The IL-6, TNF-alpha, and TGF-β Levels in Serum and Tissue in Children with Treated by Different Burn Dressings......
Prof. Mehmet Demircan, Dr. Kubilay Gürünlüoğlu

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SUPRATHHEL REDUCES THE SYSTEMIC OXIDATIVE STRESS IN PATIENTS WITH BURNS - MORE THAN SILVER PRODUCTS

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THE IL-6, TNF-ALPHA, AND TGF-β LEVELS IN SERUM AND TISSUE IN CHILDREN WITH TREATED BY DIFFERENT BURN DRESSINGS

Authors:
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Poster No: 354
The IL-6, TNF-alpha, and TGF-β Levels in Serum and Tissue in Children with Treated by Different Burn Dressings

Introduction: The Interleukine-6 (IL-6), TNF-α cytokines play an important role in the inflammatory response in burn trauma. They rise in the first week and then return to normal levels in 5 weeks. They are responsible for many systemic effects during burns. After burn trauma, TGF-β plays an important role in wound healing, in providing tissue tensile strength and tissue elasticity. Our aim was to investigate how three different wound dressings; polylactic membrane (PLM), hydrofiber dressing with silver (HFA), and Autograft, used in burn treatment were able to change IL-6 and TNF-α level in wound and serum, and also to determine how these treatments affect both the serum level of TGF-β and the expression in the burned tissue.

Methods: There were three groups, each consisting of 20 patients. A different dressing was applied to each group. Serum and tissue samples were collected at the end of 4 weeks of treatment. There were three groups (PLM, HFAg and control), each consisting of 22, 21 and 22 children with partial thickness burns, respectively. A different dressing was applied to each group. Serum were collected at the end of 4 weeks of treatment. In these cases we investigate how IL-6, TNF-α, and TGF-β levels changed.

Results: The levels of IL-6, and TNF-α was lower significantly in PLM and HFA groups then in other groups, p<0.01. The level of TGF-β was higher significantly in PLM group then in other groups, p<0.01.

Conclusions: The reasons of faster wound healing and lesser scar in patients treated with PLM may be these significant lower inflammatory response (IL-6 and TNF-α) and higher serum level of TGF-β.

Applicability of Research to Practice: Clinically faster wound healing and lesser scar.

Material & Methods: There were three groups (PLM, HFAg and control), each consisting of 22, 21 and 22 children with partial thickness burns, respectively. A different dressing was applied to each group. Serum were collected at the end of 4 weeks of treatment. In these cases we investigate how IL-6, TNF-α, and TGF-β levels changed.

In burns, IL-6 concentrations are significantly increased when compared to IL-6 levels in non-burn volunteers. Detection of IL-6 in serum is significantly greater in non-surviving versus surviving burn patients at all time points between the time of admission and time of death or discharge. TNF-α is an important factor in wound healing due to its role in the early immune response when secreted by activated macrophages. TNF-α may also influence wound healing through direct action on keratinocytes and endothelial cells, thereby impacting epithelialization and vascularization. Therefore TNF-α may be a good therapeutic target to improve wound healing in burns. Transforming growth factor (TGF)-beta is essential for activation and proliferation of fibroblasts during the initial stage of wound healing. After burn trauma, TGF-β plays an important role in wound healing, in providing tissue tensile strength and tissue elasticity.

Aim: To investigate how two different wound dressings (PLM, HFAg) used in partial thickness acute burn treatment were able to change IL-6, TNF-α and TGF-β level in serum.

Abbreviations: HFAg: Hydrofiber with silver PLM: Polylactic membrane

The IL6, TNF-α, and TGF-β Levels in Serum in Children with Treated by Different Burn Dressings

Silver based dressings have been used for many years. Are they still gold standard? Well, are they safer than other dressing?
Introduction: There is a lot of literature about the application of keratinocytes in deep second degree burns but there is still a lack of the effect of dressings on keratinocytes. Polylactic membranes have demonstrated usefulness in the treatment of superficial and partial thickness burns because of pain reduction, ease of application, reduced workload and good clinical results. This paper presents the results of 103 patients treated with sprayed keratinocytes and covered with polylactic membranes.

