Flash-lamp pulsed-dye laser treatment of port-wine stains in childhood. A case of technology assessment

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Costs of treatment of port-wine stains with the flash-lamp pulsed-dye laser in relation to the timing of treatment

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Abstract

Objective - A port-wine stain (PWS) is a disfiguring congenital vascular malformation that grows proportionally with the child. The progression of these lesions through life and their psychological implications that occur during socialization in childhood make early treatment desirable. It is believed that PWS in children are smaller and thinner, treatment at an early age would not only be desirable but also more efficient. This study was undertaken to determine whether early treatment of the PWS is less costly than treatment at an advanced age.

Study-design - A prospective comparative study was set up of 100 patients with a facial PWS, treated with a SPTL-1 flash-lamp pulsed-dye laser (FPDL). Equal numbers of patients were assigned to 4 age groups (0-5, 6-11, 12-17 and 18-31 years). Direct medical costs (health services costs) and direct non-medical costs (traveling and out-of-pocket expenditures) related to the laser treatment were valued. Indirect costs generated by time lost from work were not included in the economic evaluation.

Results - 91 Patients were included in the economic evaluation. All patients received 5 treatments of the entire PWS. The average direct medical costs per patient of 5 treatments of the entire PWS did not differ significantly between the four age groups (p=0.80). Calculated costs were influenced by the differences in procedure, treatment with or without anesthetics, related to the age of the patient and size of the PWS.

Conclusions - Although PWS are generally smaller in children, the number of visits, pulses needed and treatment costs were not lower, because (young) children were more difficult and less efficient to treat than adolescents and adults.
Introduction

PWS are congenital dermal vascular malformations that occur with an incidence of 0.3%-0.5%.\textsuperscript{1,2} PWS grow proportionally with the child.\textsuperscript{3} Untreated birthmarks darken with age to a red-purple color, and by middle age they are often raised and nodular.\textsuperscript{4}

A major goal in treating (facial) PWS is to avoid the progression of these lesions through life and the consequent psychological complications during socialization in childhood.\textsuperscript{5}

Laser surgery has been introduced as an effective treatment of these vascular lesions. Treatment with older lasers, like the argon laser often was ineffective and could cause formation of scar tissue and permanent hypopigmentation in children.\textsuperscript{6,7} The development of the flash-lamp pulsed-dye laser (FPDL) has enabled treatment in childhood. This laser type produces selective photothermolysis of cutaneous ectatic blood vessels. It also shows minimal thermal damage, there is no clinical evidence of complications as seen with older lasers (e.g. argon, continuous wave dye and carbon dioxide lasers).\textsuperscript{4,8,9}

It has been assumed that infants and children can be treated more successfully than adults. Children have a thinner skin, a smaller PWS surface area and a less ectatic structure of the abnormal bloodvessels in the superficial dermis.\textsuperscript{10} As a result, it is expected that infants and children require fewer laser treatments and fewer laser pulses for the eradication of the PWS, compared to adolescents and adults. The costs of treatment should consequently be lower at an early age. A number of studies with the FPDL have supported this hypothesis, although most of these studies did not include controls and were retrospective in design.\textsuperscript{3,6,11,12}

This prospective, comparative study was undertaken to determine whether early treatment of the PWS is less costly than treatment at a later stage in life. We report on a series of 91 consecutive patients with untreated facial PWS, who were treated with a FPDL over a study period of 3 years.
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Material and methods

Study-design

In a prospective, comparative study consecutive patients with untreated PWS in the face or neck were assigned to 4 age groups. Age categories were defined as follows: 0-5, 6-11, 12-17 and 18-31 year. Enrollment in an age category was stopped when 25 patients had entered. All patients were treated in the department of Plastic and Reconstructive Surgery in the Academic Medical Center at the University of Amsterdam, the Netherlands, between December 1991 and March 1995. Oral informed consent was obtained from the patients or their parents or guardians.

Treatment

Patients were treated with a Candela SPTL-1 flash-lamp pumped pulsed dye laser, with rhodamine in methanol as the dye, an emission wavelength of 585 nm, a pulse duration of 450 microseconds, a repetition rate of 1 pulse per 3 seconds (0.33 Hz) and a circular 5 mm spot. Treatments were performed with a maximum spot overlap of 20%. Before actual treatment started patients received a test patch to verify clinical response.

Patients were treated initially in an outpatient setting. To relieve pain during treatment, the PWS was cooled with water drenched gauze dressings. If necessary EMLA-cream® and/or nerve blocks were used. Most children had EMLA® applied to their lesions at least one hour before treatment, occluded with Tegaderm®. If those analgesic methods were insufficient Dormicum® was added for sedation. In some cases general anesthesia in a day-care unit was necessary, containing halothane in combination with nitrous oxide, oxygen and additional pain control. Patients treated under general anesthesia stayed on average 2 hours on the recovery-room and required minimal postoperative care.

