The use of OPAL001 filtrate and cream in the treatment of chronic pressure ulcers

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Abstract

Residents at the Quadriplegic Centre located in Perth, Western Australia, were studied. The Quadriplegic Centre is a 100-bed hospital for the specialist management of people with paralysis as a consequence of spinal cord injury or diseases of the spinal cord. Clinical staff at the Quadriplegic Centre became aware of the OPAL001 filtrate and cream, derived from pawpaw (papaya) and peach, and the apparent efficacy in healing various types of ulcers. Staff initiated a trial involving patients that had suffered Stage II-IV pressure ulcers, including some of more than 5 weeks' duration that were difficult to heal. Daily treatment consisted of application of the filtrate to the ulcer and the cream to the surrounding skin with non-adherent dressing. Treatment appeared to be effective, and persistent large and deep ulcers were healed. There was improved mobility among patients, as well as less turning and bedside care. A retrospective cost analysis shows savings arose from reduced nursing care and fewer products being used for wound care. The preliminary data presented show some evidence for OPAL001 therapy reducing costs and improving outcomes; the situation where costs decrease and health outcomes improve is both unusual and highly desirable for healthcare decision makers. A randomised clinical trial is required to show that these observations are real effects from therapy.

Introduction

Quadriplegics are at high risk for developing pressure ulcers. Up to 85% of spinal cord injured people will develop one or more pressure ulcers in their lifetime, with 70% developing multiple ulcers [1]. Once established, these wounds become chronic, and healing is difficult. The physical and mental health of the affected individual is likely to be compromised. The increased burden on scarce healthcare resources is considerable. A pressure ulcer of Stage II or higher has been calculated to increase patient costs by a factor of 2.7 [2], while the annual cost of pressure ulcers to the American and Australian healthcare systems is estimated at $US3.6 billion [3] and $A285 million [4], respectively. Patients that were admitted to US hospitals for treatment of pressure ulcers stayed nearly 13 days [5], and pressure ulcers were found to independently extend length of stay for patients admitted to Australian hospitals by 4.1 days [6]. The mean charge for hospital stays – principally for pressure sores – was $US37,800 in the US, although charges varied by payer. The average charge billed to Medicaid was $US39,100, while an average charge of $US25,600 was billed to the uninsured [5]. An effective treatment is not available but would have great value for patients, carers and payers of healthcare.

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Several residents at the Quadriplegic Centre had suffered with pressure ulcers of particular tenacity and longevity. Either because of their overall health status, their nutrition, their tissue fragility, or their lifestyle choices (including choices causing non-compliance with standard ulcer care provided by the Quadriplegic Centre), they had Stage II-IV pressure ulcers. Some of the residents' ulcers had existed for up to 2 years. The pharmacist and staff at the Quadriplegic Centre became aware of OPAL001 filtrate and cream, which are derived from pawpaw and peach. Because of the need for a new approach to treatment for this group of patients with intractable ulcers, the Centre became the location for a research trial. The aim for this paper is to describe the experience of using OPAL001 products on selected patients residing at the Quadriplegic Centre. The observed clinical and economic consequences of the therapy are summarised.

Methods

Setting

The Quadriplegic Centre is a 100-bed specialty hospital in Perth, Western Australia. The Quadriplegic Centre provides high-level residential care for persons with paralysis as a

consequence of spinal cord injury or disease of the spinal cord. The Centre promotes excellence in spinal nursing and aims to provide its clients with a level of care that will enable them to remain free of medical, physical and psychological complications, so that they can pursue their lives and abilities to the fullest extent. Consequently, residents at the Quadriplegic Centre spend most of their days in wheelchairs, participating in many of the available activities. The nursing staff monitor skin integrity diligently, and the Centre provides measures to prevent the formation of pressure ulcers. Nevertheless, pressure ulcers may develop as a result of the residents' lifestyle choices or may occur when they are on leave or in hospital for acute treatment. Pressure ulcers occur most commonly on the sacrum, ischium, trochanters and heels.

