Therapeutic Breakthroughs and Persistent Challenges in Umbilical Granuloma: Evidence-Based Insights

Siddharth Singh[1], Deepika Raina[2], Prachi Mall[2], Chestha Goyal[3], Loveleen Kaur[3], Hitesh Chopra[4] and Tabarak Malik[5]

ABSTRACT

There are many umbilical medical issues have been reported by medical experts among neonates. Umbilical granuloma brings attention towards more its self and parent's concerns because of their lesion appearance with discharge. It develops due to the overgrowth of granulation tissue and also leads to the associated subclinical infections. The diagnosis of umbilical granuloma can be done clinically in certain cases Ultrasound can be done where lesion is to differentiate between granuloma / polyp. There are various treatment options are available such as topical salt therapy, silver nitrate therapy, corticosteroid therapy, topical antibiotics, electro-cauterization, ligation, and last surgical excision. This review elaborates on all the treatment options with their clinical corroborations and limitations. The effective treatment approach includes silver nitrate and common salt. The first line treatment for umbilical is Silver nitrate which is supported by randomized trials but sometimes results in periumbilical burns. Recent trials shows safer treatment which is safer approach.

Keywords: Umbilical granuloma, Salt therapy, Silver nitrate cauterization, Topical corticosteroids, Doxycycline therapy

[1]Faculty of Pharmacy, School of Pharmaceutical & Population Health Informatics, DIT University, Dehradun, Uttarakhand, India
[2]School of Pharmacy, Graphic Era Hill University, Dehradun, Uttarakhand, India
[3]Chitkara College of Pharmacy, Chitkara University, Patiala, India
[4]Department of Biosciences, Saveetha School of Engineering, Saveetha Institute of Medical and Technical Sciences, Chennai - 602105, Tamil Nadu, India
[5]Department of Biomedical Sciences, Institute of Health, Jimma University, Ethiopia

Correspondence to: Deepika Raina, deepikaraina0@gmail.com

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Introduction

It has been found that roughly 10% of drugs prescribed for children are either off-label or unlicensed, while the WHO reports that roughly 50% of medication issued for long-term diseases is not taken as advised. There are some well-known paediatric therapeutic tragedies have been reported such as sulfanilamide elixir and thalidomide cases. Therapeutic disasters in children influenced legislatures to mandate extensive testing of new drugs before they could be distributed across state lines. These legislations strive to lower the mortality rate for infants and young children, stop infectious disease propagation, encourage healthy lifestyles for a long life free of sickness, and assist in easing the issues faced by kids and teenagers with chronic illnesses. From preventative health care to the diagnosis and treatment of acute and chronic disorders, paediatric care covers a wide range of medical services.[1–3]

Abraham Jacobi (1830–1919) is widely regarded as the pioneer in the field of pediatrics. The pediatrics population is bifurcated into various subsets with the difference in anatomy and physiology, age followed by development skills. This features either inherent or environmental adaptations made many obstacles in many aspects such as formulation administration, toxicity, safety, therapeutic efficacy, and acceptability. In addition, these above-discussed features cannot neglect by formulation scientists for a pediatric population of all possible ages while developing formulation.[4–6]

The most common medical issue among neonates is the umbilical granuloma. Umbilical granuloma, a red, wet tissue fleshy lump develops on the baby's navel (belly button) in the weeks after the detachment of the umbilical cord. An umbilical granuloma affects around 1 in every 500 newborns. An umbilical granuloma is caused by the umbilical ring failing to properly epithelialize and the skin's natural healing process being outpaced by the proliferation of fibroblasts. The umbilical cord serves as a link between the developing child and the mother inside the womb. The umbilical cord is not required after delivery. After being clamped, it is removed. This results in the formation of a tiny stump. Most of the time, the umbilical cord stump typically dries out and comes off the infant within the first few weeks of life. However, a granuloma can occasionally develop after the stump is removed. It resembles a little stalk or mass of pinkish-red tissue. It is possible that the granuloma is wet and draining fluid. It is possible that the surrounding area is irritated or diseased. For the initial assessment of umbilical lesions, ultrasonography (US) is the imaging modality used. It is benign in nature with no nerve supply that made it sense and rarely cause infection omphalitis. Its treatment differs as per different geographical locations worldwide. The most common treatment approach that offers topical therapy is salt treatment (silver nitrate and copper sulphate) and oral usage of antibiotics. Apart from this, ethanol and clobetasol propionate wipes, electrocauterization, cryotherapy, double ligature method, and surgical excision.[7–11]

Research Method

An intense literature search was done using engines like PubMed, Scopus, and Google Scholar from 2010–2024. The key words used were "umbilical granuloma," "salt therapy," "silver nitrate," "corticosteroids," "antibiotics," "surgical excision," and "neonates".

