**EVIDENCE SUMMARY**

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| Topic | Burns |
| Subtopic | Management |
| Intervention | Aloe vera |
| Question (PICO) | In people with burns (P), does applying Aloe vera on the burn (I), compared to not applying Aloe vera on the burn (C), influence survival, functional recovery, pain, complications, time to resumption of usual activity, restoration to the pre-exposure condition, time to resolution of the symptoms (O)? |
| Search Strategy | Databases The Cochrane Library (systematic reviews and controlled trials) using the following search strategy:1. [mh “Burns”] OR burn:ti,ab,kw OR burns:ti,ab,kw OR burned:ti,ab,kw OR “thermal injury”:ti,ab,kw OR “thermal injuries”:ti,ab,kw OR scald\*:ti,ab,kw2. [mh “Aloe”] OR aloe\*:ti,ab,kw3. 1-2 ANDMEDLINE (via PubMed interface) using the following search strategy:1. “Burns”[Mesh] OR burn[TIAB] OR burns[TIAB] OR burned[TIAB] OR “thermal injury”[TIAB] OR “thermal injuries”[TIAB] OR scald\*[TIAB]2. "Aloe"[Mesh] OR aloe\*[TIAB]3. 1-2 AND Embase (via Embase.com interface) using the following search strategy:1. 'Burn'/exp OR burn:ab,ti OR burns:ab,ti OR burned:ab,ti OR ‘thermal injury’:ab,ti OR ‘thermal injuries’:ab,ti OR scald\*:ab,ti2. 'aloe'/exp OR aloe\*:ab,ti3. 1-2 ANDSystematic reviews, retrieved with the above searches, were used to identify additional individual studies. Following systematic reviews provided additional studies:Norman, 2017Hekmatpou, 2019Included articles, retrieved with the above searches, were used to identify additional studies by searching (1) reference lists and (2) 20 first related citations in MEDLINE (via PubMed interface). |
| Search date | 31/08/2020 |
| In/Exclusion criteria | **Publication language:** Include: English.**Publication type:** Include: articles published in a peer-reviewed journal. Exclude: conference abstracts, conference papers, (clinical) trial registrations, dissertations, letters to the editor. **Study design**: Include: a systematic review: inclusion of the studies of the systematic review if the search strategy and selection criteria are clearly described and if at least the Cochrane Library, MEDLINE and Embase are searched. Inclusion of a systematic review as a source of studies if the search strategy and selection criteria are clearly described and at least two databases have been searched of which one is the Cochrane Library, MEDLINE or Embase.An experimental study: inclusion in case of one of the following study types: (quasi or non-) randomised controlled trial, controlled before and after study or controlled interrupted time series, and the data are available. An observational study: inclusion in case of one of the following study types: cohort and case-control study, controlled before and after study or controlled interrupted time series, and the data are available. Exclude: case series, cross-sectional studies**,** animal studies, *ex vivo* or *in vitro* studies, studies reporting no quantitative data, studies reporting only means, but no SDs, effect sizes, p-values. Studies with less than 3 participants per group.**Population:** Include: People with burns.**Intervention:** Include: Treatment with Aloe Vera. Exclude: Any other type of acute burn management, combination preparations of Aloe Vera and other active substances (e.g. other herbal extracts).**Comparison:** Include: Any other type of acute burn management, no burn management.**Outcome:** Include: Functional recovery, time to recovery, prevalence of adverse events. |

