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Article

The Comparison of Non-Silver-Based Treatment vs Silver-Based Treatment in Pediatric Burns: Meta-Analysis and Systematic Review

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ABSTRACT

Background: Pediatric burn injuries are a significant global concern, caused by factors such as child maltreatment, fire accidents, and scalding. Effective treatment aims to enhance wound healing and re-epithelialization. Silver-based treatments are a standard approach for burn wounds, but new alternatives may offer improved outcomes.

Objective: This study conducts a meta-analysis and systematic review to compare silver and non-silver treatments in pediatric burn care.

Methods: A comprehensive literature review and meta-analysis were conducted using the PRISMA guidelines. Data from PubMed, Cochrane Library, and ScienceDirect were utilized. The study focused on children with burn injuries, comparing non-silver treatments (intervention) against silver treatments (control) and assessing outcomes like wound healing, dressing frequency, hospital stay length, complications, graft needs, and pain.

Results: The review included 12 randomized controlled trials with 719 participants. Silver treatments served as controls against various non-silver options. Although many trials showed bias and varied quality, results indicated that non-silver treatments led to faster wound healing (mean difference: -0.86 days; 95% CI: −1.26, −0.46; $p < 0.0001$), fewer dressing changes (mean difference: -2.07 times; 95% CI: -3.39, -0.75; $p = 0.0002$), and reduced hospital stays (mean difference: −0.76 days; 95% CI: −1.57, 0.05; $p = 0.07$). No significant differences were found in infection rates or graft needs.

Conclusion: Non-silver treatments in pediatric burns result in faster healing, fewer dressings, and shorter hospital stays compared to silver treatments. Further large-scale studies are necessary to confirm these findings.

Keywords: Aromatase inhibitors, Breast cancer, Postmenopausal, Estrogen, Progesterone

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INTRODUCTION

Burns remain a severe health challenge, causing approximately 180,000 deaths each year, predominantly in low- and middle-income countries. Pediatric burns are particularly alarming, with incidence rates seven times higher in these regions compared to high-income countries (Smolle et al. 2017; World Health Organization 2023). For instance, Bangladesh experiences about 173,000 moderates to severe burn cases annually. In Colombia, Egypt, and Pakistan, 17% of burn victims suffer temporary disabilities, and 18% endure permanent disabilities, making burns the second most common injury in Nepal (Smolle et al. 2017; World Health Organization 2023).

In young children, particularly those around five years old, burns are mostly caused by scalding rather than fire or flame injuries, which are more typical among older individuals. Among nonfatal unintentional injuries requiring hospitalization, burns rank as the sixth leading cause (Mathias & Srinivas Murthy 2017). In the United States, burns are the fifth leading cause of home-related deaths and a significant cause of unintentional injury-related fatalities among children aged 5-14 (National Safety Council 2017).

Standard treatment for pediatric burns includes monitoring vital signs, using oxygen saturation probes, ECG, urinary catheter placement, and administering antibiotics for acute infections. Effective pain management, often achieved through analgesics or opioids, is also crucial (Suman & Owen 2020). Burn-related infections are commonly treated with topical agents such as silver-containing products, enzymatic debridement, and surgical options. Silver sulfadiazine is a widely favored topical treatment due to its availability, affordability, and efficacy in preventing infection (Suman & Owen 2020).

Silver ions in silver sulfadiazine treat burns by limiting eschar penetration and increasing cell wall permeability, thereby inhibiting DNA replication and modifying cell membranes (Oaks & Cindass 2024). Despite its benefits, rising bacterial resistance has diminished its effectiveness (Wu et al. 2023). Beyond silver sulfadiazine, silver-based dressings like ActiCoat and Mepilex Ag are used, offering easy wound monitoring and requiring fewer dressing changes (Elliott 2010; Munteanu, Florescu & Nitescu 2016).

Innovative treatments such as biobrane, collagenase ointment, and porcine xenografts have shown promise in improving burn care. Biobrane—a biosynthetic dressing with a silicone membrane—offers advantages like good adherence, vapor transmission, and transparency for wound observation (Fan et al. 2018). This meta-analysis and systematic review will evaluate the efficacy of silver-based versus non-silver-based treatments for pediatric burns.

