Laser therapy versus cryotherapy of lentigines: A comparative trial

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Background: Lentigines are common sun-induced benign melanocytic proliferations. Many therapies have been advocated, but few have been systemically evaluated.

Objective: We studied the effectiveness of two laser modalities in comparison with liquid nitrogen cryotherapy for lentigines.

Methods: We conducted a randomized, controlled, prospective trial comparing liquid nitrogen cryotherapy, argon laser light delivered by a Dermascan shuttered delivery system, and low-fluence carbon dioxide laser irradiation in the treatment of solar lentigines at 99 sites in 13 patients.

Results: Cryotherapy was more likely to produce substantial lightening than either argon or CO₂ laser treatment, which gave similar results (p < 0.05 for both comparisons). The odds of an excellent result were about 50% higher with cryosurgery than with CO₂ or argon laser therapy.

Conclusion: Liquid nitrogen cryotherapy was superior to argon and CO₂ laser therapy in the treatment of benign epidermal pigmented lesions. This study demonstrates that comparative rather than uncontrolled studies are needed to judge the relative efficacy of therapies for benign pigmented lesions such as lentigines.

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In the past decade several laser systems have been developed. Sponsors claim these systems are safe and effective for the treatment of common benign pigmented epidermal and dermal lesions. Many of these medical devices have been approved by the U.S. Food and Drug Administration for the treatment of lentigines.

We have been struck by the frequency with which patients seek laser treatment with the belief that lasers are not only more effective but less likely to scar than older, conventional, and often far less expensive therapies. Yet even for the most widely recognized cutaneous laser applications, few if any well-controlled comparative studies assess the relative efficacy and safety of these high-technology treatments in comparison with traditional therapies.

In open trials our group previously demonstrated that two laser technologies, low-fluence carbon dioxide laser (CO₂) and the argon laser light delivered by a Dermascan shuttered delivery system (ADS) could reduce the cutaneous hypopigmentation of solar lentigines. The utility of these and other new treatments on benign epidermal pigmentation can be best established through trials that compare newer technologies with each other and with long-established treatments. We performed a randomized controlled trial that demonstrates that more complex technology is not always an improvement.

MATERIAL AND METHODS

This trial compares CO₂, ADS laser surgery, and cryosurgery with liquid nitrogen (LN₂) for the treatment of lentigines. The techniques for each laser system have been previously detailed.

One dermatologist (J. A. L.) treated all areas of hyperpigmentation within a 4 cm² area at each site. Assignment to treatment sites was established on the basis of random numbers, with allocation of three sites to each laser for every two sites treated with LN₂. Any portion of a lentigo outside the designated area was not treated. For each patient four to nine areas that included one or more
Table I. Distribution of assessments of photographs by therapy*

<table>
<thead>
<tr>
<th>Therapy</th>
<th>CO₂ (n = 152)</th>
<th>ADS (n = 148)</th>
<th>LN₂ (n = 96)</th>
<th>All photographs (n = 396)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lightening (%)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>6</td>
<td>7</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Slight</td>
<td>28</td>
<td>26</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>Moderate</td>
<td>32</td>
<td>33</td>
<td>31</td>
<td>32</td>
</tr>
<tr>
<td>Substantial</td>
<td>28</td>
<td>26</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>Normal skin</td>
<td>5</td>
<td>5</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Unable to evaluate</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Textural change (%)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>77</td>
<td>90</td>
<td>87</td>
<td>84</td>
</tr>
<tr>
<td>Minimal</td>
<td>19</td>
<td>8</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Moderate</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Good result (%)*</td>
<td>61†</td>
<td>62‡</td>
<td>75</td>
<td>65</td>
</tr>
<tr>
<td>Excellent result (%)*</td>
<td>23†</td>
<td>25‡</td>
<td>37</td>
<td>27</td>
</tr>
</tbody>
</table>

*One percent to 3% of photographs could not be evaluated and were excluded.
†p < 0.05 compared with cryosurgery (excluding photographs that could not be evaluated).
‡p < 0.1 compared with cryosurgery.