Characteristics of included studies

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| **Author, year, Country** | **Study design** | **Population** | **Comparison/Risk factor/Exposure**  | **Remarks** |
| Heck, 1981, United States | Experimental: Randomized controlled trial | 18 patients with moderate to deep second-degree burns from 2 to 12% of total body surface area | Intervention: Aloe vera cream (commercially available)Comparison: Silvadene (silver sulfadiazine)All patients received identical wound care with cleansing and debridement. After application of the cream, wounds were covered with a light gauze bandage. Wounds were cared for every other day. | Wounds were evaluated every other day. Unclear how data on established bacterial infections and adverse reactions were collected.Discrepancy for patient healing times between data as described in text and data in table 4. Data from text were extracted. |
| Khorasani, 2009, Iran | Experimental: Randomized controlled trial (within subjects design) | 30 patients, aged 33±11 years old, 25 males and 5 females, with two same site, second-degree burns (such as on the hands or feet) from 10-40% total burn surface area | Intervention: Aloe vera creamComparison: silver sulfadiazineWounds were cleaned with water or normal saline solution and the topical agent was applied directly to wound. | Identified from the systematic review of Norman, 2017.[Data regarding infection was not extracted as this was based on wound swabs] |
| Moghbel, 2007, Iran | Experimental: Non-randomized controlled trial (within subjects design) | 30 patients, aged 20-50 years, 20 males and 10 females, with second degree burns on both hands | Intervention: Aloe vera topical formulation produced by the researchersComparison: silver sulfadiazine 1% creamBurn wounds were treated twice daily.Intervention and comparison treatments were used on each hand symmetrically. | Identified from the systematic review of Hekmatpou, 2019.To quantify the rate of burn wound healing, every 24h the outline of the burn wound was traced on a sterilized transparent plastic sheet The area of the burn wounds on the first day were considered as 100% (0% healing) and the wound areas on subsequent days were compared with the wound on the initial day. Pathological changes, e.g. granulation tissue formation and reepithelization in wounds and their comparison with the normal tissue part were inspected medically by the specialist doctor.[Data is unclearly reported. Only data with clear p-value available mentioned in text extracted] |
| Shahzad, 2013, Pakistan | Experimental: Randomized controlled trial | 50 patients, ages 15-65 years, 26 males and 24 females with second degree burns who presented within 24 hours and had total burn surfacearea <25 % | Intervention: Aloe vera gel (98 % of unrefined gel from innerleaf of the plant)Comparison: silver sulfadiazineWounds were cleaned with pyodine scrub and normal saline and the topical agent was applied. Wound dressing was done twice a day until healing wascomplete. | At the time of change of dressing details regarding the condition of the wound such as signs of wound infection, condition of surrounding unburned tissues, discharge, smell, necrotic tissue and state of epithelialization was noted on every 3rd day. Subjective factors such as pain and local irritation were recorded regularly.The wound progression was measured by calculating percentage rate of change. Pain relief was noted by visual analogue scoring system (1-10). Pain was considered as severe for score 6-10, moderate 3-5, and mild less than 3. Pain was considered relieved if patient scored 0-1.[data regarding wound colonization not extracted as this was based on swabs and infection of the wound itself was also reported; data regarding complete/incomplete healing based on scar formation not extracted] |
| Thamlikitkul, 1991, Thailand | Experimental: Randomized controlled trial | 38 patients, aged 18 years [0.3-46] (aloe) and 25.2 years [0.2-62] (silver sulfadiazine), with first or second-degree burns | Intervention: Aloe vera mucilage (glue-like substance produced by the plant) Comparison: silver sulfadiazineTopical applications were applied twice daily until burns healed or patient left hospital. | Retrieved from Norman, 2017Each patient was assessed daily for healing, side effects and satisfaction with the treatment. |
| Visuthikosol, 1995, Thailand | Experimental: Non-randomized controlled trial (within subjects design) | 27 patients, 18 males and 9 females, with partial thickness burns with total body surface area >2%. Full thickness burns and other injuries could be present in other areas. | Intervention: Aloe vera cream Comparison: vaseline gauzeThe distal part of the limb with the wound was dressed with aloe vera cream and an equal size of the proximal part was dressed with Vaseline gauze alone. Dressing was changed twice daily. | The wound was clinically inspected and photographed on day 1,7,14 and 21, or until full epithelialization. |

Synthesis of findings

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| **Outcome** | **Comparison/Risk factor/Exposure** | **Effect Size** | **#studies, # participants** | **Reference** |
| Time to healing (days) | Aloe vera cream vs silver sulfadiazine | Not statistically significant:13.00±6.63 vs 16.15±5.94MD: -3.15, 95%CI [-8.97;2.67] ¥(p=0.29)\* | 1, 9 vs 9 § | Heck, 1981 |
| Statistically significant:15.9±2 vs 18.73±2.65MD: 2.83 £(p<0.0001)*In favour of Aloe vera* | 1, 30 vs 30 (within subjects design) § | Khorasani, 2009 |
| Healing (%) based on area on day 3 | Statistically significant:(p<0.001) £*In favour of Aloe vera* | 1, 30 vs 30 (within subjects design) § | Moghbel, 2007 |
| Adverse reactions | Not statistically significant:0/9 vs 0/9 §RR: not estimable | 1, 9 vs 9 | Heck, 1981 |
| Established bacterial infection | Not statistically significant:0/9 vs 0/9 §RR: not estimable |
| Time to healing (days) | Aloe vera mucilage vs silver sulfadiazine | Statistically significant:11±4.18 vs 24.24±11.16MD: -13.24, 95%CI [-17.91;-8.57] \* ¥(p<0.0001)*In favour of aloe vera* | 1, 25 vs 25 § | Shahzad, 2013 |
| Efficacy (epithelialization when leaving the hospital cured/improved vs not improved) | Not statistically significant:19/20 vs 15/18 §RR: 1.14, 95%CI [0.91;1.43] \* ¥(p>0.05) | 1, 20 vs 18  | Thamlikitkul, 1991 |
| Side effects (irritation/itching) | Not statistically significant:7/15 vs 7/15 §RR: 1, 95%CI [0.47;2.15] \* ¥(p>0.05) | 1, 15 vs 15  |
| Infections | Not statistically significant:3/25 vs 4/25 §RR: 0.75, 95%CI [0.19;3.01] ¥(p=0.69)\* | 1, 25 vs 25 § | Shahzad, 2013 |
| Time taken for pain relief (days) | Statistically significant:21 vs 26MD: -5 £(p=0.01)*In favour of aloe vera* |
| Patient satisfaction (satisfied vs not satisfied) | Not statistically significant:8/9 vs 5/8 §RR: 1.42, 95%CI [0.79;2.55] \* ¥(p>0.05) | 1, 9 vs 8  | Thamlikitkul, 1991 |
| Time to healing (days) | Aloe vera cream vs Vaseline gauze | Statistically significant:11.89±4.39 vs 18.18±8.87MD: -6.29 £(p<0.002)*In favour of Aloe vera* | 1, 27 vs 27 (within subjects design) § | Visuthikosol, 1995 |