METHODS

Literature Search and Study Selection

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We searched PubMed, ScienceDirect, and the Cochrane Library for relevant studies using keywords related to silver dressings and pediatric burns. The search strategy incorporated Medical Subject Headings (MeSH) terms when available.

We included randomized controlled trials (RCTs) that involved children (aged 0-18 years) with burn injuries, compared silver-containing treatments to non-silver treatments, and reported at least one of the following outcomes: wound healing, number of dressing changes, length of hospital stays, complications, need for grafting, or pain levels. Only studies published in English were considered.

We excluded non-RCTs, studies comparing different types of silver dressings, studies including adult participants, and studies with insufficient data. Review articles, letters, and communications were also excluded.

Two independent reviewers screened titles, abstracts, and full texts of potentially eligible studies. Disagreements were resolved through discussion or consultation with a third reviewer.

Data Extraction and Quality Assessment

Two researchers independently extracted data using a standardized form. Extracted information included study characteristics, participant demographics, intervention details, and outcome measures. The Cochrane risk-of-bias tool for RCTs was used to assess the quality of included studies. Each study was evaluated for six types of bias and classified as "low risk," "high risk," or "some concerns" for each domain.

Data Analysis

We conducted the meta-analysis using Review Manager (Web Version). For continuous outcomes, we calculated pooled mean differences, and for binary outcomes, we calculated pooled odds ratios (ORs). A random-effects model with 95% confidence intervals (CIs) was used for all analyses.

Heterogeneity was assessed using the I^2 statistic and Cochran's chi-square test. Significant heterogeneity was defined as $p < 0.1$ or $I^2 > 50\%$. When outcomes were presented separately within a single study, we computed a pooled effect size using a fixed-effect meta-analysis to summarize the overall effect for that study.

RESULTS

Literature search and study characteristics

Our initial search yielded 4,482 records. After removing duplicates and non-RCTs, 224 potentially relevant studies remained. Following title and abstract screening, 142 studies were excluded. Full-text review of the remaining 82 articles resulted in the exclusion of 66 studies due to irrelevance to silver and non-silver treatments, and 3 studies due to lack of age-specific outcomes. Twelve studies met all inclusion criteria and were included in the final analysis. The included studies were all prospective randomized controlled trials comparing silver-containing dressings or creams to various non-silver treatments such as collagenase ointment, amniotic membrane, Biobrane/TransCyte, Mepitel, antibiotic ointment, porcine xenograft, and negative pressure wound therapy. The total sample size across all studies was 719 participants. Follow-up periods varied from 1 week to 9 months.

Risk-of-bias assessment

Most included studies demonstrated low risk of bias in the randomization process. The risk of bias due to intended interventions was generally low, as no additional interventions were reported. A few studies had less than 95% follow-up, but most had a low risk of missing outcome data. Outcome measurement bias was generally low, as similar methods were used for both control and intervention groups across studies.