Inclusion criteria: Randomized controlled trials (RCTs), prospective and retrospective observational studies/ case report and series on the treatment of umbilical granuloma in neonates and infants (Figure 1).

Exclusion criteria: Manuscript which were not in English, studies not focused on neonatal umbilical lesions, and manuscripts which were devoid of treatment outcomes. The search was conducted through the titles and abstracts of the references of the database followed by full length manuscript to find relevancy (Table 1).

Ethical approval: This study was a secondary analysis based on the currently existing data and did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper

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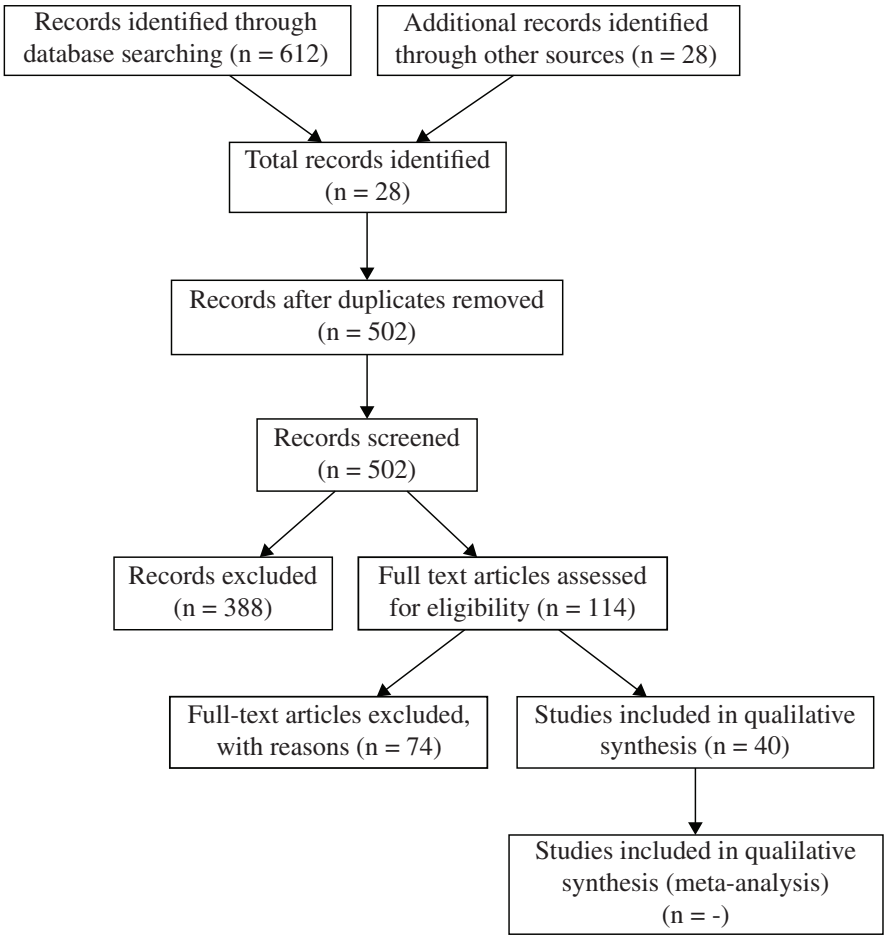

Fig 1 | Study selection process for selection of UG

Table 1 | Level of evidence and risk of bias

Study	Design	Sample Size	Intervention/Comparator	Primary Outcome	Level of Evidence	Risk of Bias
Ogawa et al., 2018	RCT	≈204–207 neonates	Silver nitrate vs topical steroid	Healing at 3 weeks (~91% vs 90.4%)	1b	Some concerns
Brødsgaard et al., 2015	RCT	109 infants	Silver nitrate vs clobetasol vs ethanol	Healing / resolution rates	1b	Some concerns
Chung et al., 2022	Pilot RCT	64 infants	NaCl vs $CuSO_4$	Complete healing (90% vs 69.7%)	1b	Some concerns
Janyoungsak et al., 2022	Double-blind RCT	100 infants	3% vs 30% NaCl	Healing by granuloma size	1b	Low–Some concerns
Copper sulphate vs Salt (2015, 2017)	Prospective / Retrospective cohort	40–84 infants	Salt vs $CuSO_4$	Cure rate	2b	Moderate–Serious
Abdoufatouh, 2021	Comparative cohort	50 infants	Salt vs clobetasol	Cure rate	2b	Serious
Badebarin, 2018	Prospective cohort	50 infants	Salt vs electrocautery	Healing success	2b	Serious
Wang, 2015	Cohort	84 infants	Topical doxycycline	Lesion resolution	2b	Moderate
Multiple Salt Series (17, 36, 76, 25 cases)	Case series	17–76 infants	Salt therapy	Resolution rates, recurrence	4	Moderate
Ethiopia case (2018)	Case report	1 infant	Salt therapy	Resolution, no recurrence	5	Low

Diagnosis of the Umbilical Lesions

The main reason for the delayed diagnosis of umbilical granuloma is because it mimics/ may coexists with other conditions. To avoid further complications the delay should be avoided.

