Topical Chemotherapy in Cutaneous T-cell Lymphoma

Positive Results of a Randomized, Controlled, Multicenter Trial Testing the Efficacy and Safety of a Novel Mechloretamine, 0.02%, Gel in Mycosis Fungoides

Stuart R. Lessin, MD; Madeleine Duvic, MD; Joan Guitart, MD; Amit G. Pandya, MD; Bruce E. Strober, MD, PhD; Elise A. Olsen, MD; Christopher M. Hull, MD; Elizabeth H. Knobler, MD; Alain H. Rook, MD; Ellen J. Kim, MD; Stuart R. Lessin, MD; Madeleine Duvic, MD; Joan Guitart, MD; Amit G. Pandya, MD; Bruce E. Strober, MD, PhD; Uma Sundram, MD; Hong Wu, MD, PhD; Youn H. Kim, MD

Objective: To evaluate the efficacy and safety of a novel mechloretamine hydrochloride, 0.02%, gel in mycosis fungoides.

Design: Randomized, controlled, observer-blinded, multicenter trial comparing mechloretamine, 0.02%, gel with mechloretamine, 0.02%, compounded ointment. Mechloretamine was applied once daily for up to 12 months. Tumor response and adverse events were assessed every month between months 1 and 6 and every 2 months between months 7 and 12. Serum drug levels were evaluated in a subset of patients.

Setting: Academic medical or cancer centers.

Patients: In total, 260 patients with stage IA to IIA mycosis fungoides who had not used topical mechloretamine within 2 years and were naive to prior use of topical carmustine therapy.

Main Outcome Measures: Response rates of all the patients based on a primary clinical end point (Composite Assessment of Index Lesion Severity) and secondary clinical end points (Modified Severity-Weighted Assessment Tool and time-to-response analyses).

Results: Response rates for mechloretamine gel vs ointment were 58.5% vs 47.7% by the Composite Assessment of Index Lesion Severity and 46.9% vs 46.2% by the Modified Severity-Weighted Assessment Tool. By the Composite Assessment of Index Lesion Severity, the ratio of gel response rate to ointment response rate was 1.23 (95% CI, 0.97-1.55), which met the prespecified criterion for noninferiority. Time-to-response analyses demonstrated superiority of mechloretamine gel to ointment (P < .01). No drug-related serious adverse events were seen. Approximately 20.3% of enrolled patients in the gel treatment arm and 17.3% of enrolled patients in the ointment treatment arm withdrew because of drug-related skin irritation. No systemic absorption of the study medication was detected.

Conclusion: The use of a novel mechloretamine, 0.02%, gel in the treatment of patients with mycosis fungoides is effective and safe.

Trial Registration: clinicaltrials.gov Identifier: NCT00168064


Mechloretamine (methyl-bis[2-chloroethyl]amine) hydrochloride, commonly known as nitrogen mustard, is an alkylating agent. First reported in 1946 to be active in lymphoid malignant neoplasms, mechloretamine was the first systemic chemotherapy agent to be approved in the United States for the treatment of Hodgkin disease, lymphosarcoma, chronic myelocytic or lymphocytic leukemia, polycythemia vera, bronchogenic carcinoma, and mycosis fungoides (MF), the most common type of cutaneous T-cell lymphoma (CTCL). Successful use of mechloretamine as a topical agent in the treatment of MF-CTCL was first reported in the late 1950s and provided a rationale for skin-directed chemotherapy that minimized systemic toxic effects. Initially, lyophilized mechloretamine was dissolved into water and painted onto the skin. Application of aqueous solutions was complicated by high rates (≥67%) of delayed-type cutaneous hypersensitivity, often limiting its prolonged use.
Subsequently, mechlorethamine was compounded into petrolatum-based ointments, which resulted in lower and tolerable rates of delayed-type cutaneous hypersensitivity (≤10%).