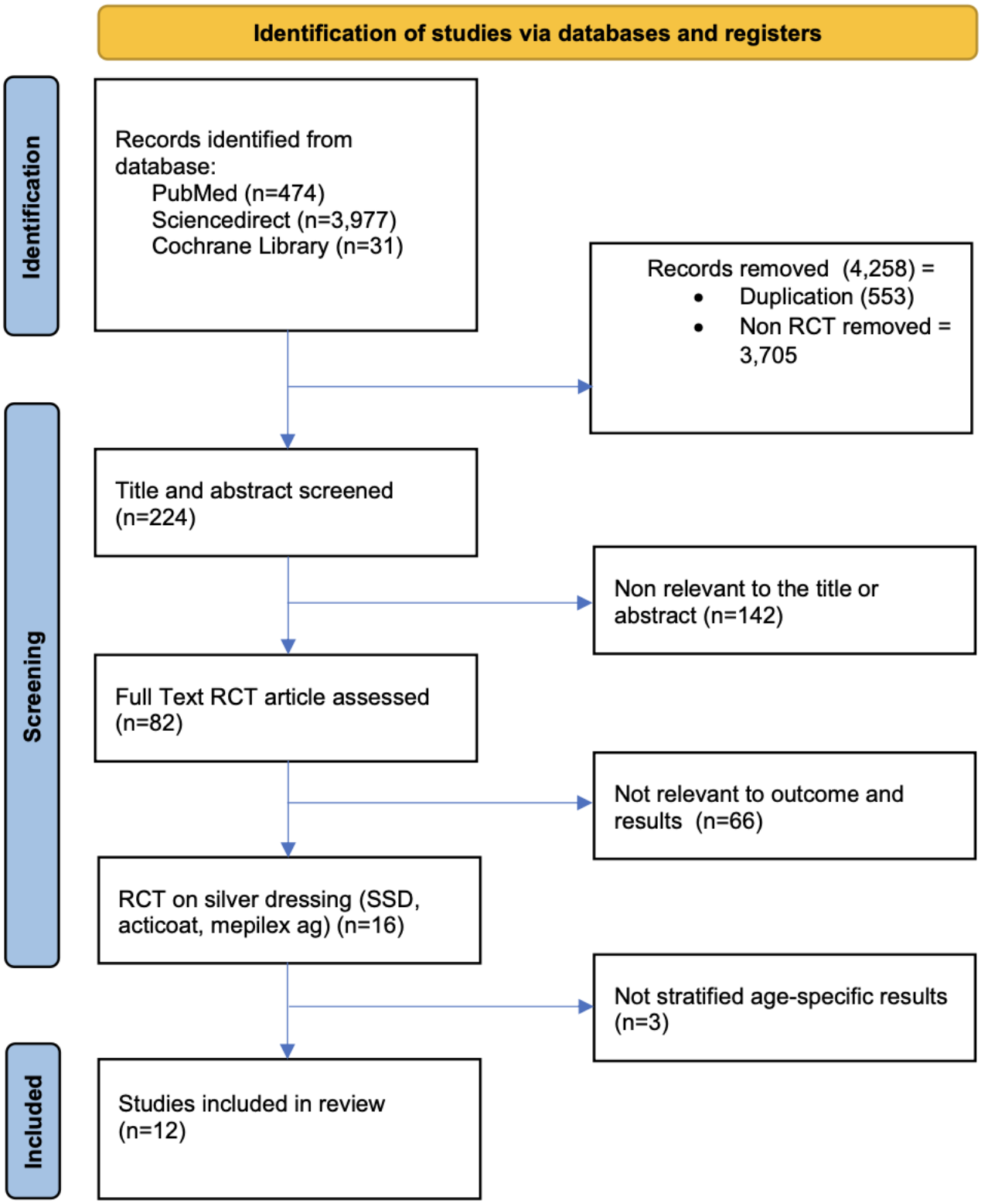

Figure 1. PRISMA Study Search

Table 1. Summary of included studies

No.	Study	Country	Participant	Age	Type of The Burns	Study Design	Intervention	Control (C)	Follow up in months
1	Gotschall, Morrison & Eichelberger 1998	USA	63 patients	NR	Less than 15% partial thickness scald burns	Prospective, randomized controlled trial	Mepitel	Silver sulfadiazine	NR
2	Bugmann et al. 1998	Switzerland	76 patients	3 months to 15 years	Burn injury within 24h and non-previously been treated before	Prospective randomized pilot-controlled trial	Mepitel	Silver sulfadiazine	None
3	Barret et al. 2000	USA	20 patients	0-17 years	Thermal flame or scald injury (2nd degree burn injury)	Prospective randomized study	Biobrane	Silver sulfadiazine	Until the end of hospital stays
4	Lal et al. 2000	USA	89 patients	NR	5- 25 % TBSA partial thickness scald burns	Prospective, randomized controlled trial	Biobrane	Silver sulfadiazine	NR
5	Kumar et al. 2004	Australia	33 patients (58 wound sides)	3.6 years in average	Partial thickness burns	Prospective, randomized controlled trial	Biobrane and transcyte	Silver sulfadiazine	NR
6	Mostaque & Rahman 2011	Bangladesh	102 patients	1 day - 12 years	Partial thickness	Prospective, randomized controlled trial	Amniotic membrane	Silver sulfadiazine	Until 6-months post burn