Study design and participants

The Quadriplegic Centre staff selected a total of 11 patients with pressure ulcers for treatment with OPAL001 products. In seven of these patients, conventional therapy was ineffective and ulcers were long-standing (5 weeks' to 2 years' duration) and problematic. An additional four patients with new (up to 1 week's duration) Stage II and III ulcers were selected to participate. For each patient, the topical OPAL001 treatment consisted of the filtrate being applied to the ulcer and the cream being applied to the surrounding skin on a daily basis, with an appropriate non-adherent dressing to cover.

Phoenix Eagle Company Pty Ltd [Mount Lawley, Western Australia] is the manufacturer of the OPAL products and is developing OPAL001 for the treatment of wounds. OPAL products are created by applying the patent-pending OPAL process to one or more fruits. The OPAL process comprises controlled heating of the flesh of fruit, then alkalinising the fruit puree with sodium bicarbonate, and filtering the resulting suspension. The filtrate derived from a particular fruit can be used on its own, or filtrates derived from different fruits can be mixed – OPALA is the extract resulting from applying the OPAL process to pawpaw; OPALM is the extract resulting from applying the OPAL process to peach. OPAL001 is a mixture of OPALA and OPALM.

OPAL001 is the primary product formulation used in the treatments described in this paper. OPAL001 is used in both filtrate and cream form. Where the authors refer to 'OPAL001 filtrate' or 'filtrate', the reference is to the pure filtrate obtained from the OPAL process applied to the raw materials, Where the authors refer to 'OPAL001 cream' or 'cream', the reference is to the cream made by emulsifying the OPAL001 filtrate with almond oil, cocoa butter, and bees' wax.

Data sources / measurement

With the exception of one patient, who was deceased at the time this retrospective study was undertaken, all patients that had been treated with OPAL001 products between October 2003 and June 2004 were interviewed and examined in November 2007. All patients' medical records were examined, and the staff that had treated the patients using the OPAL001 products were interviewed. The clinical outcomes from all 11 patients are shown in Table 1. In addition, the clinical outcomes from treating four patients that were compliant with the OPAL001 treatment regimen – that were considered representative of the compliant group's outcomes, and for whom reliable medical data were available at the time of this study – are described as individual case studies here.

A senior nurse at the Quadriplegic Centre and one of the authors conducted a detailed cost analysis that describes the 12 weeks prior to the onset of therapy and 48 weeks after. The standard nursing care plan, nursing flow chart and skin integrity chart were interrogated. Values for the following variables were recorded: number of turns in a 24 hour period; number of wound swabs taken; number and type of oral or intramuscular antibiotics prescribed for infection of the pressure ulcer; number of days in acute care for treatment of the pressure ulcer; number of surgical procedures for the pressure ulcer; number of outpatient appointments for the pressure ulcer; number of doctor visits for the pressure ulcer; number of other clinical services for the pressure ulcer; number of dressings used, including other products for wound dressing/care; and duration of nursing time spent on wound dressing/care.

Quantitative variables and statistical methods

Market prices were attached to each unit of resources used and the duration of nursing time for care calculated. This described the number of turns in a 24 hour period and the nursing time spent on wound dressing/care. Cost outcomes were estimated for each of the six patients for whom reliable economic data were available, including the four patients whose clinical outcomes are described below. Means and standard errors for cost outcomes were calculated for each of the 60 weeks. The method of moments was used to fit a data likelihood function for the purpose of describing a cost parameter and so specify a prior distribution for cost outcomes that captures the variance among the set of data (Figure 1). A gamma distribution was chosen because it represents the likelihood for positive continuous variables, especially those that describe resource use such as length of stay of cost outcomes – Gamma(α,β), mean=α/β, variance=α/β^2, shape parameter α, scale parameter β. Random re-samples (n=1000) were taken from the prior distribution of cost outcome over the 60 weeks of data collection. This number of re-samples is sufficient to give a stable posterior distribution.