Large, uncontrolled case series have documented the efficacy and safety of mechlorethamine formulations in the treatment of MF-CTCL, with overall response rates of 63% to 83% (in clinical stages I-III). Complete responses to topical mechlorethamine in early-stage (stage IA) MF-CTCL are associated with a lower risk of disease progression. As such, topical mechlorethamine is considered a primary therapy for MF-CTCL in treatment guidelines.

Despite the well-documented clinical experience with topical mechlorethamine treatment of MF-CTCL, no topical mechlorethamine formulation has been approved by the US Food and Drug Administration. This has become problematic for physicians and patients for several reasons. Pharmacy-compounded mechlorethamine formulations are not subject to rigorous quality assurance, such as evaluations of potency and stability. Furthermore, most health insurance formularies rarely include compounded medicines or those without Food and Drug Administration approval. In addition, petrolatum-based ointments may often be difficult to apply to the skin, are esthetically unappealing, and can compromise patient compliance. To address these needs, a randomized, controlled, observer-blinded, multicenter trial was conducted to evaluate the efficacy and safety of a novel mechlorethamine, 0.02%, gel (hereafter gel) vs mechlorethamine, 0.02%, compounded ointment (hereafter ointment) in MF.

PATIENT ELIGIBILITY

Established patients with MF-CTCL having persistent or recurrent stage IA, IB, or IIA disease and no history of progression beyond T2N1M0B0 (stage IIA) with at least 1 prior treatment were eligible for the study. Patients previously treated with topical carmustine were excluded, as were patients treated with topical mechlorethamine within 2 years or with radiation therapy (local or total body) within 1 year. A skin biopsy specimen of a representative lesion, obtained within 90 days before study initiation and after a 4-week washout period of treatments directed at the disease, was deemed diagnostic of MF-CTCL using the histologic criteria previously used in clinical trials for MF and incorporating a diagnostic algorithm for defining early MF-CTCL. Patients with histologic variants, folliculotropic or syringotropic MF, or large-cell transformation (LCT) were eligible. Participants were free of concurrent illness or infection, met laboratory inclusion criteria, and had completed an adequate washout of MF-CTCL therapies for 4 weeks before the start of the trial. Male and female study patients were required to use contraception during the trial, and women could not be pregnant or breastfeeding. Institutional review board approval of the clinical trial, and women could not be pregnant or breastfeeding. Male and female study patients were required to use contraception during the trial. Male and female study patients were required to use contraception during the trial.

STUDY DESIGN

This study was a randomized, controlled, observer-blinded, multicenter trial involving 13 academic medical or cancer centers in the United States and was registered as a pivotal phase 2 trial (clinicaltrials.gov Identifier: NCT00168064). Patients were randomized to receive mechlorethamine hydrochloride, 0.02%, gel or ointment. The gel was manufactured under US Food and Drug Administration–approved good manufacturing practice guidelines and was formulated to enhance the ease of application to the skin. The comparator ointment was compounded into a petrolatum-based vehicle as previously described. Mechlorethamine was applied once daily to specific lesions or to the total skin surface (depending on the T classification) for up to 12 months. If new lesions appeared in untreated areas, as is common with the initiation of topical mechlorethamine therapy, patients were converted from spot treatment to regional or whole-body treatment. A temporary reduction in daily application frequency (every other day or less frequently) was permitted for skin adverse events (AEs). Tumor response and AEs were assessed (by observers S.R.L., M.D., J.G., A.G.P., B.E.S., E.A.O., C.M.H., E.H.K., A.H.R., E.J.K., M.F.N., D.M.A., A.B.K., G.S.W., and Y.H.K.) blinded to treatment type) every month between months 1 and 6 and every 2 months between months 7 and 12. The target enrollment of 260 patients was achieved in the study.