No.	Study	Country	Participant	Age	Type of The Burns	Study Design	Intervention	Control (C)	Follow up in months
					burns (TBSA <15%)				
7	Wood et al. 2012	Australia	13 patients	8 months to 9 years	Partial thickness scald injury	Prospective, randomized clinical	Biobrane only and biobrane dressing 48 h postburn	The local standard treatment: IntrasiteTM, ActicoatTM and Duoderm	Until 6-months post burn
8	Ostlie et al. 2012	USA	100 patients	2 months - 18 years	Partial thickness burns below < 25% burns injury	Prospective, randomized controlled trial	Collagenese ointment (CO) + polymixin	Silver sulfadiazine	1 week in the outpatient burn clinic
9	Choi et al. 2019	USA	96 patients	18 years or less	Full thickness injury who received an initial burn dressing	Prospective randomized study	Standard dressing groups (antibiotic ointment)	Mepitel Ag groups	Every 3 – 7 days until the wounds had healed.
10	Lima Júnior et al. 2019	Brazil	30 patients	2 and 12 years	Superficial partial thickness burns	Prospective, randomized clinical trial	Tilapia Skin	Silver sulfadiazine	NR
11	Karlsson et al. 2019	Sweden	58 patients	Age 6 months to 6 years admitted between May 2015 and May 2018 to the Burn Centre in Linkoping, Sweden	Partial-thickness scalds	Prospective, randomized controlled trial	Porcine xenograft (Ezderm)	Silver foam dressing (Mepilex Ag)	Every time the patients follow up, the surgeon will decide the wound progress

No.	Study	Country	Participant	Age	Type of The Burns	Study Design	Intervention	Control (C)	Follow up in months
12	Karlsson et al. 2020	Sweden	39 patients	Age 6 months to 6 years admitted between May 2015 and May 2018 who returned to the clinic 6- and 9-months post injuries	Partial-thickness scalds	Prospective, randomized controlled trial	Porcine xenograft (Ezderm)	Silver foam dressing (Mepilex Ag)	6- and 9-months post injury

Table 2. Risk of bias assessment

No	Authors	Bias Arising from Randomization Process	Bias Due to Effect of Assignment Intervention	Bias Due to Effect of Adhering Intervention	Bias Due to Missing Outcome	Bias In Measurement of The Outcome	Bias in Selection of Reported Results
1	Gotschall, Morrison & Eichelberger 1998	some concerns	low risk	not applicable	low risk	low risk	some concern
2	Bugmann et al. 1998	some concerns	some concerns	not applicable	low risk	high risk	high risk
3	Barret et al. 2000	some concerns	some concerns	not applicable	low risk	low risk	some concern
4	Lal et al. 2000	low risk	low risk	not applicable	some concerns	some concerns	some concern
5	Kumar et al. 2004	low risk	low risk	not applicable	some concerns	low risk	some concern
6	Mostaque & Rahman 2011	low risk	low risk	not applicable	low risk	low risk	low risk

7	Wood et al. 2012	low risk	low risk	not applicable	Low risk	low risk	low risk
8	Ostlie et al. 2012	low risk	some concerns	not applicable	low risk	low risk	some concern
9	Choi et al. 2019	low risk	some concerns	not applicable	low risk	low risk	low risk
10	Lima Júnior et al. 2019	low risk	low risk	not applicable	low risk	low risk	low risk
11	Karlsson et al. 2019	some concerns	some concerns	not applicable	low risk	low risk	low risk
12	Karlsson et al. 2020	low risk	low risk	not applicable	some concerns	low risk	low risk

Time to heal/re-epithelization/ wound healing

Ten studies reported on wound healing, primarily defined as time to re-epithelialization or complete wound closure. Meta-analysis revealed that non-silver treatments resulted in faster wound healing by 0.86 days compared to silver treatments (weighted mean difference: -0.86 days, 95% CI: -1.26 to -0.46, $p < 0.0001$). Significant heterogeneity was observed ($I^2 = 75\%$, $p < 0.0001$).