Mean ± SD (unless otherwise indicated), MD: mean difference, RR: risk ratio, SD: standard deviation

\* Calculations (SD, MD, 95%CI and/or p-value) done by the reviewer using Review Manager software

£ No raw data or SDs available, effect size and CI cannot be calculated

¥ Imprecision (large variability of results)

§ Imprecision (limited sample size or low number of events)

Study limitations

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| **Author, Year**  | **Lack of allocation concealment** | **Lack of blinding** | **Incomplete accounting of outcome events** | **Selective outcome reporting** | **Other limitations** |
| Heck, 1981 | Lack of randomization: Unclear, only stated that patients were randomly assigned with no information on how randomisation was performed.Lack of allocation concealment: Unclear, no information provided on allocation concealment. | Participants: Unclear, no information provided on whether patients were blinded.Personnel: Unclear, no information provided on whether personnel was blinded.Outcome assessors: Unclear, no information provided on whether outcome assessors were blinded. The outcomes measured do involve some judgement. | No, outcome data seems to be available for all included patients. | No, no protocol available but all relevant outcomes seem to be reported. | Data unclearly reported and differs between text and table. |
| Khorasani, 2009 | Lack of randomization: Unclear, patients were randomized but no further information on method of randomization.Lack of allocation concealment: Unclear, no information provided on allocation concealment. | Participants: No, participants were blinded.Personnel: No, nurses were blinded.Outcome assessors: Unclear, not mentioned whether expert surgeons who performed assessments were blinded. | No, outcome data seems to be available for all included patients. | Yes, no explicit reporting of adverse effects or infections. | Within subjects design and statistical analysis was probably not adequately adjusted. |
| Moghbel, 2007 | Lack of randomization:Yes, study most likely not randomized.Lack of allocation concealment:Not applicable. | Participants: Unclear, study was double blind but unclear who is blinded.Personnel: Unclear, study was double blind but unclear who is blinded.Outcome assessors: Unclear, study was double blind but unclear who is blinded. | No, outcome data seems to be available for all included patients. | Yes, no reporting of adverse effects or infections. | Within subjects design and statistical analysis was probably not adequately adjusted.Data unclearly reported and differs between text, table and figure. |
| Shahzad, 2013 | Lack of randomization: Unclear, patients were randomized but no further information on method of randomization.Lack of allocation concealment: Unclear, no information provided on allocation concealment. | Participants: Unclear, no information provided on whether patients were blinded. They were provided information regarding the Aloe vera gel and SSD cream but it is unclear whether patients knew the treatment they were assigned to.Personnel: Unclear, no information provided on whether personnel was blinded.Outcome assessors:Unclear, patients assessed pain and it is unclear whether they were blinded. It is not described who performed the other assessments. | No, outcome data seems to be available for all included patients. | No, no protocol available but all relevant outcomes seem to be reported. |  |
| Thamlikitkul, 1991 | Lack of randomization: Unclear, patients were randomized using stratified randomisation but no further information on sequence generation.Lack of allocation concealment: Unclear, no information provided on allocation concealment. | Participants: Unclear, no information provided on whether patients were blinded.Personnel: Unclear, no information provided on whether personnel was blinded.Outcome assessors: Unclear, no information provided on whether outcome assessors were blinded. The outcomes measured do involve some judgement both from patients as well as those assessing healing. | No, patients who are not included in the outcomes ‘side effects’ and ‘patient satisfaction’ were young children or did not want to comment on the treatment, but were accounted for. | No |  |
| Visuthikosol, 1995 | Lack of randomization:Yes, study was not randomized.Lack of allocation concealment:Not applicable. | Participants: Unclear, no information provided on whether patients were blinded.Personnel: Unclear, no information provided on whether personnel was blinded.Outcome assessors: Unclear, no information provided on whether outcome assessors were blinded. | No, outcome data seems to be available for all included patients. | Yes, adverse effects (which were minor) not adequately reported and could not be included in synthesis of findings. | Within subjects design and statistical analysis was probably not adequately adjusted. |