RESPONSE CRITERIA

The primary efficacy end point was the Composite Assessment of Index Lesion Severity (CAILS). Up to 5 index lesions were identified at baseline and were assessed throughout the study in all the patients. Because the study also included regional and total skin surface applications, the Modified Severity-Weighted Assessment Tool (mSWAT) was used as a secondary efficacy end point in all the patients. A determination of the percentage involvement of total body surface area and, if applicable, an assessment of clinically abnormal lymph nodes (≥1.5 cm in diameter) were completed at baseline and throughout the 12-month study. The CAILS and mSWAT scores were calculated at baseline (day 1), and at each study visit the tumor response was determined using standard oncology criteria for complete response (100% improvement, with a score of 0), partial response (50% to <100% reduction from the baseline score), and stable disease (<50% reduction from the baseline score). Confirmed responses were those observed for at least 4 weeks. A patient was considered to have progressive disease if his or her CAILS score was at least 25% above the baseline score. Because the appearance of new lesions is common with the initiation of topical mechlorethamine application, investigators’ S.R.L., M.D., J.G., A.G.P., B.E.S., E.A.O., C.M.H., E.H.K., A.H.R., E.J.K., M.F.N., D.M.A., A.B.K., G.S.W., and Y.H.K. discretion and patient best interest determined if a patient was withdrawn from the study when progressive disease was documented. Duration of response was defined in the clinical trial protocol as the time from the first appearance of a confirmed response to the first assessment at which loss of response (<50% improvement from the baseline CAILS score) or progressive disease was documented. An additional definition for loss of response, an increase in CAILS score greater than the sum of the lowest CAILS score (nadir) plus 50% baseline CAILS score, was used based on consensus guidelines recommendations. As with progressive disease, investigator discretion and patient best interest determined if a patient was withdrawn from the study when loss of response was documented.

SAFETY EVALUATION

Standard laboratory blood tests (chemistries and complete blood cell count with differential cell count), physical examinations, and AE monitoring were used to evaluate patient safety. Toxic...
effects were evaluated and graded according to the National Cancer Institute Common Toxicity Criteria of Adverse Events, version 3.0. Adverse events were recorded and classified by standardized Medical Dictionary for Regulatory Activities query and Medical Dictionary for Regulatory Activities preferred terms. Systemic absorption of mechlorethamine was measured with a high-performance liquid chromatography serum assay from a subset of patients who agreed to have blood levels evaluated on day 1 (0, 1, 3, and 6 hours after application) and at 4 weeks. Treatment-limiting AEs were defined as grade 3 or 4 local dermal irritation (on a 4-point scale per protocol and by the National Cancer Institute Common Toxicity Criteria of Adverse Events) that did not resolve to grade 2 or lower within 2 weeks off the study drug. Grade 3 or 4 local dermal irritation associated with a positive patch was considered allergic contact dermatitis; other manifestations were considered irritant contact dermatitis. For grade 3 or 4 local dermal irritation, treatment frequency was suspended or reduced for up to a maximum of 4 weeks and was resumed after irritation improved to grade 2 or lower. Therapy for skin irritation included topical emollients and systemic antihistamines, but the use of topical or systemic corticosteroids was prohibited. Patients with positive–patch test results (allergic contact dermatitis) associated with grade 3 or 4 rashes were withdrawn from the study. Patients were evaluated for the development of squamous cell carcinomas of the skin for an additional 12 months after treatment.

STATISTICAL ANALYSIS

A noninferiority statistical end point was chosen to show that a novel mechlorethamine gel formulation is statistically (and clinically) not inferior to a pharmacy-compounded mechlorethamine ointment given that their performance would be expected to be similar. All the randomized patients were included in the intent-to-treat (ITT) population and were evaluated by CAILS as the primary efficacy end point. All the patients who were treated for at least 6 months were included in the protocol-defined efficacy-evaluable (EE) population. The safety population included all the patients who used any study medication. Noninferiority of gel to ointment was established if the lower bound of the 95% CI around the ratio of the response rate (complete response plus partial response for gel or ointment) was at least 0.75. The Kaplan-Meier method was used to calculate the time to first confirmed response and the duration of response curves. Treatment arms were compared using a log-rank statistic.