Methods: Retrospective quality control in 103 patients from 2003 to 2018, in which partial-thickness burns were treated with sprayed keratinocytes and covered with polylactic membranes. From 2003 to 2015 evaluation of burn depth was done on clinical aspects, from 2016 to 2018 laser Doppler imaging was used. People were included, when the time of healing was expected to be longer than 15 days.

Results: There were 67 male and 36 female patients with an average TBSA of 17.8% ±14.8 median: 14. The average second-degree burn was 8.52 %(± 9.8), the average 3rd° burn was 9.47% plus ±12. 2. Age was in average 39 years (median 42). No significant difference could be found between male and female in age and TBSA distribution. Average abbreviated burn severity index was 5.97, interestingly in women significantly higher. Nearly all patients had significant comorbidities.

Source of injury was an explosion (18), flame (55), scald burn(17), contact burn (2), electricity (2), suicide attempt(6) and others (2).

The operation was started on average four days (±3 ) after the injury (median 3.0). Sprayed keratinocytes were applied in average 12 days after the 1st operation (±7.6). Using laser Doppler imaging the time for keratinocytes application was reduced to 7.6 days. Three different cell types were applied to twelve different regions. Healing time (time to 99% healing) was on average 8. 33 days (median: 7). The total treatment time to healing was shorter in the non-cultured cell suspension treated patients due to the lacking necessity of preculturing cells. In 6 patients retransplantation had to be done. The last control was performed on average 96 days (± 368) after spraying. Scar was visible in 4; pigment changes happened in 9, hypertrophic scarring in 5 patients, Infections were suspected or confirmed in 6.

Conclusions: polylactic membranes proved to be an adequate dressing for sprayed keratinocytes in deep 2nd° burns. There was no need for frequent dressing changes. Infections in other areas of the body did not spread on the wounds covered with polylactic membranes. Other than predicted 91% of the wounds were healed within 14 days. Twelve cases treated with not cultured cells and polylactic membranes were completely healed within 15 days.

Applicability of Research to Practice: Immediate.
Polyactic membranes proved to be an adequate dressing for sprayed keratinocytes in deep partial thickness burns

Description of Patients:

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>TBSA</th>
<th>- Percentage</th>
<th>Treatment modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15 years</td>
<td>Male</td>
<td>103</td>
<td>8,37 ± 3,47</td>
<td>BiPET</td>
</tr>
<tr>
<td>≥ 15 years</td>
<td>Female</td>
<td>51</td>
<td>8,17 ± 5,24</td>
<td>BiPET</td>
</tr>
</tbody>
</table>

How did LDI influence the time of healing?

- Polyactic membranes protected children from wound-associated infections.
- Polyactic membranes supported a short healing time in deep partial thickness burns after spraying with keratinocytes independently from cell type used.
- Polyactic membranes showed a low complication rate.

Implications for further RCT:
- Use of sprayed keratinocytes and dressing with polyactic membranes could shorten wound healing and maybe impatient time.
- Use of sprayed keratinocytes without culturing and dressing with polyactic membranes can shorten healing time and maybe impatient time more effectively compared to culturing keratinocytes.
- Results only difficulty comparable to literature, PRT needed.

Lessons Learned:
- Polyactic membranes showed a low complication rate.
- Polyactic membranes supported short healing time in deep partial thickness burns after spraying with keratinocytes independently from cell type used.
- Polyactic membranes protected the wounds from infections from not wound-associated sources.

Limitations:
- Retrospective evaluation over 15 years with different treatment standards.