During each visit the largest possible area of the PWS was treated. In most patients one treatment of the entire PWS required several visits. The average period between 2 visits was 8.5 weeks (sd. 3.2).

Cost-calculations

Cost-calculations were set up to reflect a societal perspective. Costs of medical care, related to the laser treatment or the PWS, were divided into
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direct medical and direct nonmedical costs. The direct medical costs represent the health services costs of patients undergoing treatment. These costs include operating costs, direct labour of the plastic surgeon and other provider services (staff time), used materials and supplies, equipment, drugs, devices, outpatient visits and additional care. Cost-calculations were based on actual resource use in routine care during the laser treatment and calculated unit prices. Direct nonmedical costs contain costs outside the health care system because of treatment. Direct nonmedical costs reflect family and patient expenses, such as the use of camouflage and travel costs.

A prospective resource data collection was set up. Data related to direct medical costs were registered: treatments, with or without general anesthesia, use of medication and disposables, and the number of outpatient visits. The following additional data were retrieved from hospital databases and financial reports: the average professional wages (the attending plastic surgeon, anesthetist and ward nurse), expenditures per work unit (medical staff, office and board of the department plastic surgery), hospital overhead (such as domiciliary services, housing, board) and capital costs (equipment, buildings and land) to be allocated to the department of plastic surgery. Overhead and capital costs were allocated in a stepwise fashion to the medical services.

Complementary data on direct medical costs (such as other consulted health services, the actual use of drugs and devices), direct nonmedical costs and indirect costs (days of absence from paid employment during the period following treatment onset) were collected using repeated postal questionnaires. Adolescents and parents of children were asked to report the number of days missed from school or day-care. Questionnaires were sent by mail to the patients between January-March 1994 and May-July 1995, both with one consecutive reminder. In the two youngest age groups (0 to 5 and 6 to 11 year) these questionnaires were addressed to the parents.

The costs per visit were calculated with a standard base rate covering costs of staff and use of facilities, to which was added a sliding scale, taking into account the number of pulses and the time to treat the PWS.

The costs of drugs, devices and camouflage were based on official Dutch retail prices. Travel costs were calculated based on defined general cost-guidelines related to transport mode.¹⁴
The time horizon of this cost-analysis was limited to 5 treatments of the entire PWS, because most patients (89%) did not finish treatment within 3 years. Protocol driven costs were excluded from the calculations.

**Analysis**

Per age group the average direct medical costs per patient were calculated. Data were normalized using the natural log transformation. Statistical analysis included one-way ANOVA to compare costs between age groups. Within each group, the direct medical costs per patient were related to the size of the untreated PWS. Covariance analysis was used to compare costs, adjusted for age-related differences in size, between the age groups.

Descriptive statistics were used to report direct nonmedical costs and indirect costs. Indirect costs generated by time lost from work for patients were not valued. Per age group the average number of days of absence from paid employment related to one visit was recorded and reported. For the adolescents and the children the average number of days missed from school or day-care, because of treatment, was calculated.

Calculated costs were expressed in constant 1994 Dutch Guilders (DGL) using retail prices, and were discounted at 5%. To eliminate differences in price levels costs were converted into pounds sterling with purchasing power parities (PPP: 1 DGL = 0.30 £), based on the Gross Domestic Product (GDP), instead of the currency exchange rate.

**Results**

The results of the cost evaluation are based on the data of 91 patients. Nine patients had to be excluded from the analysis, because they did receive less than 5 treatments of the entire PWS within the study period.

Table 1 shows the characteristics of 5 treatments of the entire PWS per age group. The number of visits and the average duration per visit were generally similar for all groups. General anesthesia was only used in the pediatric population (0-5 and 6-11 year): 15 children (30%) were treated under general anesthesia. These treatments covered 11.4% of the total number of visits.
Table 1. Treatment characteristics: 5 treatments of the entire PWS (test patch included).