Reason behind Umbilical Granuloma

The baby and mother connect through each other by an umbilical cord in the gestation period. The umbilical cord is made up of connective tissues and blood vessels that supply essential requirements to the foetus for

Table 2 | Risk of bias

Study Design	Risk-of-Bias Tool (Domains)	Reviewers & Unit of Judgment	Output Artifact	GRADE Starting Level	Pooling Rule	Notes/Guardrails
Randomized controlled trials (RCTs)	RoB 2 — randomization; deviations from intended interventions; missing outcome data; outcome measurement; selection of reported result	Two independent reviewers; third-party adjudication; per outcome	RoB 2 traffic-light table (per outcome/study)	High (rate down as needed)	Meta-analysis if ≥2 clinically similar RCTs; random-effects by default	Pre-specify primary timepoint for "cure/resolution"; handle multi-arm trials via relevant contrasts only
Nonrandomized comparative (cohort, CBA, etc.)	ROBINS-I — confounding; selection; classification of interventions; deviations; missing data; outcome measurement; selection of reported results	Two independent; third-party adjudication; per outcome	ROBINS-I domain-justifications table	Low (rate down/up as appropriate)	Pool only if confounding addressed and clinical/methodological homogeneity acceptable	Pre-specify key confounders: infant age, granuloma size/characteristics, prior treatment, setting
Observational cohorts with limited confounder control	Newcastle–Ottawa Scale (NOS) — selection; comparability; outcome	Two independent; study-level	NOS star table	Low	No quantitative pooling unless designs comparable and risk acceptable; otherwise narrative	Use primarily for feasibility and harms signals
Case reports / case series	CARE checklist — reporting quality	Two independent; study-level	CARE checklist summary	Very low	Do not pool; narrative (ranges/medians) only	Avoid causal language; use for context and adverse events only

Table 3 | Disease coexisting with umbilical granuloma

Condition	Key Features	Role of Imaging	Management/Referral
Umbilical Polyp	Bright-red, firm nodule; ectopic intestinal/urinary mucosa; does not regress with salt or silver nitrate.	Not routinely required unless lesion is atypical.	Surgical excision.
Patent Omphalomesenteric (Vitellointestinal) Duct	Persistent feculent or bilious discharge from umbilicus.	Ultrasonography may reveal communication with ileum.	Surgical referral required.
Urachal Anomalies (patent urachus, sinus, cyst)	Urinary discharge at umbilicus or infra-umbilical swelling.	Ultrasound first-line; MRI/CT if diagnosis remains uncertain.	Pediatric surgical evaluation.
Omphalitis	Erythema, swelling, tenderness, purulent discharge; may have systemic signs.	Routine imaging not required unless abscess suspected.	Medical emergency: start antibiotics; surgical drainage if abscess.