RESULTS

PATIENT CHARACTERISTICS

Figure 1 shows the flow of patients assessed, enrolled, randomized, and followed up throughout the trial. Table 1 gives the baseline characteristics of all 260 patients enrolled and summarizes the similarities between the 2 treatment arms. Overall, 59.2% of patients were male, and 40.8% were female; 74.2% were of white race/ethnicity, 13.3% were African American, and 12.3% were of other races/ethnicities. The median age was 58 (range, 11-88) years. Overall, 54.2% of patients had stage I disease at baseline (58.5% in the gel treatment arm and 50.0% in the ointment treatment arm), and 44.2% of patients had stage IB disease at baseline (40.0% in the gel arm and 48.5% in the ointment arm). Two patients in each treatment arm had stage IIA disease at baseline. The median number of prior treatments was 2 (range, 1-12).

EFFICACY

The CAILS treatment response rates are summarized in Table 2. In the ITT population, the confirmed response rate (complete response plus partial response) was higher for the gel treatment arm (58.5%) than for the ointment treatment arm (47.7%). By the CAILS, the ratio of gel response rate to ointment response rate was 1.23 (95% CI, 0.97-1.55), which met the prespecified criterion for noninferiority (Figure 2). In the EE population, a confirmed CAILS treatment response was achieved in 76.7% of patients in the gel arm vs 58.9% of patients in the ointment arm (ratio of gel response rate to ointment response rate, 1.30; 95% CI, 1.06-1.61) (P = .01) (Figure 2).

Subset analysis by strata revealed a relative balance between 141 patients in stratum 1 (stage IA) and 119 patients in stratum 2 (stage IB or IIA). Stratum 1 patients...
demonstrated a 59.2% overall CAILS treatment response rate (among the ITT population) in the gel treatment arm vs 40.0% in the ointment treatment arm (ratio of gel response rate to ointment response rate, 1.48; 95% CI, 1.05-2.14). Stratum 2 patients showed a 57.4% overall CAILS treatment response rate for the gel arm vs 40.0% in the ointment treatment arm (ratio of gel response rate to ointment response rate, 1.48; 95% CI, 1.05-2.14). Stratum 2 patients showed a 57.4% overall CAILS treatment response rate for the gel arm vs 40.0% in the ointment treatment arm (ratio of gel response rate to ointment response rate, 1.48; 95% CI, 1.05-2.14). Stratum 2 patients showed a 57.4% overall CAILS treatment response rate for the gel arm vs 40.0% in the ointment treatment arm (ratio of gel response rate to ointment response rate, 1.48; 95% CI, 1.05-2.14). 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Most AEs in both treatment arms were skin related, with at least 1 AE considered related to the study drug. And 50.4% of patients who received ointment reported skin irritation at the time of the last visit. Sixty-two percent (61.7%) of patients who received gel arm and 37.7% in the ointment arm reached a 50% reduction. Fifteen patients randomized to the gel treatment arm and 46.2% for the ointment treatment arm maintained their response through the end of the trial (12 months). Based on the Kaplan-Meier analysis, no statistically significant difference between the 2 treatment arms was observed with respect to duration of response (P = .48, log-rank test), and further analysis estimated that at least 90% of responses (using the consensus guidelines) will be maintained for at least 10 months, the maximum follow-up period in the trial (Figure 4).

The mSWAT secondary efficacy end point demonstrated similar results, with response rates of 46.9% for the gel treatment arm and 46.2% for the ointment treatment arm (response rate ratio, 1.02; 95% CI, 0.78-1.32) in the ITT population. In the EE population, the response rates were 63.3% for the gel arm and 55.8% for the ointment arm (response rate ratio, 1.14; 95% CI, 0.89-1.49) (Figure 2).