Literature:
The treatment of epidermal and deep dermal wounds with polylactid based membrane and foam structures: 8 years perspective and outlook

Session Title: Management-of-Burns-in-Developing-Countries 1

Burn injuries are a major cause for hospitalization and are associated with significant morbidity and mortality particularly in children under the age of four years. Over 50% of burn injuries involve the head and neck region and can be caused by flame, electric current, steam, chemicals and hot substances. Hot liquids are the most common cause of these injuries in the pediatric group. In the last 40 years the management of Burns has changed dramatically, one of those changes is the early escharectomy during the first 72 Hrs. With these we can decrease the colonization and bacterial propagation and decrease the possibility the SRIS presentation, less pain and adequate healing. Suprathel™ is a polylactide-based membrane, alloplastic, absorbable skin substitute that is highly permeable to oxygen and water vapor, providing a particularly favorable environment for wound healing. We have been used Suprathel™ in the past 8 years. Suprathel™ was applied cutting it to make easier the adapt to the irregular surface. Adequate debridement using a.........
Improvement in acute healing and scaring of deep dermal and partial thickness burn wounds after enzymatic debridement by application of platelet rich fibrin (PRF) – first experiences

Presenting Author: Dr. Alexandra Schulz
Co Author: Wolfram Heitzmann, Paul Christian Fuchs, Jennifer Schiefer
Institution: Cologne Merheim Medical Center, Cologne, Germany

Abstract No: 77
Heading: Improvement in acute healing and scaring of deep dermal and partial thickness burn wounds after enzymatic debridement by application of platelet rich fibrin (PRF) – first experiences

Session Title: Wound-Management-and-Infection-Control
Abstract Body: Question This study evaluates the supportive effect of PRF on spontaneous healing in deep dermal and partial thickness burn wounds (hands and faces) after enzymatic debridement with NexoBrid with special respect to pain, healing time and aesthetic and functional outcome. Methods: After enzymatic debridement PRF is produced from the patient’s own blood and applied on the wound surface according to manufacturer’s instructions. Suprathel is used as final dressing. The first dressing change takes place on the fifth day. Pain and wound healing are evaluated closely until wounds are completely closed (defined as the Results: Since November 2017, 10 burn wounds (3 faces and 7 hand burns) were debrided enzymatically and treated with PRF. In the beginning of our learning curve, we found the manufacturing process of PRF challenging. Application and wound healing were uneventful. Patients reported no pain during treatment. Wounds healed without infection in any case with good functional and aesthetic results after up to 12 months. Conclusion: First experiences in 10 burn wounds let us assume that the application of PRF on partial thickness and deep dermal burn wounds after enzymatic debridement is suitable to reduce wound healing time and improve scaring........
SPRAYED EPITHELIAL AUTOGRAGTS COVERED WITH POLYLACTIC TEMPLATES IN DEEP DERMAL BURNS

Authors:

Presenting Author: Dr. Bernd Hartmann
Co Author: Frank Sander, Claudia Belfekroun, Herbert Haller
Institution: Burn Center Unfallkrankenhaus Berlin, Germany

Abstract No: 142
Heading: Sprayed epithelial autografts covered with polylactic templates in deep dermal burns

Session Title: Wound-Management-and-Infection-Control 2
Abstract Body: Introduction: Treatment of deep dermal burns always has been challenging in various aspects. Methods have been developed to support faster healing like CelluTome [2] or spraying procedures of cells [3]. This presentation describes our way and short time results of 120 patients treated with sprayed cells.

Methods and material: Treatment with epithelial cells has been done since 2003 in our unit. After checking the influence of different spraying methods and pressures on the vitality of sprayed cells since 2005 epithelial cell suspensions of different sources in different locations of body were used. After promising results in a retrospective evaluation the method was used in more than 110 patients. Discussion: Different sources of cells have been used by us. The correct range of pressure during application is important which lead to the development of an applicator. Quality control was done in a retrospective study. Although there were excellent cosmetic results in deep burns the method has its limitations. Results: Treatment with sprayed epithelial cells after different methods of necrosectomy reduces the rate of grafts and can show a very good cosmetic result. When there were no dermal remnants, secondary grafting had to be done. Covering with a polylactic template (Suprathel®) proved to be a simple and easy method reducing pain and workload. Short-time results of ........
The use of Suprathel in deep partial-thickness burns: long-term follow-up results of a prospective trial

Presenting Author: Dr. Paul Wurzer
Co Author: David Benjamin Lumenta, Janos Cambiaso Daniel, Christian Smolle, Alexandru Christian Tuca, Raimund Winter, Michael Schintler, Lars-Peter Kamolz
Institution: Division of Plastic, Aesthetic and Reconstructive Surgery, Department of Surgery, Medical University of Graz, Graz, Austria