Table 4 | Pragmatic management algorithm for umbilical granuloma

Decision Node	Key Criteria	Action (Clinic vs. Home)	Escalate/Refer When…	Follow-up & Monitoring
1) Initial triage	Typical UG: soft, moist, pink-red nodule (~1–10 mm), serous ooze. Concern: feculent/bilious discharge (OMD), urine leak/infra-umbilical swelling (urachal), firm bright-red deep nodule (polyp), omphalitis (erythema, fever, purulence).	If typical & well infant ⇢ proceed. Any red flag ⇢ clinic evaluation; avoid cautery.	Red-flag discharge, systemic signs, deep/atypical mass.	N/A at this step.
2) Choose setting	Home: classic ≤3 mm, sessile, no infection, reliable caregivers. Clinic: >3 mm, pedunculated, friable/bleeding, dermatitis, prematurity, prior failure, or diagnostic doubt.	Home = table salt protocol. Clinic = $AgNO_3$ or topical steroid.	Uncertain diagnosis or unreliable caregivers.	N/A at decision step.
3) Home management (NaCl)	Classic ≤3 mm; no concern.	Clean/dry ⇢ protect perilesional skin (petroleum jelly) ⇢ small pinch NaCl to cover ⇢ occlude 30 min ⇢ wipe off; BID for 3–5 days (max 2 cycles).	No flattening/dryness after ≤1 week; worsening ooze/bleed; irritation/infection.	Tele/photo day 3–4; in-person 1–2 wk. Stop if erosions/irritation.
4) Clinic first-line	Larger/atypical but likely UG; no infection.	$AgNO_3$ 75% stick: dry lesion, petroleum-jelly ring, minimal touch; repeat weekly ×1–3.	No response after 2–3 sessions; significant bleed; suspected tract.	Review 7–10 days after each session. Watch for chemical burns; irrigate spills with saline.
5) Clinic alternative	Avoiding caustics or $AgNO_3$ unavailable.	Topical corticosteroid (e.g., betamethasone/clobetasol) BID 2–3 wk.	No response by 2–3 wk; atrophy/telangiectasia.	Recheck 2–3 wk; stop if atrophy/irritation.
6) Selective options	Pedunculated stalk; refractory; center preference.	Double-ligature for pedunculated; electrocautery/cryotherapy for refractory; $CuSO_4$ clinician-only (burn risk).	Persistent/recurrent lesion; diagnostic uncertainty.	Standard wound care; check 1–2 wk.
7) Imaging / referral	Suspicion of tract/remnant or atypical/deep lesion.	Ultrasound ± Doppler for urachal/OMD remnant; surgical referral if positive/suspected.	Any positive imaging or persistent red-flag discharge.	As per surgical plan; ensure infection surveillance.
8) Omphalitis pathway	Erythema, warmth, tenderness, fever, purulence.	Avoid cautery. Start antibiotics per protocol; consider admission if systemic signs.	No improvement in 24–48 h; systemic illness.	Close clinical review within 24–48 h.
9) Caregiver instructions	Applies to all pathways.	Keep area dry; fold diaper down; avoid rubbing. Return for fever, spreading redness, malodor/pus, bleeding, or no improvement.	Any red-flag symptom as above.	Provide written safety-net; document caregiver teaching.

its development. After the completion of the gestation period and removal and clamping of the cord, Umbilical cord separation has been suggested to get underway with thrombosis and constriction of the umbilical vessels followed by other events such as collagenous degeneration, granulocyte and phagocyte-mediated necrosis, and cord tissue infraction (Table 2). By the second or third week after birth, the stump has already begun to dry out, shrink, and separate from the rest of the body. There is no such specific time duration that has been marked out for delayed cord separation, perhaps cord separation beyond three weeks considered is extremely delayed. There are several possible reasons for delayed cord separation such as cesarean route delivery, systemic antibiotics use, infections, prematurity and low birth weight, leukocyte adhesion deficiency, urachal remnants, and topically applied anti-microbial agents. This delay in detachment leads to cord infection due to bacterial growth and that is further responsible for the neonate's morbidity and mortality. Sometimes it is not necessary that delayed cord separation always ends up with the infection. Granulation tissue may remain as a tiny mass at the base after cord separation. The tissue, which ranges in size from 1 mm to 10 mm and is typically a pale pink color, is made up of fibroblasts and capillaries. Due to their excessive size, they can easily see through the naked size, and they release odorless discharge. Its assessment can also be performed through an optical magnifier. Whilst small sessile umbilical granuloma can diagnose through an otoscope. An umbilical granuloma is suspected if there is persistent serous or serosanguinous discharge at the umbilicus. The appearance of craggy umbilical stump, periumbilical erythema, purulent drainage, and discoloration in umbilical and near surrounding tissues indication of an infection called omphalitis (Table 3). The most common microbes are *Staphylococcus aureus*, Escherichia coli, clostridium, klebsiella, etc.

Treatments and Clinical Corroborations

There are numerous treatments available for umbilical granuloma, but lack of scientific and clinical evidence hinders its treatment avenue. The first line treatment is silver nitrate application and the next options are salt application, topical antibiotics and steroids, and topical antiseptics, in addition, granuloma excision requires a surgical procedure. These options are being sought due to these factors: I) certain cases of silver nitrate application not working; II) the need for a medical practitioner to apply it; and III) the potential for a periumbilical burn with chemical cauterization IV) New-born surgeries raise anxiety among parents.[12–16]

Topical Therapies

There are various topical therapies have been reported in the treatment of umbilical granuloma such as salt treatment, topical corticosteroids, silver nitrate, and topical antibiotics. Topical corticosteroids have great potential in the treatment of dermatological diseases that have depicted symptoms like hyperproliferation, inflammation, and immunological responses. These diseases are psoriasis, atopic dermatitis, lichen sclerosis, phimosis, eczema, and many more.[17,18] The administration of topical corticosteroids also depends upon the type of delivery vehicle used and in addition, vehicle selection criteria depend upon the affected site and lesion morphology.[19]

