtained from each of the guardians of the participants. All agreed not to be treated with other modalities. A history was obtained at the beginning of the study regarding duration of lesions, contact with fomites, swimming and kick board usage, previous therapies, family history of MC and underlying diseases. Tissue was extracted for typing the MC virus prior to treatment. The treatment and control groups were classified by residual lesions. The treatment group was treated with PDL (585 nm) (Candela, model SPTL-1b, 7 mm diameter at fluences 7.0 J/cm²) and no treatment was given to the control group.

At the second visit (2nd week), the percentage cure in both the treatment and control groups as well as the side effects were recorded. The treatment was repeated for persistent lesions in the treatment group.

At the last visit (4th week), the percentage cure and side effects were assessed for

both groups.

At the end of the study, all remaining lesions were treated by the method selected by the patient and guardian.

Laboratory test

DNA was extracted from stored tissue (-70°C) using QIAamp[®] DNA mini Kit (GmbH, Hilden, Germany) and subjected directly to PCR-based amplification. The PCR was performed using primers to amplify the p43K protein gene. The primers consisted of a forward primer MCVF (5'-TCAAATACGGAGGCGCG TGC-3') and reverse primer MCVR (5'-GGGC TTGCCGGGCAG-3'). The cycle conditions were initially pre-denaturation at 94°C for 1 minute, followed by 35 cycles of denaturation at 94°C for 30 seconds, annealing at 54°C for 30 seconds and extension at 72°C for 1.30 minutes. Amplicons were analysed by electrophoresis on 2% agarose gel, stained with ethidium bromide and observed under UV light. Amplicons were purified with a gel-extraction kit (Perfectprep Gel Cleanup; Eppendorf). DNA sequencing analysis of the PCR products was performed with a Perkin-Elmer 310 sequencer. Viral subtypes were identified using BLAST analysis.

Statistical analysis

Statistical analysis was descriptive (average, standard deviation, frequency). Since the data did not have a standard distribution, testing for differences was performed using non-parametric tests (Wilcoxon signed ranks test, Kruskal Wallis test, Mann-Whitney *U* test). The program used for statistical analysis was SPSS 11.5 for Windows.

RESULTS

There were 20 patients with a male:female ratio of 9:1 and an average age of 5.2 years. The duration of disease varied from 7 days to 3 years (average 5 months). Further data can be seen in Table 1.

Table 1
Basic data for patients included in this study.

| No | Sex | Age (yrs) | Duration (days) | Skin type ^a | Fomites ^b | Swimming | Kick board | Previous treatment | Underlying disease |
|----|-----|-----------|-----------------|------------------------|----------------------|----------|------------|--------------------|--------------------|
| 1 | M | 2.00 | 7 | 5 | 1,2,3 | | | | |
| 2 | M | 6.00 | 1,095 | 4 | | | | | HIV |
| 3 | M | 3.42 | 30 | 2 | 3 | | | | |
| 4 | F | 5.00 | 90 | 3 | | | | | |
| 5 | M | 4.00 | 90 | 4 | 3 | Yes | Yes | | |
| 6 | M | 1.75 | 30 | 3 | | | | | |
| 7 | M | 9.00 | 150 | 4 | | Yes | Yes | | |
| 8 | M | 3.50 | 120 | 3 | | | | | |
| 9 | M | 5.00 | 365 | 4 | | | | | |
| 10 | M | 7.00 | 60 | 4 | | Yes | Yes | | |
| 11 | F | 13.00 | 90 | 4 | | | | duofilm® | |
| 12 | M | 1.67 | 14 | 3 | 1,2,3 | | | | |
| 13 | M | 5.00 | 90 | 3 | 3 | Yes | | curette | AR |
| 14 | M | 5.00 | 60 | 4 | | Yes | | cimetidine | |
| 15 | M | 10.00 | 60 | 4 | 3 | Yes | | curette | |
| 16 | M | 11.58 | 30 | 4 | 1,2,3 | Yes | Yes | | |
| 17 | M | 2.75 | 365 | 4 | 3 | | | | |
| 18 | M | 3.00 | 14 | 4 | 1,2,3 | | | | |
| 19 | M | 2.00 | 120 | 3 | | | | | AR |
| 20 | M | 3.75 | 60 | 3 | 1,2,3 | | | | spastic diplegia |

^a2=fair skin, brown hair, brown eye; 3=white skin, dark brown hair, brown eye; 4=light brown skin, dark brown hair, dark eye; 5=brown-skinned individuals

^b1 = shirts; 2= trousers; 3 =towel; HIV = human immunodeficiency virus; AR = allergic rhinitis

Molluscum contagiosum subtype

Analysis of the 20 patients after running through BLAST analysis and comparing them with sequences in the GenBank revealed all isolates were subtype 1 (GenBank accession no EF138604-EF138623).

Percentage of cure

After the first treatment, 70.5% (95%CI = 58.5-82.5) of the treatment group lesions were healed. In the control group, 7 patients (15.3%, 95%CI = 2.5-28.0) had their lesions spontaneously resolve. After the second treatment, an additional 10.6% (8.3-50.0%, 95% CI = 3.6-17.5) and 8% of lesions resolved in the treatment and control groups, respectively (Table 2). The difference in cure rates between the two groups was statistically significant for

both treatments ($p < 0.01$).

Associating factors influence on cure of lesions

Sex, underlying disease, skin type, fomites, swimming and kick board usage were not significantly associated with the cure of lesions ($p > 0.05$).