**Certainty of the body of evidence**

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|  | **High [A]** | Downgrading due to |
| **Limitations of study design** | -1 | See table ‘Study limitations’ |
| **Imprecision** | -1 | Limited sample sizes, low number of events and large variability of the results |
| **Inconsistency** | 0 |  |
| **Indirectness** | 0 |  |
| **Publication bias** | 0 |  |
| **CERTAINTY (GRADE)** | **Low [C]** |  |

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| **Conclusion** | There is limited evidence in favour of Aloe vera. In making this evidence conclusion we place a higher value on time to healing and pain-related outcomes over infections, side effects and patient satisfaction; and we place a higher value on imprecise but statistically significant outcomes over imprecise and not statistically significant outcomes.It was shown that Aloe vera cream resulted in a statistically significant decrease of time to healing and healing % based on area on day 3, compared to silver sulfadiazine and Vaseline gauze (Khorasani 2009, Moghbel 2007, Visuthikosol 1995). It was shown that Aloe vera mucilage resulted in a statistically significant decrease of time to healing and time taken for pain relief, compared to silver sulfadiazine (Shahzad 2013).A statistically significant increase time to healing, when using Aloe vera cream, compared to silver sulfadiazine, could not be demonstrated (Heck 1981). Furthermore, a statistically significant increase in epithelialization efficacy when using Aloe vera mucilage, compared to silver sulfadiazine, could not be demonstrated (Thamlikitkul 1991).A statistically significant increase of infections, when using Aloe vera creme or Aloe vera mucilage, compared to silver sulfadiazine, could not be demonstrated (Heck, 1981, Shahzad 2013). A statistically significant increase of side effects when using Aloe vera cream and Aloe vera mucilage, compared to silver sulfadiazine, could not be demonstrated (Heck 1981, Thamlikitkul 1991).Finally, a statistically significant decrease of patient satisfaction when using Aloe vera mucilage, compared to silver sulfadiazine, could not be demonstrated(Thamlikitkul 1991).Evidence is of low certainty and results cannot be considered precise due to limited sample sizes, low numbers of events and large variability of results. |
| **Reference(s)** | **Articles**Heck E, Head M, Nowak D. *Aloe vera (gel) cream as a topical treatment for outpatient burns*. Burns 1981, 7(4):291-294.Khorasani G, Hosseinmehr S, Azadbakht M, Zamani A, Mahdavi M. *Aloe versus silver sulfadiazine creams for second-degree burns: a randomized controlled study.* Surg Today. 2009;39(7):587-91.Moghbel A, Ghalambor, A; Allipanah S. *Wound healing and toxicity evaluation of Aloe vera cream on outpatients with second degree burns*. Iranian Journal of Pharmaceutical Sciences 2007, 3(3):157-160.Shahzad MN, Ahmed N. *Effectiveness of Aloe Vera gel compared with 1% silver sulphadiazine cream as burn wound dressing in second degree burns*. Journal of the Pakistan Medical Association 2013, 63(2):225-230.Thamlikitkul V, Bunyapraphatsara N, Riewpaiboon W, Theerapong S, Chantrakul C, Thanaveerasuwan T, Nimitnon S, Wongkonkatape S, Riewpaiboon A, Tenambergen E. *Clinical Trial of Aloe vera Linn. For Treatment of Minor Burns.* Siriraj Hosp Gaz 1991, 43(5):313-316Visuthikosol V, Chowchuen B, Sukwanarat Y, Sriurairatana S, Boonpucknavig V. *Effect of aloe vera gel to healing of burn wound a clinical and histologic study.* J Med Assoc Thai. 1995 Aug;78(8):403-9.**Systematic reviews**Hekmatpou D, Mehrabi F, Rahzani K, Aminiyan A. *The Effect of Aloe Vera Clinical Trials on Prevention and Healing of Skin Wound: A Systematic Review*. Iran J Med Sci 2019, 44(1):1-9.Norman G, Christie J, Liu Z, Westby MJ, Jefferies JM, Hudson T, Edwards J, Mohapatra DP, Hassan IA, Dumville JC. *Antiseptics for burns*. Cochrane Database of Systematic Reviews 2017, 2017(7). |
| **Evidence used for** | Guideline |
| **Project** | AFAM 2021 |
| **Reviewer(s)** | Bert Avau + Anne-Catherine Vanhove |

Opmerkingen voor de dienst Eerste hulp:

Aloe vera versnelt misschien de heling, maar er zijn ook studies die geen significant verschil aantonen. Pijn zou ook sneller afnemen. Infectie of neveneffecten komen mogelijks niet meer voor en patiënten lijken niet ontevredener.

Aloe kan aangeraden worden, maar het bewijs blijft beperkt.