Corticosteroids Therapy

Corticosteroids have the potential to suppress the proliferation of keratinocytes and fibroblasts followed by a deleterious effect on inflammatory cell survival, development, and immunological function.[20] designed multicenter randomized controlled trials to evaluate the efficacy impression in umbilical granuloma-suffered neonates with 0.05% betamethasone valerate ointment and silver nitrate cauterization respectively.[21] The 207 neonates with umbilical granuloma were assigned to 18 hospitals followed by 2 clinics in Japan under the time period of three years from 2013 to 2016. The 20% of silver nitrate treatment once a week was given to 104 patients whilst the remaining 100 patients received the topical steroids ointment twice a day. The parents were advised and informed about some side effects such as local infection, itching, pigmentation, stinging, and for avoiding occlusive dressings and normal baths for 24 h in both treatment groups. It was found that both the treatment groups exhibited almost similar types of healing responses within 3 weeks. The topical steroid ointment and silver nitrate received groups depicted 91% and 90.4% respectively. Furthermore, topical steroid treatment was suggested as feasible, cost-effective, and safe in comparison to silver nitrate treatment. The long-run use of topical corticosteroids leads to the side effects such as bacterial infections, skin atrophy, and paradoxical inflammatory responses but treatment for neonatal umbilical granuloma often lasts no longer than a month, thus this is not a major worry. The less cost and high effectiveness of silver nitrate credits point to their account but its iatrogenic periumbilical burns are still reported followed by medical staff and parent's concerns.[21]

In another randomized study, three different treatments were given to 109 patients that have been divided into three different groups. The first group has 32 patients who received 99% silver nitrate topical treatment and the second group has 33 patients that received clobetasol propionate 0.05% and the last group has 44 patients who were treated with ethanol wipes. It was found that silver nitrate and topical steroid-treated groups exhibited better healing results compared to ethanol wipes-treated group. The silver nitrate and clobetasol propionate treated groups depicted identical healing time and resolution rates. It was concluded that clobetasol propionate treatment can be done at home and silver nitrate treatment at the clinic efficiently in the umbilical granuloma (Table 4).[22]

Silver Nitrate Therapy

Silver nitrate is preferred as the first-line conventional treatment option because of its antiseptic property

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followed by astringent effects. Silver nitrate-based pencil-like preparations should be applied to the lesion carefully to prevent chemical burns on the nearby skin. As a result, for chemical cauterization, sticks or Q tip applicators made of 75% silver nitrate and 25% potassium nitrate (HemoStop™, Bray™, Grafco™, etc.) should be selected. The umbilical area should be washed with an antiseptic solution and wiped with a sterile sponge prior to applying silver nitrate. In addition, extra care needs to be taken while applying the applicator to the granulation tissue. But it also made negative impressions on healthy tissues such as chemical burns and as well as it also required a specialist and the high cost hinders its treatment roadmap.[23–26]

Salt Therapy

In 1972, Schmitt reported the first example of salt being used to treat umbilical granuloma, and in 1983, Kesaree provided additional details on the procedure. Salt has a remarkable effect on the umbilical granuloma's tissues. The high amount of sodium causes granulation tissue to dry out and die off because they attract and absorb water from the cells. Even, this treatment approach does not cause any effect on the normal tissues and is even cheap compared to other available treatments followed by ease of application and rapid resolution,[27,28] recruited 17 infants of 1–4 months aged who were suffering from umbilical granuloma.[9] They applied common and covered it with occlusive tape after clearing the administration site and taking follow-up for 24 h. After the removal of the occlusive tape, the size of the granuloma tissues was analyzed. It was found that granuloma size was alleviated in all 17 infants. In addition, the shrunken tissues were easily cleaned without leaving any residue, and there was no recurrence in the three-month follow-up period (Figure 2).

Fig 2 | (A) Umbilical granuloma (B) Alleviation of granuloma after salt treatment[33] data derive from published sources