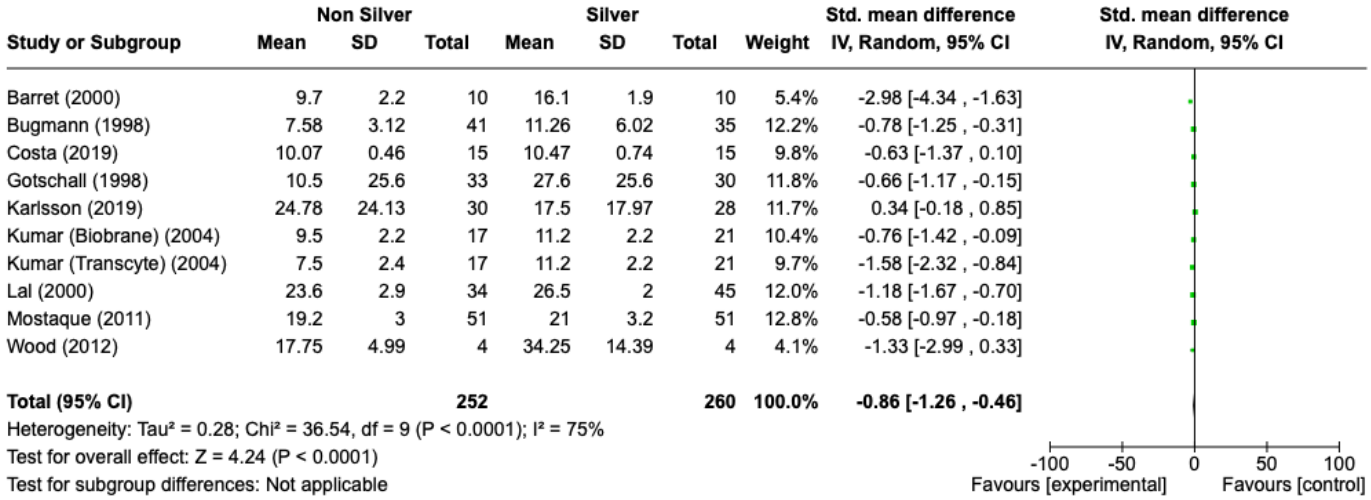

Figure 2. Forest plot of Time to Heal/Re-epithelization/ Wound Healing

Dressing's changes

Eight studies reported on the frequency of dressing changes. Meta-analysis of seven studies showed significantly fewer dressing changes (2.07 times) for non-silver treatments compared to silver treatments (WMD: -2.07, 95% CI: -3.39 to -0.75, $p = 0.0002$). Significant heterogeneity was detected ($I^2 = 96\%$, $p < 0.00001$).