Results

Clinical outcomes

For each patient, a summary of the length of time the ulcer had previously existed, the time to observable improvement

and the time to complete closure are shown in Table 1. All patients, including the non-compliant patients, showed significant, rapid improvement with treatment with the OPAL001 products; all but two non-compliant patients, for whom treatment was discontinued, achieved complete wound closure.

Case I

A 70 year old male was the first to be treated with OPAL001 at the Quadriplegic Centre [note that, in all cases, age refers to the dates of treatment, not the dates of examination by the authors]. He sustained a T10 spinal cord injury in 1998 and a stroke in 1999. He developed a Stage II pressure ulcer to his buttock close to the gluteal crease. Although the resident was encouraged to stay in bed, he chose to spend the day in his wheelchair so he could paint and smoke. Despite best practices treatment, the ulcer showed no signs of healing at 2 months. He had spent 10 days in bed, while the OPAL001 cream was applied to the skin surrounding the ulcer, again with no improvement. Following that period, the OPAL001 filtrate was applied directly into the wound, with continued application of cream; within 24 hours of this combined treatment, granulation commenced. The wound was completely healed within 6 days, without scar. He has had no recurrence.

Case II

This 68 year old female resident had suffered from multiple sclerosis for 35 years, resulting in incomplete quadriplegia. She was admitted to the Quadriplegic Centre in October 2001 after having undergone Z-plasty for a chronic pressure ulcer over her left ischium. The wound had not healed and had developed into a Stage IV pressure ulcer, with a sinus tunnelling in the subcutaneous tissue (60ml of saline could be flushed into the wound), and excoriation of the surrounding skin. She had a poor appetite and was reluctant to drink water.

During the following 2 years the sinus was treated with a variety of medications, including acetic acid to control *Pseudomonas aeruginosa*. At times the wound improved enough to allow the resident to sit in her wheelchair for short periods of time, but it never developed significant granulation. The flushed solution was a brownish yellow and malodorous; a large absorbent dressing was needed to control the drainage. Initially, OPAL001 cream was applied daily directly onto the excoriated area, whilst vinegar continued to be syringed into the sinus. There was an immediate reduction in the inflammation of the excoriated skin.

Three weeks later, OPAL001 filtrate replaced the vinegar solution for treatment of the sinus. Within 2 days of commencing treatment with OPAL001 filtrate, the colour of the fluid became transparent, and the sinus started to close. In 2 additional weeks, the wound was sufficiently healed for the resident to be able to sit in her wheelchair for short periods of time. The pressure ulcer was completely healed within 3 weeks. She has had no recurrence.

Case III

This 72 year old female resident was quadriplegic from multiple sclerosis of 24 years' duration. She had a percutaneous

Table 1. Summary of clinical results for ulcers in all patients treated with OPAL001. (Roman numerals given for cases are described in more detail in the text).

Case no.	Location of ulcer	Stage of ulcer	Time ulcer had existed	Time to observable improvement	Time to complete healing
1 (I)	Buttock	II	2 months	24 hours	6 days
2	Buttock	II	6 weeks	48 hours	2 weeks
3	Buttock	II	1 week	48 hours	15 days
4 (III)	Buttock	II	5 weeks	immediate	1 week
5	Foot	II	new ulcer	48 hours	N/A
6	Ankle	II	2 years	immediate	N/A
7	Buttock	II	new ulcer	24 hours	5 days
8	Hip	III	1 week	24 hours	2 weeks
9	Heel	III	13 months	48 hours	14 weeks
10 (II)	Buttock	IV	2 years	sinus: 48 hours	3 weeks
11 (IV)	Hip	IV	19 months	48 hours	3 weeks

endoscopic gastrostomy tube inserted because of her inability to feed herself. She had a very supportive family that took her out on frequent occasions, which meant she sat in her wheelchair for long periods of time. In October 2003, over a period of 2-3 weeks, a Stage I pressure ulcer developed over the sacral area. Despite standard preventive treatment such as towelling the skin dry following showering and toileting and the fitting of an appropriate cushion in the wheelchair, the skin broke and the pressure ulcer developed to Stage II, with the surrounding skin becoming inflamed. The resident was confined to bed, and the wound was treated with betadine and tegaderm dressing for 1 week then a biatain dressing was applied for 1 week. Neither of these treatments appeared to have any effect on the wound.