The compared clinical trials study was performed by using copper sulphate and common salt therapies among 84 infants in the age group of 2 weeks– 4 months who were suffering from umbilical granuloma. These 84 infants were divided into two groups, the first group of 40 infants was treated with salt therapy twice a day for continuously three days, and another group of 44 infants was treated with copper sulphate once a day for 10 minutes under authorized personnel from the outpatient clinic department. It was revealed that the copper sulphate-treated group exhibited a 95.5 % cure rate whilst the salt-treated group depicted a 55 % cure rate at the end of the first week. In addition, 8 infants did not show any response from the salt therapy treated group at the end of the third week. Overall, it was concluded that copper sulphate has remarkable properties in the treatment of umbilical granuloma with no side effects or relapse in comparison to salt treatment therapy.[29] In another clinical study, 60 umbilical granuloma-suffering patients were recruited aged between 2 weeks to 4 months. They used the lottery method and bifurcated 60 infants into two groups. Group A has 30 infants and was treated with copper sulphate and Group B of 30 infants received salt therapy twice a day for consecutive three days. It was found that the copper sulphate treatment received group depicted an excellent healing process with a 100 % cure rate whilst a 53.3% cure rate was observed in the salt therapy.[30–32] A case report of an 18-day-old female infant with a yellowish discharge after cord separation was presented in the outpatient department of an Ethiopia-based hospital. The patient returns after five days with purulent discharge from a two-day umbilical swelling but no other complaints. The medical experts cleaned the administration site and applied cooking salt twice a day to the entire lesions and a gauze dressing was applied to the region and maintained in place for 30 minutes every time. After three times salt therapy was applied, the granuloma's color improved and its size decreased, and no recurrence was seen throughout the three months of follow-up.

Conducted a multicenter randomized controlled trial at three different units to compare the effects of copper sulphate and table salt (NaCl) on 64 umbilical granuloma suffering subjects.[34] The 31 infants received salt therapy twice a day for five days in a row while 33 received copper sulphate treatment by experts. The results revealed that salt therapy exhibited

a 90% completed healing rate whilst $CuSO_4$ depicted a 69.7% healing rate. Overall, salt therapy is effective, readily available, cheap, and safe compared to copper sulphate therapy.[34,35] The randomized and controlled clinical studies were performed with the envisaged to measure the influence of salt in comparison to clobetasol propionate on umbilical granuloma infants. They recruited 50 umbilical granuloma infants and bifurcated them into two groups, Group A treated received salt therapy while Group B received clobetasol propionate therapy. There was a statistically significant discrepancy between groups A (98.80 ± 4.4) and B (70.4 ± 33.1) after one week of treatment, nevertheless, after three weeks there was no longer a significant difference found in both groups (Group A 100.00 versus Group B 92 ± 27.7). Overall, investigators found that salt therapy was a successful, low-cost, and complication-free option for treating umbilical granulomas. In a retrospective study, 36 infants who were suffering from umbilical granuloma and treated with common salt twice a day for three days continuously. It was found that 96% of cases healed completely after three treatment cycles without any side effects.[36]

After getting salt therapy twice a day for a period of six days in a row, found that 69 out of 76 patients who were suffering from umbilical granuloma displayed a remarkable rate of healing. Janyoungsak[37] and Alatwani[38] designed a randomized, double-blind, and comparative study to determine the effect of 3% and 30% NaCl solution in umbilical granuloma patients. They used stratified block-of-four randomization techniques to divide 100 subjects into two groups. One group has 48 patients with a granuloma size range < 3mm in those 16 patients received 3% NaCl and 32 patients received 30% NaCl solution. Whilst another group has 66 patients with a granuloma size range ≥ 3mm in those 32 patients received 3% NaCl and 34 patients received 30% NaCl solution. The therapy was given three times a day for 2 weeks continuously and if no response was observed further silver nitrate was used as a treatment option. The patients with a granuloma size range of < 3 mm showed a 100% healing rate and patients with a granuloma ≥3 mm size range depicted 90.6 % effectiveness on receiving 3% NaCl and 97.1% at 30% NaCl solution. In addition, parents have not been reported any adverse events and also convinced of treatment efficacy. Another prospective study was designed and enrolled 32 subjects aged between 15 to 27 days and treated with half a teaspoon salt and a full teaspoon delivery mode from 1 to 7 days. All the patients were found with no lesions in both modes of delivery with no recurrence after a one-month follow-up.[39]

Antibiotics Therapy

It has been reported that antibiotics like doxycycline and tetracycline have been found effective in umbilical granuloma treatment due to their anti-bacterial, anti-inflammatory, and hyperosmotic dehydration properties. In this regard,[40] designed clinical examinations on 84 infants and divided them randomly into two groups, the inpatient group has 24 subjects and the outpatient group has 40 subjects aged between 28 days to 129 days. Both groups received topical doxycycline once a day for 5 days in a row. The lesion was found shrunken, turned into dark color in dried form, and removed easily in one-time application in 22 patients, and one patient showed similar results after two applications followed by one patient undergo for surgery. Simultaneously in the outpatient group with a single application, 47 people were healed completely whilst 13 patients required a second topical application in that 9 patients were cured completely and 4 patients underwent lesion removal surgery. Hence, doxycycline therapy was found safe with no adverse events and recurrence even after 3 to 13 months of follow-up (Table 5).[41]