Abstract No: 145
Heading: The use of Suprathel in deep partial-thickness burns: long-term follow-up results of a prospective trial

Session Title: Wound-Management-and-Infection-Control 2
Abstract Body: Deep partial-thickness burns can be covered with different kind of materials and techniques; one of them is Suprathel, a polylactide-acid based membrane. The aim of this study was to intraindividually compare its long-term outcome with the results obtained by use of autologous skin grafts in patients suffering from deep dermal burns. A prospective trial was designed in order to assess skin quality and scar formation by use of subjective (Vancouver Scar Scale; Patient and Observer Scar Assessment Scale) and objective (noninvasive cutometry) burn scar assessment tools. All items of the Patient and Observer Scar Assessment Scale, except vascularity, were found to be noninferior in the areas covered with the temporary skin substitute vs autologous skin.

Results of objective scar evaluation showed comparable viscoelastic parameters without reaching noninferiority. Overall, the outcome of deep dermal burns covered with Suprathel revealed satisfactory results in terms of scar formation and skin quality as compared with autologous skin. This paper supports its use in deep partial-thickness burns, where autologous skin donor sites require either to be reserved for coverage of full-thickness skin defects in severe burns or to be saved for reduction of additional morbidity in selected patient collectives....
Abstract Body: In this study, we evaluated and compared the effect of treatment with a hydrofiber dressing with silver (HFAg), a polylactic membrane (PLM) and autografts on systemic oxidative stress in systemic inflammatory reaction in thermal burn injuries in children. This prospective study was conducted in children (age, 1–16 years) of both sexes affected by thermal injury to 20–50% of their total body surface area (TBSA), including deep burns to 10 % TBSA. Serum malondialdehyde (MDA), total antioxidant capacity (TAC), total oxidant capacity (TOC), glutathione (GSH), and telomerase levels were examined, and the results were analyzed statistically. HFAg, PLM®, and the autograft groups had higher levels of MDA than those in the control group, demonstrating increased levels of oxidative stress after burn injury. Serum telomerase levels in the HFAg and autograft groups were significantly higher than those in the PLM® and in the control group signaling increased cellular damage and oxidative stress. The TAC level of the PLM group was quite high, whereas TOC level was significantly lower which indicates a lower level of inflammatory response to the burn injury under the PLM dressing. Based on the TOC, TAC, and telomerase levels, PLM demonstrated a strong antioxidant capacity due to fast progress of wound healing. PLM demonstrated the most effective reduction of triggering oxidative stress.......
**Introduction** Burns result in local tissue damage and response caused by both local and systemic oxidant changes due to systemic mediators associated with increased free radical activity and lipid peroxidation (1). On the other hand, it causes a significant decline in total antioxidant status and in antioxidant sweeping capacity when compared to a control (2). This results in oxidative stress that activates hepatic hypermetabolism and protein synthesis, both of which have adverse effects wound healing (3,4).

**Aim of the study** To evaluated and compared the effect of treatment with a hydrofiber dressing with silver (HFAg) (Aquacel® Ag), a polylactic membrane (PLM) (Suprathel®) and autografts on systemic oxidative stress in systemic inflammatory reaction in thermal burn injuries in children.

**Methods** After approval by the Inonu University Clinical Research Ethics Committee, a prospective randomized and paired match study was conducted in children (age, 1–16 years) of both sexes affected by thermal injury to 20–50% of their total body surface area (TBSA), including deep burns to 10 to [6–10]% of their TBSA. The control group included normal children (age, 1–16 years) of both sexes.

- The PLM group (n = 20) was dressed with a synthetic copolymer composed of DL-lactide (>70%) and ϵ-caprolactone (PLM) (PMI Polymedics) every 7 days (5).
- The HFAg group (n = 20) was dressed with a hydrofiber dressing containing silver (Aquacel® Ag) (Convatec) every 7 days (6).
- The Autograft group (n = 20) was dressed with antiseptic gauze wrapped with silver sulfadiazine (PansAG®) (Velfina S.A., Campulung, Romania) every 3 days.