Figure 1. Method of moments.

We used the method of moments to fit this distribution with the expected value and variance of the distribution given by $E[0] = \alpha\beta$ and $var[0] = \alpha\beta^2$.

We set the observed sample statistics reported equal to the expressions of the mean and variance for the Gamma distribution with the re-arranged expressions solved as follows

$$\alpha = \frac{\bar{u}^2}{s^2} \quad \text{and} \quad \beta = \frac{s^2}{\bar{u}}$$

On the third week OPAL001 treatment was commenced with application of OPAL001 cream to the skin surrounding the pressure ulcer. Since no effect was seen in 2 days, the cream was ceased and OPAL001 filtrate was applied daily directly onto the wound. The pressure ulcer immediately showed signs of granulation. On the third day the wound was sufficiently granulated for the resident to resume her normal activities of daily living in her wheelchair. The wound was completely healed in 4 additional days. This resident's wound was particularly challenging to treat, as heavy sweating prevented adhesion of dressings to her buttocks. The nursing staff had anticipated that the healing time would be protracted, as the wound remained uncovered. Surprisingly, however, the gel-like nature of the filtrate adhered sufficiently to the wound to allow it to remain moist. She has had no recurrence.

Case IV

This 70 year old female resident was admitted to the Quadriplegic Centre in 1998, having been confined to a wheelchair since 1968 with polyarthritis. Although she had a limited range of mobility, she had full sensory perception. Due to strong analgesics, her appetite was poor. She insisted on sitting in her wheelchair for extended periods during the day so she could smoke. This combination of factors not only hindered the healing of the Stage I pressure ulcer that had

formed but caused it to develop into a Stage IV pressure ulcer over a period of 19 months.

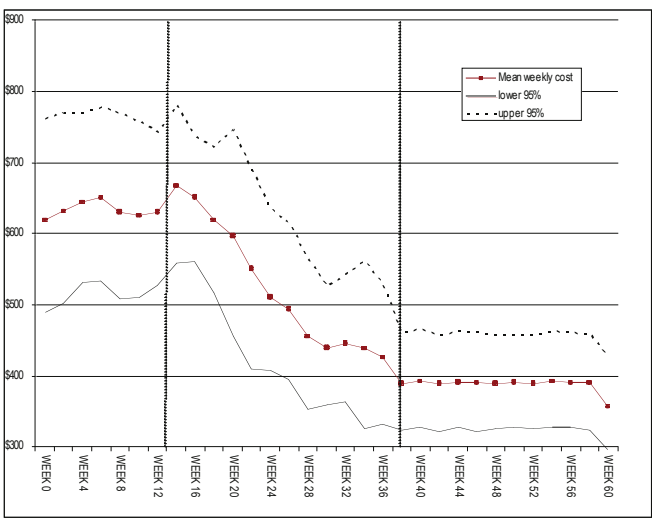
The pressure ulcer developed over the left ischium with two sinus tracks, one 13cm and the other 2cm deep. One of the sinuses was packed with 2 metres of ribbon gauze soaked in saline. There was a large amount of exudate, which necessitated covering the wound with a non-adhesive absorbent dressing. The exudate was malodorous and coloured with a mixture of blood and pus, clearly indicating that the ulcer was infected, although there were no signs of bacteraemia. The ulcer had been treated with various products including intrasite gel, biatain, calcium alginate and kaltostat over the 19 month period prior to OPAL001 treatment. The resident consented to bed rest for 1 month prior to commencing the OPAL001 treatment, with no change in the appearance of the wound.

In October 2003 the resident underwent daily treatments to the pressure ulcer and sinus with OPAL001 products. The cream was applied in the morning to the surrounding skin, and the filtrate was syringed into the sinus in the evening. After 48 hours the exudate became transparent and decreased in volume. After 72 hours it was apparent that granulation was rapidly ascending from the base. The resident's wound was granulated within 2 weeks, allowing her to resume her normal activities of daily living in her wheelchair. Complete re-epithelialisation occurred after 3 weeks of treatment with OPAL001 products. With the healing of this Stage IV ulcer, she was left with a small depression on her buttock. She has had no recurrence.