The complete response rates ranged from 11.5% to 18.9% in both treatment arms of the ITT and EE populations. Thirty-three percent of patients in the gel arm and 23.8% of patients in the ointment arm achieved a 90% reduction from the baseline CAILS score, while 52.3% in the gel arm and 37.7% in the ointment arm reached a 75% reduction. Fifteen patients randomized to the gel arm and 10 patients randomized to the ointment arm had progressive disease at some time during the study. However, most patients continued with treatment. Seven patients in the gel arm who continued with treatment achieved a confirmed response. Eight patients (5 in the gel arm and 3 in the ointment arm) met the criterion for progressive disease without influencing their T classification at the time of the last visit.

SAFETY AND TOLERANCE

No drug-related severe AEs were reported during the trial. Sixty-two percent (61.7%) of patients who received gel and 50.4% of patients who received ointment reported at least 1 AE that was considered related to the study drug. Most AEs in both treatment arms were skin related, characterized mainly as local dermatitis (skin irritation) (Table 3). The incidence of skin irritation was higher in the gel arm (P = .04). No statistically significant differences were observed in the overall incidence of AEs or any other subcategory between the gel and ointment arms.

The difference in skin irritation among patients in the gel arm is primarily due to an increased incidence of moderate or moderately severe (grade 2 or 3) local dermal irritation. However, no difference was found between the 2 treatment arms with respect to the number of patients who withdrew from the trial because of protocol-defined treatment-limiting skin AEs (26 of 128 [20.3%] in the gel arm vs 22 of 127 [17.3%] in the ointment arm) (P = .63). The data showed that most withdrawals for treatment-limiting skin AEs occurred within the first few months and that 89.2% occurred before month 6.

Although patch testing was not routinely required in this trial, the incidence of treatment-limiting skin AEs (21 of 128 [16.4%] in the gel arm and 16 of 127 [12.6%] in the ointment arm) can be used as a conservative estimate of allergic contact dermatitis. Of 21 patients in the gel arm who withdrew from the study because of treatment-limiting skin AEs, 13 had a positive–patch test result, and 8 were not tested; of 16 patients in the oint-
ment arm who withdrew for the same reason, 11 had a positive–patch test result, 2 had a negative–patch test result, and 3 were not tested.

Clinical laboratory monitoring (hematology and serum chemistry parameters at baseline and at months 4, 8, and 12) demonstrated no systematic pattern of change in any laboratory value measured, consistent with a lack of systemic absorption. In addition, high-performance liquid chromatography serum assays performed in 16 patients who received gel (at 0, 1, 3, and 6 hours after application on day 1 and at week 4) revealed no detectable blood levels or evidence of systemic absorption of mechlorethamine (data not shown).

The development of secondary nonmelanoma skin cancers was monitored throughout the 12-month trial and during an additional 12-month follow-up period. Eleven patients (3 in the gel arm and 8 in the ointment arm) were diagnosed as having 20 nonmelanoma skin cancers. These included 10 basal cell carcinomas (5 occurring in a treatment area), 9 squamous cell carcinomas of the skin (1 occurring in a treatment area), and 1 Merkel cell carcinoma (not occurring in a treatment area). Most nonmelanoma skin cancers occurred on sun-exposed areas and in patients who had a history of skin cancer or who had received prior skin-directed therapies, including phototherapy, for the treatment of MF.

**COMMENT**

After decades of reported use of topical mechlorethamine in MF-CTCL, to our knowledge, this clinical trial is the first to date to evaluate the efficacy and safety of topical mechlorethamine chemotherapy by comparing a novel mechlorethamine, 0.02%, gel with a compounded mechlorethamine, 0.02%, ointment in stage IA to IIA MF-CTCL. The enrollment of 260 patients represents the single largest controlled clinical trial in MF-CTCL for any given treatment. A noninferiority analysis was chosen to show that the gel formulation is statistically (and clinically) not inferior to the ointment. As measured by the primary CAILS efficacy end point within the ITT population, the overall response rates (complete response plus partial response) were 58.5% for the gel treatment arm compared with 47.7% for the ointment treatment arm. The ratio of gel response rate to ointment response rate was 1.23 (95% CI, 0.97-1.55). The ratio in each stratum was also within the protocol-specified limit for noninferiority (≥0.75). Differences in the ratios between stratum 1 (stage IA) and stratum 2 (stage IB to IIA) may be related to advanced disease of patients in stratum 2 or to patient compliance (with more effort required to treat larger areas) and varied application methods (regional vs total body) allowed in the protocol. Therefore, the clinical trial's statistical primary end point was achieved and demonstrated the efficacy, safety, and tolerability of a novel mechlorethamine, 0.02%, gel formulation.