<table>
<thead>
<tr>
<th></th>
<th>0 - 5 year (n=25)</th>
<th>6 - 11 year (n=25)</th>
<th>12 - 17 year (n=19)</th>
<th>18 - 31 year (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>7/18</td>
<td>10/15</td>
<td>5/14</td>
<td>5/17</td>
</tr>
<tr>
<td>Size PWS (cm²)¹</td>
<td>68 (58)</td>
<td>119 (145)</td>
<td>96 (82)</td>
<td>111 (142)</td>
</tr>
<tr>
<td>Average visits per patient ¹</td>
<td>10 (4)</td>
<td>11 (5)</td>
<td>10 (6)</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Total treatment duration (year) ¹</td>
<td>1.5 (0.4)</td>
<td>1.3 (0.4)</td>
<td>1.4 (0.6)</td>
<td>1.2 (0.5)</td>
</tr>
<tr>
<td>Number of pulses per visit ¹</td>
<td>171 (263)</td>
<td>217 (333)</td>
<td>223 (156)</td>
<td>225 (176)</td>
</tr>
<tr>
<td>With general anesthesia</td>
<td>621 (443)</td>
<td>1000 (806)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Without general anesthesia</td>
<td>89 (52)</td>
<td>160 (129)</td>
<td>223 (156)</td>
<td>225 (176)</td>
</tr>
<tr>
<td>Time per visit (minutes) ¹²</td>
<td>28 (26)</td>
<td>31 (27)</td>
<td>30 (12)</td>
<td>31 (15)</td>
</tr>
<tr>
<td>With general anesthesia</td>
<td>79 (31)</td>
<td>100 (54)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Without general anesthesia</td>
<td>18 (7)</td>
<td>26 (11)</td>
<td>30 (12)</td>
<td>31 (15)</td>
</tr>
</tbody>
</table>

¹ mean (standard deviation).
² preparation time included.

In Table 2 the average direct medical costs per patient of 5 treatments of the entire PWS are reported, with or without general anesthesia. The costs included a single outpatient visit before treatment, a test treatment and all other visits needed.

The direct medical costs for children included the use of general anesthetics so these cases have the added costs of surgery facilities. The average direct medical costs per patient in the two youngest age groups (0-5 and 6-11 year) were influenced by the high costs of treatment with general anesthesia and the relatively low costs of treatment without general anesthesia. During the visits with general anesthesia the entire PWS of children could be treated, implying a higher number of pulses and a longer per visit duration.
Table 2. Average direct medical costs per patient of 5 treatments of the entire PWS.

<table>
<thead>
<tr>
<th></th>
<th>0 - 5 year (n=25)</th>
<th>6 - 11 year (n=25)</th>
<th>12 - 17 year (n=19)</th>
<th>18 - 31 year (n=22)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laser treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.80</td>
</tr>
<tr>
<td>[range]</td>
<td>[129-4600]</td>
<td>[154-4739]</td>
<td>[120-3835]</td>
<td>[100-5206]</td>
<td></td>
</tr>
<tr>
<td>With general</td>
<td>1973 (1223)</td>
<td>2142 (1430)</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>anesthesia (£)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without general</td>
<td>565 (288)</td>
<td>819 (786)</td>
<td>1036 (880)</td>
<td>916 (1054)</td>
<td>--</td>
</tr>
<tr>
<td>anesthesia (£)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication and</td>
<td>12.3 (13.9)</td>
<td>11.1 (7.8)</td>
<td>5.1 (4.4)</td>
<td>4.5 (6.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>devices £</td>
<td></td>
<td></td>
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</tbody>
</table>

1 mean (standard deviation).

Treatment without general anesthesia was less efficient in (young) children, because children became (highly) anxious and pain-sensitive during treatment. For these reasons only a small number of laser pulses and a short treatment time per visit were achieved. Without the use of general anesthesia only a small surface area of the PWS could be treated during 1 visit. Adults were less pain-sensitive and endured a longer treatment time and a larger number of pulses per visit. The average direct medical costs in the older groups (12-17 and 18-31 year) were substantially lower, because patients needed no general anesthesia during treatment and care could be provided by usual outpatient facilities. Costs in adults were influenced by a larger time period and more pulses per visit. The average costs, for 5 treatments of the entire PWS showed no statistically significant differences between the age groups (p=0.80).

In Table 2 the average costs per patient of drugs and devices needed within the treatment period are presented. The costs of drugs and devices represent the use of Tegaderm® (occlusive dressing), Vaseline, Penatrase® and palliative drugs. Parents of children reported more use of palliative care after treatment than adolescents and adults.
Figure 1. Cumulative direct medical costs of 5 treatments related to the absolute surface of the port-wine stain.
In Figure 1 the direct medical costs per patient of 5 treatments of the entire PWS are related to the absolute size of the PWS. After adjusting for differences in size of the lesion by covariance analysis, we found significant cost differences ($F=26.5$, $p<0.01$) across the 4 age groups. After back-transformation the geometric means of the direct medical cost data were £928, £687, £728 and £568, respectively.

Fifteen patients (17%) covered their PWS with camouflage make-up. All these patients received a questionnaire to report their use of camouflage. Twelve patients reported a reduction in the application of camouflage, following treatment. In the two youngest groups, only 1 patient (aged 10) used camouflage. Seven patients aged 12 to 17 and 7 patients in the oldest age group (18-31 year) covered up their PWS. The average costs of camouflage per patient within the period of 5 treatments in these two age categories were £119 (sd. 192) and £139 (sd. 149), respectively. All adults (18-31 year) reported daily use of camouflage.