Side effects

The treatment was well tolerated. Only temporary pigmentary changes occurred in 13 patients (65.0%). Two patients (10.0%) had skin erythema, and 11 patients (55.0%) had hypopigmentation.

DISCUSSION

To decrease confounding factors and selection bias, we designed a study with a

Table 2
Percent cure after treatment in treatment and control groups.

| | 1 | 2 ^b | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 ^d | 12 | 13 ^e | 14 ^d | 15 ^d | 16 | 17 | 18 | 19 ^e | 20 ^c |
|------------------------|------|----------------|----|-----|------|-----|-----|------|--------------|-----|-----------------|------|-----------------|-----------------|-----------------|------|-----|----|-----------------|-----------------|
| Laser # 1 | | | | | | | | | | | | | | | | | | | | |
| Cure (%) | 50 | 78.6 | 60 | 80 | 37.5 | 100 | 100 | 61.5 | 62.5 | 80 | 66.7 | 100 | 60 | 60 | 100 | 71.4 | 100 | 0 | 91.7 | 50 |
| Control # 1 | | | | | | | | | | | | | | | | | | | | |
| Cure (%) | 0 | 8 | 0 | 0 | 0 | 0 | 40 | 0 | 0 | 0 | 0 | 16.7 | 0 | 33.3 | 0 | 0 | 0 | 50 | 57.1 | 100 |
| Laser # 2 | | | | | | | | | | | | | | | | | | | | |
| Cure (%) | 12.5 | 0 | 0 | 20 | 25 | - | - | 15.4 | ^a | 20 | 0 | - | 40 | 20 | - | 0 | - | 0 | 8.3 | 50 |
| Control # 2 | | | | | | | | | | | | | | | | | | | | |
| Cure (%) | 0 | 8 | 0 | 0 | 0 | 0 | 0 | 0 | ^a | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - |
| Laser treatment | | | | | | | | | | | | | | | | | | | | |
| Total cure (%) | 62.5 | 78.6 | 60 | 100 | 62.5 | 100 | 100 | 76.9 | 62.5 | 100 | 66.7 | 100 | 100 | 80 | 100 | 71.4 | 100 | 0 | 100 | 100 |
| Control group | | | | | | | | | | | | | | | | | | | | |
| Total cure (%) | 0 | 16 | 0 | 0 | 0 | 0 | 40 | 0 | 0 | 0 | 0 | 16.7 | 0 | 33.3 | 0 | 0 | 0 | 50 | 57.1 | 100 |

^a = patient lost to follow-up; ^b = patient with human immunodeficiency virus infection; ^c = patient with spastic diplegia; ^d = patient with previous treatment; ^e = patient with allergic rhinitis

matched control group because molluscum contagiosum infection can resolve spontaneously. By identifying the MC subtype in our study we found our findings supported by data from Japan (Gottlieb and Myskowski, 1994; Hanson and Diven, 2003) in which subtype 1 was the most prevalent MC subtype. Yamashita *et al* (1996) found the ratio for MC subtypes 1 and 2 was 13:1, and MC subtype 2 was isolated in 75% of HIV patients. In this study, we had only one HIV patient with MC subtype 1. Due to the small sample size the overall prevalence of MC subtypes could not be elucidated.

The efficacy of PDL in the treatment group was significantly better than the control group (p<0.01). The mechanism of action is photocoagulation which selectively damages abnormal vessels and surrounding connective tissue. The heating effect activates the release of various growth factors, which brings about an increase in T lymphocytes which is capable of eliminating poxvirus (Michel, 2004). Our findings support studies in Western countries which found that PDL is effective in MC treatment, however, our cure rate (overall 81.1%) was lower than that reported by Hammes *et al* (2001) (overall 100%) and Hughes (1998) (99.0% after single treatment), even though the energy density (fluence) in our study was the same as that of Hughes (1998). Hughes (1998) used 2 different spot sizes and fluences to match the diameter of the lesions: 3 mm at fluences of 7.0-8.0 J/cm² and 5 mm at fluences of 6.8-7.2 J/cm², while a 7 mm spot size at a fluence of 7.0 J/cm² was utilized in our study. The difference in cure may be due to inappropriateness of energy density (Hughes, 1998), since Caucasian subjects possess different skin types

from our population.

The HIV patient (number 2) had a 78.6% cure without any change in his immune status (%CD4 count = 3.0, actual CD4 count = 285) during the period of treatment.

The efficacy of PDL in different MC subtypes could not be evaluated since only MC subtype 1 was found in our study.

Side effects in our study were dyspigmentation in all 13 patients. These transient changes were not reported in previous studies. This may be due to the different subject skin types in our study compared to previous studies which were on Caucasians (Hughes, 1998; Hammes *et al*, 2001; Michel, 2004). There were no secondary infections in this study, similar to previous reports.

Our study supports previous studies (Gottlieb and Myskowski, 1994; Husar and Skerlev, 2002; Hanson and Diven, 2003) concerning several factors (sex, underlying disease, skin type, fomites, swimming and kick board), which had no effect on the efficacy of treatment or recurrence.

We believe appropriate energy density is needed to maximize the efficacy of PDL in MC treatment in Thai children as well as to lessen the side effects. A larger sample size is needed to evaluate the overall epidemiological data for MC subtype in Thai children and the efficacy of PDL therapy by MC subtype.

In summary, pulsed dye laser is an efficacious alternative treatment in molluscum contagiosum infection with mild and transient side effects. It is bloodless, and an excellent choice for HIV patients and patients who fail other therapies.

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