Ligation and Surgical Excision

There some umbilical granulomas hard to remove and treat due to their growing site at the umbilical pit. To overcome the side effects such as burning issues after silver nitrate application and no therapeutic response from salt therapy, the double-ligating method has been used in that 3–0 and 4–0 silk sutures used for the ligation. The superficial hold ligature is positioned in the first step of the double-ligature surgery to stabilize the granuloma. A more accurate and deeper ligation must be applied at the lesion's base during the second step. Similar to the original umbilical cord remnant, the granuloma turns necrotic and falls off in 7–14 days. Bleeding is one of the major concerns during this process because of the deep, large, and friable lesions.[12,25]

Designed a prospective study in that 105 umbilical granuloma and umbilical polyps suffering infants have recruited and divided into groups by chit method. Group A has 70 patients treated with surgical excision and Group B has 35 received the silver nitrate cauterization therapy.[41] The 100% successfully completed alleviation was found in Group A whilst a 57.14% and 34.29% healing response was observed after the first treatment and second treatment attempts respectively. For the unresponsive patients, a surgical excision technique was performed. In addition, only 4 patients depicted minimal perilesional burn in Group B, and no postoperative complications were observed in Group A with no recurrence even after 6 months of follow-up. Overall, it was concluded that silver nitrate should be preferred as a first-line treatment option in umbilical granuloma and umbilical polyps perhaps surgery excision is the treatment of choice.[41,42]

In the case of large granulomas, surgical excision has been recommended to be performed for the granuloma removal. Even, dual therapy such as chemical cauterization and surgical excision can be the treatment of choice pragmatically in wide root granulomas. Apart from surgical excision, electrocautery and cryotherapy have been used perhaps their limitations such as skin discoloration and clinical requirements hinder their uses.[42,25] In a clinical study, 50 infants were enlisted and split into two groups equally, respectively. There are a total of 25 infants in each group; the first set received salt therapy, while the second set had

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Table 5 | Level of evidence (Oxford CEBM 2011)

Therapy	Protocol	Sample Size & Design	Resolution Time	Adverse Events	Follow-up	Level of Evidence*	Treatment Feasibility
Salt (NaCl)	Table salt applied locally, 2×/day for 3–5 days	RCTs (31–60 infants); cohort studies (36–76 infants); case reports	Cure rates 90–100% in RCTs (Chung 2022; Janyoungsak 2022); ~96% in observational studies	Minimal; no recurrence, no reported burns	1–3 months	Level 1–2 (high in RCTs; moderate in cohorts)	Cheap, safe, can be applied at home, good caregiver acceptance
Silver Nitrate	75% silver nitrate sticks, clinic application once weekly	RCTs (100–207 infants); prospective studies	Cure rates ~90–95% (Ogawa 2018); similar to corticosteroids	Chemical burns reported (iatrogenic periumbilical burns); requires clinical expertise	2–6 weeks	Level 1 (multiple RCTs)	Standard first-line in hospitals; requires trained personnel; cost moderate
Corticosteroids (e.g., 0.05% betamethasone, clobetasol)	Ointment applied 2×/day for 2–3 weeks	RCTs (100–109 infants); prospective studies	Resolution ~91% (Ogawa 2018); comparable to silver nitrate; home use feasible (Brødsgaard 2015)	Local irritation, rare infection, atrophy (not significant in short neonatal use)	2–3 weeks	Level 1 (well-designed RCTs)	Cost-effective, safe for short use; practical for home treatment
Antibiotics (topical doxycycline/ tetracycline)	Applied once daily for 5 days	Case series (84 infants)	~95% resolution; recurrence rare	No adverse events reported	3–13 months	Level 3–4 (case series; no RCTs)	Evidence limited; may be useful where infection suspected
Copper sulphate	Applied once daily for 5–10 minutes under medical supervision	RCTs (30–44 infants); comparative studies	Cure rates 95–100% (Annapurna 2015; Fiaz 2017); some studies show lower than salt	No major side effects reported	2–3 weeks	Level 2 (small RCTs, limited replication)	Effective, but regulatory/safety concerns in some regions
Surgery/Ligation/ Electrocautery	Double ligature, excision, or cautery; clinic procedure	Prospective studies (50–105 infants)	Cure rates 96–100%	Bleeding risk (ligation), perilesional burns (cautery); requires anesthesia/specialist	3–6 months	Level 2 (prospective cohorts; not randomized)	Definitive; reserved for refractory or large lesions

- Level 1 = High-quality RCTs
- Level 2 = Low-quality RCTs / cohort studies
- Level 3 = Case–control studies
- Level 4 = Case series
- Level 5 = Expert opinion