Cost outcomes

The results of the process of the random re-samples taken from the prior distribution of cost outcomes were recorded, and the mean of these re-samples and the 95% confidence intervals are plotted in Figure 2. The weekly cost of caring for the pressure ulcers is about A$640 per case for the 12 weeks prior to the start of the OPAL001 therapy. Weeks 12 to 38 are characterised by reduction in wound care costs. Weeks 38 onwards show a new equilibrium of costs of about A$390 per week. If the entire reduction in costs can be attributed to the improvements in wound condition due to OPAL001 therapy, then this appears an effective way to reduce healthcare costs for this population by around A$250 per week for each patient. Given these patients' other health needs, these cost savings are substantial.

Figure 2. Weekly costs of wound care for six cases (12 weeks prior to start of OPAL001 therapy and 60 weeks in total).



Discussion

The treatment results with the OPAL001 products were encouraging and stimulate further research questions. Large, deep wounds through Stage IV – in several cases unresponsive to best practice treatment by experienced clinical specialist nurses – were healed. The cost savings arose from improved mobility among patients, as well as less turning and bedside care, reduced nursing time devoted to wound care activities as the wound improved, and fewer products required for wound care after the wound had healed. Since the OPAL001 products are not yet commercially available and no product costs have been established, the costs of OPAL001 products were not included but the costs of administering the treatment were.

The cases reported here were not selected in any systematic way and this should not be considered a rigorous scientific study. The patients who were treated were not matched with controls, nor were patients randomly assigned to treatment or control. For these reasons the observed improvements cannot be attributed to the application of OPAL001 products. It might be that the use of the product changed some other important factors in the care process and so caused the outcomes. The non-uniform type, size, and stage of pressure ulcers across the patient population studied make it difficult to draw quantitative clinical conclusions that apply to the entire study population. There is, however, some evidence to warrant further research into the mechanism of action of this product, the clinical effectiveness and the cost effectiveness.

In wound care involving pawpaw, papain is often believed to play an active role. Indeed, papain/urea has been shown to be a superior debriding agent to collagenase [7]. There are a number of creams available that contain papain as an enzymatic debriding agent. However, none of the products contains the range of ingredients found in OPAL001, as OPAL001 is made from whole fruit. It is unclear at this time whether papain does play a role in the apparent effect of OPAL001 products. Components that may be instrumental in the spectacularly rapid healing that was observed in refractory ulcers include fruit sugars (which would be hydrating and bactericidal), vitamin C, hydroxy fruit acids (which further debride necrotic tissues), and the bicarbonate (which could

buffer the vitamin C and neutralise streptokinase). It is possible that the moderate heating in the manufacturing process makes some of the enzymes more bioavailable.

Cost savings alongside improvements in health outcomes are rare. Innovative healthcare products that are effective tend to be more costly than standard care. The situation where costs decrease and health outcomes improve is both unusual and highly desirable for healthcare decision makers. The data presented here show some evidence for OPAL001 therapy reducing costs and improving health outcomes. A randomised clinical trial is required to show that the observations are real effects from therapy. The data from the trial could be incorporated into a comprehensive decision analytic model designed to address the question of whether the therapy is cost effective compared to existing therapies.

Other information

The study was approved by the Quadriplegic Centre's Human Research Ethics Committee and conformed to the NHMRC's Statement on Human Experimentation. All patients provided appropriate informed consent before any trial-related procedures were undertaken.

The authors contracted with Phoenix Eagle Company Pty Ltd to examine and evaluate the relevant medical and economic data made available by the Quadriplegic Centre, based on the Quadriplegic Centre's clinical staff's prior treatment of the patients described herein. Both authors acted as independent observers. Associate Professor Nicholas Graves is an investor in Phoenix Eagle Company Pty Ltd. Both authors made substantive intellectual contributions to this study.

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