Serum malondialdehyde (MDA), total antioxidant capacity (TAC), total oxidant capacity (TOC), glutathione (GSH), and telomerase levels were examined, and the results were analyzed statistically.
**Findings**

**Table.** Descriptive statistics of independent groups for plasma telomerase, TOC, GSH, TAC, MDA levels.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control Group (n=20)</th>
<th>HFAg Group (n=20)</th>
<th>PLM Group (n=20)</th>
<th>Autograft Group (n=20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telomerase (ng/ml)</td>
<td>3.78 &lt;sup&gt;a,b,c&lt;/sup&gt; (1.6)</td>
<td>15.79 &lt;sup&gt;b&lt;/sup&gt; (4.92-31.83)</td>
<td>6.07 &lt;sup&gt;c&lt;/sup&gt; (4.10-19.98)</td>
<td>14.48 (5.53-32.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TAC (mmol/L)</td>
<td>0.67 &lt;sup&gt;a,b,c&lt;/sup&gt; (0.29-1.41)</td>
<td>2.51 (1.00-11.98)</td>
<td>4.23 &lt;sup&gt;c&lt;/sup&gt; (1.35-14.12)</td>
<td>2.47 (1.2-10.46)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TOC (µmol/L)</td>
<td>4.55 &lt;sup&gt;a,b,c&lt;/sup&gt; (3.55-5.34)</td>
<td>11.38 &lt;sup&gt;b&lt;/sup&gt; (8.33-16.03)</td>
<td>7.03 &lt;sup&gt;c&lt;/sup&gt; (5.75-10.79)</td>
<td>10.43 (6.47-18.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GSH (µmol/L)</td>
<td>96.15 &lt;sup&gt;a,b,c&lt;/sup&gt; (50.113.8)</td>
<td>124.38 (90.24-168.3)</td>
<td>118.33 (98.88-166.32)</td>
<td>118.83 (93.07-156)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MDA (µmol/L)</td>
<td>4.12 &lt;sup&gt;a,b,c&lt;/sup&gt; (3.2-6.04)</td>
<td>5.24 &lt;sup&gt;c&lt;/sup&gt; (4.72-5.96)</td>
<td>5.65 &lt;sup&gt;c&lt;/sup&gt; (4.51-5.64)</td>
<td>5.89 (5.24-7.39)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- Serum telomerase levels were higher in the HFAg, PLM, and Autograft groups than in the control group. No significant difference in serum telomerase levels was observed between the HFAg and Autograft groups. Its levels in the PLM group were significantly lower than in the HFAg and Autograft groups).

- Serum TAC levels were higher in the PLM, HFAg and Autograft groups than in the control group. No significant difference was observed in serum TAC levels between the HFAg and Autograft groups. Serum TAC level was almost two times higher in the PLM group than in the HFAg and Autograft groups.

- Serum TOC levels were higher in the HFAg, PLM, and Autograft groups than in the control group. No significant difference in serum TOC levels was observed between the HFAg and Autograft groups. Serum TOC level was significantly lower in the PLM group than in the HFAg and Autograft groups.

- GSH levels were higher in the HFAg and Autograft groups than in the control group. No significant differences in serum GSH level were observed between the HFAg, Autograft, and PLM groups.

- MDA levels were higher in the HFAg, PLM, and Autograft groups than in the control group. No significant difference between the HFAg and PLM groups. The Autograft group had higher serum MDA levels than the HFAg and PLM groups.
Conclusion
Silver used in the HFAg and PansAg groups also reduced the oxidative stress that occurs in patients with burns, but the effect was less than that of PLM.

Burn wounds under PLM dressings caused the lesser systemic oxidative stress response compared to silver dressings. It can be speculated that the use of PML dressings can support wound healing, reduce catabolism, MODS, renal failure and infections by reduced bacterial translocation and loss of lean body mass in a patient after a burn injury (7-9).

This is caused by the material and its strong antioxidant effect on wound healing. So, PLM consists of poly-lactate which has got strong antioxidative effects and behavior as a scavenger (10).

References