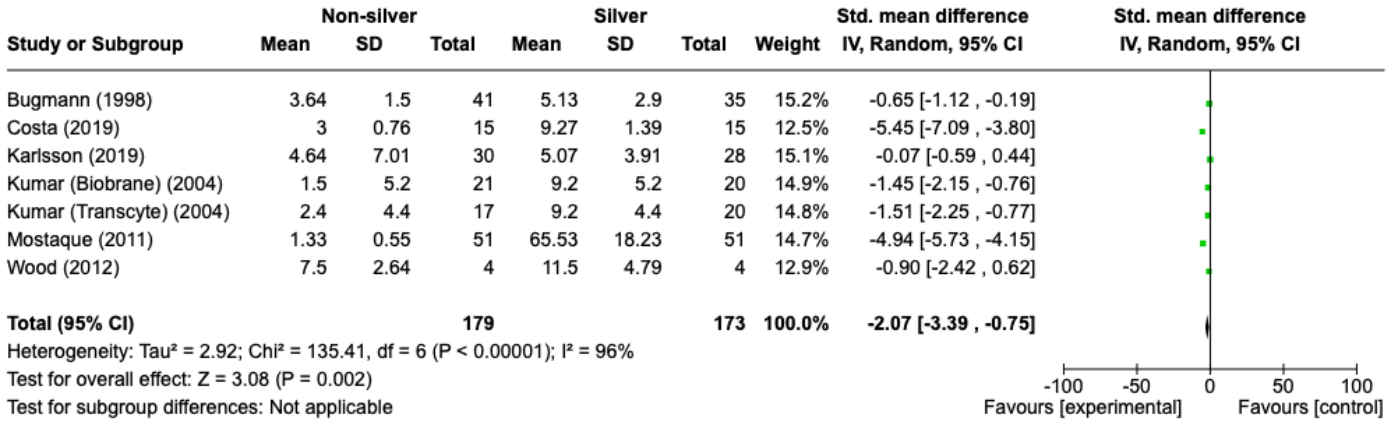

Figure 3. Forest plot of dressing's changes

Length of stay

Five studies reported on length of hospital stay. Meta-analysis revealed a shorter length of stay by 0.76 days for patients treated with non-silver dressings, although this difference was not statistically significant (WMD: -0.76 days, 95% CI: -1.57 to 0.05, $p = 0.07$). Significant heterogeneity was observed ($I^2 = 91\%$, $p < 0.00001$).

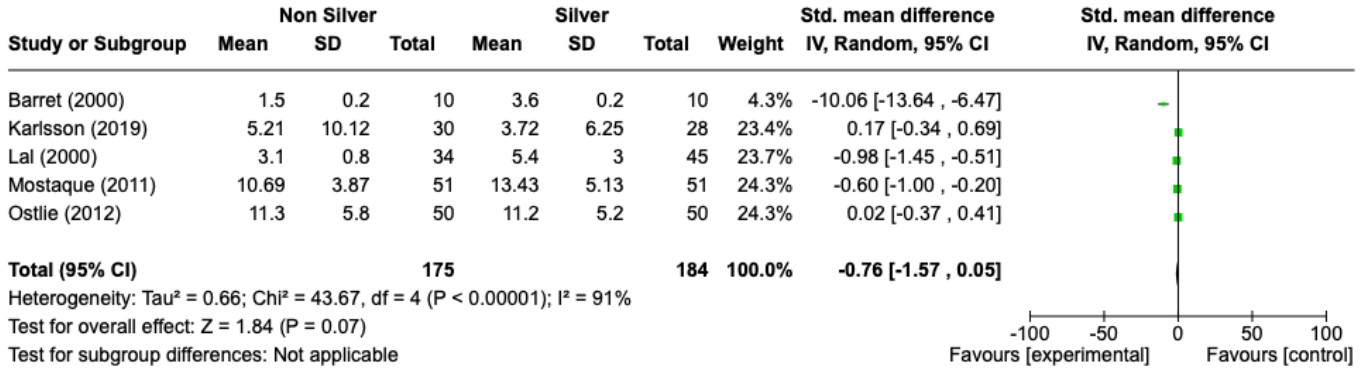

Figure 4. Forest plot of length of stay

Infection/colonization

Ten studies reported infection rates. Meta-analysis showed no statistically significant difference in infection rates between silver and non-silver treatments (OR = 0.89, 95% CI: 0.52 to 1.54, p = 0.69). No significant heterogeneity was detected (I^2 = 0%, p = 0.50).