Comparison of the overall response rate for the gel treatment arm (58.5%) in this clinical trial with previously reported response rates for topical mechlorethamine is difficult. An 83% overall response rate for compounded mechlorethamine ointment has been previously reported in retrospective case series. Several factors might account for the difference in response rates. Retrospective case series have used an EE population (often referred to as an “as treated” population) and do not include all the patients who received a particular treatment, specifically excluding those who prematurely withdrew from the study. Furthermore, one concentration of topical mechlorethamine (0.02%) was used herein throughout the trial compared with multiple and higher concentrations (range, 0.01%-0.04%) used in reported case series. In contrast to other case series, no concurrent therapies (especially topical corticosteroids) were permitted among patients during the present trial, and no additional skin-directed or systemic therapies were used in the case of unresponsive or progressive disease. Also, strict termination rules and restrictive management (concurrent use of topical corticosteroids was prohibited) of skin toxic effects (irritant and allergic contact dermatitis) were used in this clinical trial. All the aforementioned case series reported response rates using the Physician's Global Assessment in an unblinded manner, whereas in this study the CAILS was used by blinded observers.

Notably, the time-to-response analyses demonstrated that patients who were treated longer with topical mechlorethamine gel in this trial achieved greater and faster responses. These results are summarized in Figure 3.

No serious or unexpected drug-related AEs were observed with the gel or ointment. Drug-related AEs were seen in 61.7% of patients in the gel arm and in 50.4% of patients in the ointment arm. Most AEs were characterized mainly as local skin reactions, with signs and symptoms of irritant contact dermatitis or allergic contact dermatitis (Table 3). The percentages of patients who withdrew from the trial because of a drug-related skin AE were 20.3% in the gel arm and 17.3% in the ointment arm, with the occurrences of allergic contact dermatitis estimated at 16.4% and 12.6%, respectively. These rates compare favorably with the approximate 10% incidence of allergic contact dermatitis reported in the literature for compounded mechlorethamine ointments, considering the restrictive nature of the clinical trial protocol treatment adjustments (for local skin reactions) and termination rules. In the present trial, skin AEs were treated with suspension or application reduction within a 4-week period, as well as the allowed use of emollients and oral antihistamines. In contrast, clinical practice and retrospective case series used varying mechlorethamine concentrations (with dosage reduction schedules), topical corticosteroids during extended periods, and no restrictions on length of drug withheld to manage irritant and allergic contact dermatitis.

This clinical trial provided the first opportunity to date to perform high-performance liquid chromatography serum assays for mechlorethamine detection after topical application to the skin in patients with MF-CTCL. No detectable systemic absorption of study drug was found in the blood of 16 patients after mechlorethamine, 0.02%, gel application. These data, along with no observed abnormal trends in clinical laboratory values throughout the 12-month treatment period, corroborate numerous

Conflict of Interest Disclosures: Dr Lessin serves as a consultant to Ceptaris Therapeutics, Inc.

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Role of the Sponsor: Ceptaris Therapeutics, Inc, monitored the conduct of the study and provided data collection and analysis.

Additional Contributions: Cathie A. Leister, MS, performed statistical analysis of the data. We thank our study patients for their participation and the Cutaneous Lymphoma Foundation for its grassroots support of this project.