Lentigines were treated in a nearby or contralateral anatomic site.

According to established treatment protocols,11,12 a Coherent continuous-wave, CO₂ laser model 450XL with a circular spot size of 4.5 mm in diameter and an exposure time of 0.1 second, was used. Superpulsing is not possible with this laser model. Irradiances of 3, 4.5, and 6 W, yielding fluences of 3 to 5 J/cm² were administered. For ADS treatment a Coherent Radiation model 1000 argon laser and a Coherent Dermascan delivery system were used13,14 Power ranged from 0.5 to 0.9 W, yielding fluences of less than 1 J/cm² with standard techniques. Superpulsing was not used.

For cryosurgical therapy, an Owens Cryovac-R pressurized vacuum canister with a 0.3 mm tip was used. The device was held 3 cm from the lesion, and LN₂ was applied for 1 to 5 seconds after initial freezing. Photographs were taken immediately before and after all treatments, and 1 and 8 weeks later.

Four dermatologists, who did not administer treatment and who were not aware what treatment had been used, independently viewed colored slides of pretreatment and 8-week posttreatment color sites. Three raters were board-certified dermatologists experienced in the use of lasers, and one was a senior resident. Each rater separately assessed the decrease in pigmentation and textural change. Decreased pigmentation was assessed on a 5-point scale (no change; slight, moderate, or substantial change; and return to normal skin). Textural change, including loss of normal skin markings or scarring, was evaluated on a 4-point scale (no change, minimal, moderate change, and severe change). An excellent result was defined as substantial decrease in pigmentation or return to normal skin color and no textural change. A good result was defined as at least moderate lightening and no more than slight textural change. The study was performed with the approval of the Beth Israel Hospital Institutional Review Board. All patients gave their informed consent.

The distribution of categorical outcomes was compared with the chi-square test. We used multiple simultaneous logistic regression to examine the associations between a good or excellent outcome and type of treatment, site, and evaluator.

RESULTS

We studied 14 patients. One was lost to follow-up. Of 99 sites treated in these remaining 13 patients, 38 sites were treated with CO₂, 37 with ADS, and 24 with LN₂. One percent to 3% of lesions could not be evaluated because of poor photographing and were excluded from the analysis.

Treatment with LN₂ was approximately four times more likely to achieve normal skin color than ADS and CO₂ therapy (p < 0.05) (Table I). Moderate atrophy was infrequently noted for all three therapies. Lesions that displayed such changes were more likely to show lightening (p < 0.0009, Mann-Whitney test). A good or excellent result was noted in a comparable number of assessments of CO₂-and
ADS-treated sites. Achieving a good or excellent result was about twice as frequent with LN2 compared with CO2 or ADS (Table II). One rater was significantly more likely to give a good or excellent rating than other raters. Lentigines on the back were more likely to improve than were those treated at other sites (Table II).

DISCUSSION

On the basis of assessment of color slide photographs, four dermatologists compared the results of two laser treatments with an established therapy for lentigines. All three treatments did in some cases provide excellent results, and textural change was infrequent, but LN2 gave good to excellent results about twice as frequently as either laser therapy. Traditional cryosurgery is simpler, less time consuming, and far less expensive than the laser therapies we evaluated.

The certainty of our conclusion is limited by the fact that one dermatologist administered all treatments. Certainly, one person may be more skillful at one treatment than another. This physician was, however, trained by those who helped develop the laser techniques we used. There was wide variation in the judgments of the observers who viewed the same photographs. The clear variability in assessment, even when raters were uninformed as to treatment, illustrate how different raters have different definitions of a good result. Comparative studies with raters blinded to treatment can provide better information about the relative risks and benefits of both traditional and innovative therapies. The pigmented lesion pulsed-dye laser (50 nm), Q-switched Nd:YAG and Q-switched ruby laser in the treatment of lentigines is under way.

REFERENCES