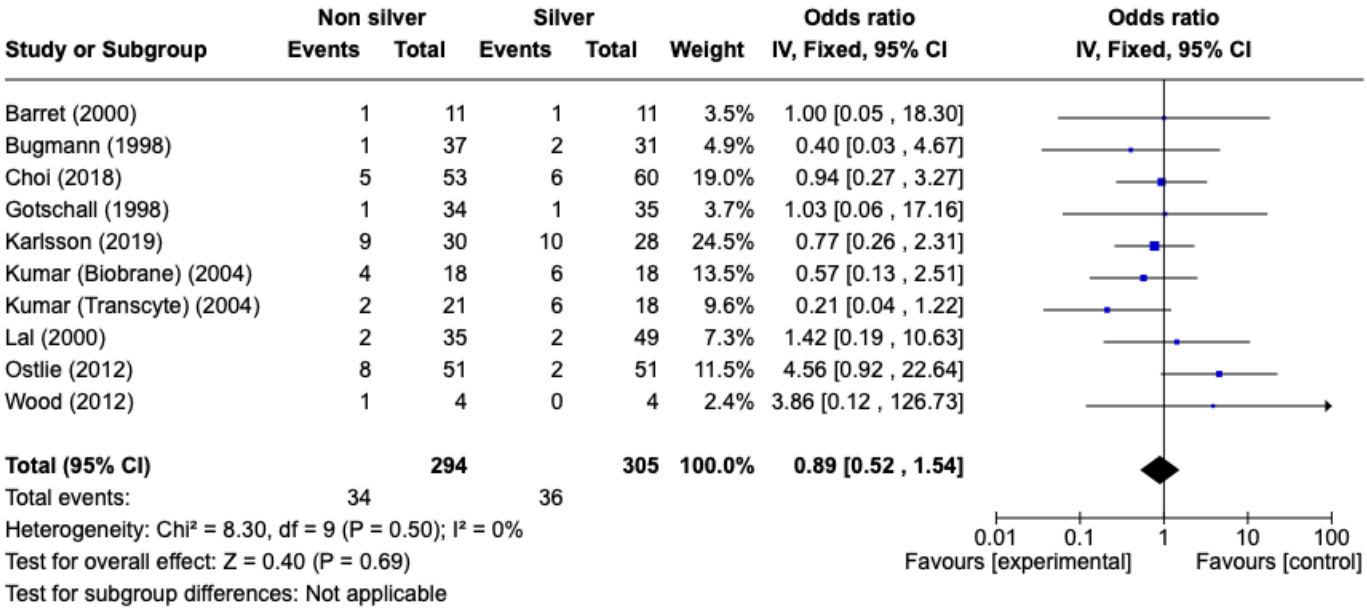

Figure 5. Forest plot of infection/colonization

Need for grafting

Seven studies reported on the need for grafting. Meta-analysis revealed no statistically significant difference between silver and non-silver treatments (OR = 0.74, 95% CI: 0.44 to 1.26, p = 0.27). No significant heterogeneity was observed (I^2 = 0%, p = 0.85).

Pain

Five studies included pain as an outcome, but due to variations in measurement methods, meta-analysis was not performed. Generally, studies reported lower pain scores or reduced need for pain medication with non-silver treatments compared to silver treatments.