Travel costs related to 5 treatments of the entire PWS were substantial and a little higher in the youngest patient groups, because the parents of these children preferred traveling by car (92%) rather than by public transport. The average travel costs in the 4 groups were £245 (sd. 193), £244 (sd. 211), £225 (sd. 137) and £186 (sd. 300), respectively.

Questionnaires were sent to 22 patients with paid employment, in the two oldest age groups, and returned by 15 (68%). In this group 7 patients reported on average 5.2 (sd. 5.3) days of absence from paid employment, after one visit. Most adults (5) were absent from work because of the blue-gray color of the treated area and the impossibility to apply the usual camouflage. Only 2 adults reported absence related to complications (slight infection) after treatment.

Questionnaires were sent to 69 (parents of) children and adolescents attending day-care or school and returned by 53 (77%). On average the youngest children, aged 0 to 5, missed day care or nursery school for 1.5 (sd. 1.3) days. Children aged 6 to 11 and 12 to 17 missed school for 1.0 (sd. 0.5) and 3.2 (sd. 4.2) days, respectively. It appeared that all children stayed at home for a longer period than just the period attending to treatment. The blue-gray color of the treated area was the most frequently reported reason for staying at home.

In this study patients from the youngest groups were mostly accompanied by both parents during treatment. On average parents took one day off per
treatment visit from their work (paid employment) to accompany the children and to take care of their children after treatment.

**Discussion**

The primary objective of an economic evaluation of the FPDL technology is to incorporate considerations of resource consumption into decisions about the effective use of this technology and the start of treatment in relation to age. In this study the average direct medical costs per patient of 5 treatments of the entire PWS did not differ significantly between age groups.

Calculated costs were influenced by differences in treatment procedure, related to age and size of the PWS. In all age groups costs of treatment increased proportionally with the absolute size of the PWS. Despite the smaller surface area of the PWS the direct medical costs were higher in the youngest age groups.

Between age groups a selective referral bias at baseline should be considered. Teenagers and adults decided to submit themselves for treatment, while (young) children were submitted by their parents. Therefore it is possible that, compared to the younger age groups, patients in the older age groups had darker PWS. For this reason, we would have expected an even stronger difference between age groups.

Our results show that optimal treatment of the PWS requires multiple visits. Only 11% of the patients finished treatment within the study period of 3 years. So we evaluated the total costs of 5 treatments of the entire PWS. The average number of visits and total treatment duration needed for these 5 treatments did not differ between the age groups. In contrast to the experiences of others we did not find that children could be treated more effective than adults. Despite a thinner skin, a smaller PWS surface area and less ectatic structure of the abnormal bloodvessels in the superficial dermis children in our study did not need fewer visits or less pulses.

In the pediatric population the use of anesthetics was not required by protocol. Nevertheless we found it necessary to treat 30% of the children (0-5 and 6-11 year) under general anesthesia, because they became highly anxious or pain-sensitive during treatment. Repeated visits without the use of anesthesia led to resentment in both children and parents. This preventive pain policy may differ between various medical centers. The need for anesthetics in the laser treatment of a pediatric population is confirmed by
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several authors. Tan et al.4, Morelli et al.20 and Alster et al.22 Also treated (very young) children but did not report the requirement of general anesthetics. Rabinowitz23 confirms our findings that the use of general anesthetics in children allows a larger surface area to be treated in a single visit.

The results shown are highly influenced by the type of laser used. As laser technology evolves treatment will become more efficient over time, because the potential repetition rate and the circular spot size of the given pulses increases, although it is not obvious whether the need for general anesthesia in children will decrease.

Larger areas and the possible treatment of the entire PWS during a visit could reduce the number of visits needed to gain optimal clearance of the PWS. A more efficient treatment scheme per visit might be able to reduce the overall amount of time lost from day-care or school and from the parents' work.

The assessment of any new technology is a complex, iterative process of which the clinical and economic considerations discussed here are only a part. This descriptive study did not confirm the hypothesis that treatment costs are lower in children than in adults. The repeated use of general anesthetics in children can be quite uncomfortable. We feel that the deleterious effects of painful procedures in childhood should not necessarily replace those of growing up with a PWS. The issue of general anesthesia and the extra costs generated should be considered by physicians, patients and health authorities. Individual assessment of pain and discomfort should guide the decision whether to use general anesthesia. The possibility to defer treatment to a later time when patients can be treated without general anesthesia should be weighed against the proportional increase in size, darkening and thickening of PWS over time.
References

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