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case series that recognized no abnormalities related to systemic absorption of topically applied mechlorethamine.6,10,11,14,15 During a 24-month observation period (12-month treatment and 12-month follow-up period), only 6 non-melanoma skin cancers (1 squamous cell carcinoma and 5 basal cell carcinomas) were detected in treatment areas. Within the limitations of the observation period and uncontrolled confounding variables, these data do not support an obvious association between the development of secondary nonmelanoma skin cancers and the daily application of topical mechlorethamine, 0.02%.

In summary, the results of this randomized, controlled, multicenter clinical trial confirm the noninferiority of a novel mechlorethamine, 0.02%, gel in the treatment of MF-CTCL compared with a compounded mechlorethamine, 0.02%, petrolatum ointment. The findings also corroborate multiple reports and case series in the medical literature spanning more than 6 decades that have affirmed the use of mechlorethamine as an effective topical chemotherapy in MF-CTCL.3,4,6-15 and its inclusion as a frontline therapy in treatment guidelines.18,19 A manufactured mechlorethamine, 0.02%, gel addresses the unmet need for good manufacturing product quality assurance that will improve drug availability for patients with MF-CTCL.
Uvulectomies and Associated Complications

Traditional uvulectomies are common therapeutic or ritualistic procedures that are performed in various countries throughout Africa and the Middle East. They have been traced back to Hippocrates (460-355), Galen (129-200), 11th century Spain, and 19th century England and France, where they were used to cure stuttering.

In the Huasa-speaking communities of Nigeria and Niger, ritualistic uvulectomy is performed as part of a Muslim naming ceremony on the seventh day after birth. This ritual is thought to prevent death from swelling of the uvula, which could burst and kill the neonate. In fact, uvula in Huasa means "throat herb" in Niger, and it is believed that the uvula should be cut prophylactically, just like weeds in the field. These ritualistic uvulectomies are usually performed by an apprenticed barber-surgeon, who identifies a diseased uvula by looking for a finger imprint after pressing on the child's forehead or by identifying a swollen, red, white, or long uvula. The barber then recites verses from the Koran and an inaudible prayer that is thought to protect the child and to guide the barber.

The uvula is completely or partially excised using a sickle-shaped knife. Hemostasis is obtained with herbal powders. The uvula is then placed on the forehead of the child and later shaped into a knife. The uvula is then recited verses from the Koran and an inaudible prayer or by identifying a swollen, red, white, or long uvula. The barber then recites verses from the Koran and an inaudible prayer that is thought to protect the child and to guide the barber. The uvula is completely or partially excised using a sickle-shaped knife. The uvula is then placed on the forehead of the child and later hangs on the wall in the child's home. During the ritual, the child's head is shaved, and a hymenectomy or circumcision may also be performed. Other variations of the practice include using a reed fork in Morocco, twisted strands of horsehair in Ethiopia, and a hot knife in Egypt.

The Kanos in Nigeria also perform uvulectomies in children and adults to prevent or treat throat infections, chronic cough, uvula swelling, swallowing troubles, difficulty in breastfeeding, speech problems, vomiting, and diarrhea. The Bedouins in Sinai believe that uvulectomies help children better tolerate thirst and prevent upper respiratory infections.

While uvulectomy bars deny any risks to the procedure, common complications include infection, hemorrhage, tetanus, fragment inhalation, diarrhea, and dehydration. Chronic complications include nasal speech, palate abnormalities, human immunodeficiency virus, obstructive sleep apnea, and snoring. One study reported a death rate of 17.2% in Nigerian infants who underwent uvulectomy. It is important for the dermatologist to recognize uvulectomy and associated complications in both the outpatient and the inpatient settings.

Rebecca Jacobson, MST
Barry Ladzinski, MD
Kachiu C. Lee, MD

Author Affiliations: Departments of Dermatology, Brown University, Providence, Rhode Island (Ms Jacobson and Dr Lee), and Duke University, Durham, North Carolina (Dr Ladzinski).

Contact Dr Lee at the Department of Dermatology, Brown University, 593 Eddy St, Ambulatory Patient Center 10, Providence, RI 02903 (kachiu@gmail.com).