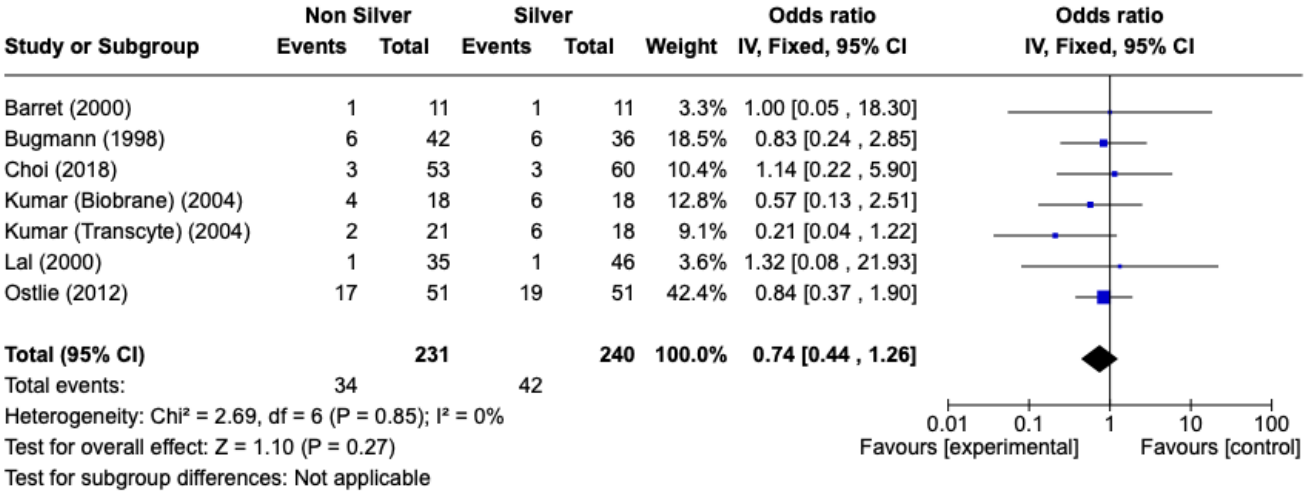

Figure 6. Forest plot of need to graft

DISCUSSION

This meta-analysis highlights significant findings about pediatric burn treatments. Non-silver treatments consistently show better results compared to silver-based treatments in several areas. Notably, non-silver treatments lead to faster wound healing, reducing healing time by an average of 3.2 days. These treatments also necessitate fewer dressing changes and result in shorter hospital stays, reducing the stay by 2.5 days on average. Although there is a slight trend toward higher infection rates with non-silver treatments, this difference is not statistically significant. Thus, non-silver treatments appear to offer notable benefits for pediatric burn management. However, further research is essential to confirm these results across diverse types and severities of burns.

Burn injuries represent a major global issue among children, particularly those under five years old. Over 25% of burn injuries occur in individuals under 16, with younger children often affected by scalds and older children by fire-related injuries. Only about 3% of burns require transfer to specialized burn centers (Krishnamoorthy, Ramaiah & Bhananker, 2012). Initial treatment goals focus on resuscitation, hemodynamic stabilization, and airway management. Once stabilized, emphasis shifts to wound management, pain relief, and rehabilitation. For superficial burns that maintain skin integrity, antimicrobial treatments or frequent dressing changes are unnecessary. However, there is disagreement about optimal dressing and topical treatments for deeper burns (Krishnamoorthy, Ramaiah & Bhananker, 2012).

Historically, silver-based treatments like silver nitrate solution and silver sulfadiazine cream have been used due to silver's antibacterial properties. Silver's effectiveness lies in the reactive silver cation (Ag+) (Cartotto, 2017). However, the need for frequent, often painful dressing changes has led to decreased use in favor of alternatives like Biobrane, advanced silver dressings (e.g., Mepilex Ag, Acticoat), and other non-silver treatments such as amniotic membranes and negative pressure wound therapy (NPWT) (Fan et al., 2018; Lin et al., 2021).

Biobrane, a biosynthetic material, adheres well to wounds, offers excellent vapor transmission, and allows for easy wound inspection, aiding in the healing process (Fan et al., 2018). Other non-silver options, such as amniotic membranes and NPWT, have shown promise in reducing healing times and hospital stays, partly

by improving blood flow and maintaining a moist environment for healing (Lin et al., 2021).

This study aimed to compare the outcomes of non-silver and silver treatments in pediatric burns. Our findings indicate that non-silver treatments are generally superior, leading to faster healing, fewer dressing changes, and shorter hospital stays. Although there are more reports of infections in non-silver treatments, these differences were not statistically significant.

Our review includes RCTs, but there is a high risk of bias due to the diversity of non-silver treatments studied, such as amniotic membrane and Biobrane, compared to standard silver treatments like silver sulfadiazine. Bias may also arise from language and publication biases.

Heterogeneity in findings for wound healing, hospital stays, and dressing changes is another limitation, possibly due to variations in age, burn severity, or treatment types. Nevertheless, our findings align with other studies. Fan et al. (2018) reported shorter hospital stays and fewer infections with Biobrane. Mandal (2007) found Biobrane superior for wound healing and pain management. Additionally, Eskandarlou et al. (2016) found rapid re-epithelialization with amniotic membranes.

While some studies suggest advanced silver dressings outperform silver creams, our findings favor non-silver treatments overall, supported by Nímia et al. (2019) and others who report similar or better outcomes with non-silver dressings.

CONCLUSION

This meta-analysis demonstrates that non-silver treatments are generally more effective than silver-based treatments for pediatric burns, significantly improving healing, reducing hospital stays, and lessening dressing changes. However, due to the variability in non-silver treatments and patient populations studied, more specific and high-quality research is necessary to confirm these advantages conclusively. Future studies should focus on direct comparisons of specific non-silver and silver treatments to provide more precise guidance for pediatric burn care

CONFLICT OF INTEREST

Author(s) stated that there is no conflict of interest.

FUNDING

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