Table 6 | Summary of the results

Study	Design	Tool	Included in Meta-Analysis	GRADE (level)	Outcome	Results
Ogawa, 2018 (PLOS One)	RCT (silver nitrate vs topical steroid)	RoB 2	Yes (if combined with other RCTs on comparable outcomes/timepoints)	High	Complete resolution by prespecified time	Multicentre; outcome-level RoB 2
Brødsgaard, 2015 (Acta Paediatr)	RCT (clobetasol vs silver nitrate)	RoB 2	Yes (if outcomes align)	High	Complete resolution	Ensure consistent definition of "cure"
Chung, 2022 (J Pediatr Surg)	RCT (salt vs copper sulfate; pilot)	RoB 2	Yes (with other salt vs $CuSO_4$ or similar)	High	Cure at 1–3 weeks	Pilot sample size; check imprecision in GRADE
Janyoungsak, 2022 (J Paediatr Child Health)	RCT (3% vs 30% NaCl)	RoB 2	Yes (salt concentration subgroup)	High	Cure/time-to-resolution	Blinding and allocation details drive RoB 2
Abdoufatouh, 2021 (Eur J Pediatr Dermatol)	Nonrandomized comparative (salt vs clobetasol)	ROBINS-I (or NOS if minimal adjustment)	Possibly (sensitivity only)	Low	Cure	Likely confounding → rate down
Annapurna, 2015 (JEMDS)	Nonrandomized comparative ($CuSO_4$ vs salt)	ROBINS-I/NOS	No in primary; sensitivity narrative	Low	Cure	Journal quality concerns; treat cautiously
Fiaz, 2017 (JMSCR)	Nonrandomized comparative ($CuSO_4$ vs salt)	ROBINS-I/NOS	No in primary; sensitivity narrative	Low	Cure	Potential predatory outlet; verify data integrity
Badebarin, 2018 (Iran J Pediatr Surg)	Nonrandomized comparative (salt vs surgery)	ROBINS-I	No (clinical heterogeneity)	Low	Cure/recurrence	Different intervention class; narrate only
Gupta, 2022 (Saudi J Health Sci)	Nonrandomized comparative (silver nitrate vs surgery)	ROBINS-I	No (heterogeneity)	Low	Cure/recurrence	Regional journal; check follow-up adequacy
Wang, 2015 (Global Pediatr Health)	Single-arm cohort (topical doxycycline)	NOS (limited); CARE elements for reporting	No	Very low (starts Low; rate down for indirectness)	Cure	Use for harms/feasibility only
Singh A., 2021 (Afr J Paediatr Surg)	Case series (salt)	CARE	No	Very low	Cure	Narrative summary only
Sthapak, 2020 (JCDR)	Case series (salt)	CARE	No	Very low	Cure	Narrative only
Alatwani, 2021 (IJMSCR)	Case series (salt; prospective)	CARE	No	Very low	Cure	Low-tier outlet; caution
Hossain, 2010 (Bangladesh J Child Health)	Case series (salt)	CARE	No	Very low	Cure	Historical context
Jois & Rao, 2021 (Aust J Gen Pract)	Systematic review of RCTs	— (not an included primary study)	—	—	—	Use to cross-check trial identification
Namba, 2023 (BMJ Open)	Protocol (SR/MA RCTs)	—	—	—	—	Not a primary study; informs methods

surgical electrocauterization. While those who underwent surgery had a 100% success rate in terms of healing their condition, those who underwent salt therapy had a 96% success rate. Neither group, however, experienced a recurrence of the disease throughout the three-month follow-up period.[42]

Result

The results are summarized in Table 6.

Conclusion

Numerous treatment options have been discussed and are available for umbilical granuloma with clinical corroborations. Topical salt therapy is one of the most preferred first-line treatment options due to its safe efficacy and cost-effectiveness. It has a tendency to absorb the water from the affected cells and does not harm normal cells. In many clinical studies, salt therapy has given remarkable results at different concentrations in a less period of time with respect to doses. In addition, salt therapy has been documented for exhibiting a better healing rate than Copper sulphate. Due to its astringent and antiseptic properties, silver nitrate is preferred as a first-line treatment option followed by salt therapy but may burns baby's tender skin. If they are used, should be used in presence by clinician themselves. However, chemical cauterization causes normal skin burning with discomfort and required clinical expertise. Some topical antibiotics such as doxycycline and tetracycline were found effective due to their anti-bacterial and anti-inflammatory activities in a clinical trial. Even, though some corticosteroids have effectiveness in umbilical granuloma but some side effects such as atrophy, hypopigmentation, and paradoxical inflammatory responses require more research shreds of evidence among the large population. And in the last, when no treatment option is working then surgery is the last option that needs to be made through laparotomy. However, correct identification and diagnosis of umbilical granuloma are necessary without delay in infants to alleviate the associated complications.

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