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Analysis of Beta-Blocker Instituted for Treatment of Hemangiomas (RABBIT Study)

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Abstract

Objective(s)—To evaluate the safety and efficacy of our institutional beta-blocker protocol for treatment of complicated infantile hemangiomas (IH).

Study design—A retrospective descriptive study of 76 infants/children with IH treated with oral propranolol at the Children's Hospital of Philadelphia between June 2008 and August 2010 was performed, assessing both the safety and efficacy of propranolol. Based on preliminary data showing hemangioma recrudescence off-treatment, we reviewed 9 additional patients with recrudescence between August 2010 and December 2011.

Results—Mild adverse events included asymptomatic bradycardia, gastrointestinal symptoms, asymptomatic hypotension, cool hands/feet, asymptomatic hypoglycemia, and sleep disturbance. 16 patients had recrudescence of IH off-treatment, with propranolol discontinued at a median age of 14 months (interquartile range 10–15 months).

Conclusion(s)—Propranolol appears to be associated with minor, not severe symptomatic adverse events. Propranolol appears to be effective in treating complicated IH. Recrudescence can occur off-treatment, even with discontinuing propranolol as late as 15 months of age.

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Disclosure Statement

Leslie Castelo-Soccio, Marissa J. Perman, and Albert C. Yan are currently serving as investigators for a Pierre Fabre clinical study. Albert C. Yan also previously served as a consultant for Pierre Fabre. All remaining authors have no conflicts of interest to report.

Keywords

Infantile hemangioma; propranolol; adverse effects; hypoglycemia; hypotension; bradycardia; recrudescence

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Introduction

Infantile hemangiomas (IH) are the most common benign tumors of infancy, with an incidence of 4–5% in the general newborn population.¹ Typically present shortly after birth, IH proliferate during the child's first year of life, with most growth occurring in the first 4–6 months (mo). Spontaneous regression follows, with most IH ceasing to involute after 3–4 years (yrs).² Residual changes such as telangiectasias, skin discoloration, and atrophic wrinkling may occur in 69% of cases.³ In the interim, IH may be complicated by bleeding, ulceration, airway obstruction or visual compromise, thereby necessitating medical treatment in approximately 10–20% of cases.

Many therapeutic modalities have been implemented in the treatment of complicated IH, including systemic corticosteroids,⁴ pulsed-dye laser,⁵ topical imiquimod,⁶ surgery, and occasionally vincristine,⁷ interferon-alpha,⁸ cyclophosphamide,⁹ sirolimus (rapamycin),¹⁰ and most recently, propranolol.¹¹ Although propranolol has been safely used for many years in infants and children for non-hemangioma indications, its now widespread use for the treatment of hemangiomas prompts the ongoing need to evaluate and establish safe and effective protocols for its use. Consequently, we investigated infants and children with IH who were treated with propranolol at our institution, the Children's Hospital of Philadelphia (CHOP), with the intention of describing our patient population and the safety and efficacy of our inpatient beta-blocker protocol, during a period when we were transitioning from exclusive use of systemic corticosteroids to oral beta-blocker therapy.

Methods

Study Design

We performed a retrospective descriptive study of 76 infants and children with complicated IH treated with propranolol at CHOP between June 2008 and August 2010, examining the safety and efficacy of propranolol therapy as administered via our institutional protocol. All subjects were evaluated for safety issues. Those who completed at least 1 mo of therapy were assessed for treatment outcome. Of note, this 1 mo duration was determined *a priori* based on anecdotal evidence that significant treatment response may not be observed within the first few weeks of treatment. Based on preliminary data showing hemangioma recrudescence in several patients who completed propranolol therapy, we performed a chart review of 9 additional patients with recrudescence of their hemangiomas following discontinuation of propranolol between August 2010 and December 2011 in order to assess possible contributing factors. Institutional IRB approval was obtained. The study was reported based on guidance from the STROBE Statement.

CHOP's institutional inpatient beta-blocker protocol was conceived by a joint clinical group, consisting of Pediatric Dermatology, Cardiology, Pharmacy, General Pediatrics, and

Neonatology, with additional input from Ophthalmology, Otolaryngology, and Plastic Surgery.

Patients less than 2 mo of age were admitted to the neonatal intensive care unit for initiation of propranolol, whereas patients over 2 mo of age were admitted to the general pediatrics inpatient service. All patients received a 12-lead electrocardiogram prior to initiating propranolol. If PHACE syndrome (posterior fossa abnormalities, hemangioma of cervical facial region, arterial cerebrovascular anomalies, cardiac defects, eye anomalies), airway involvement, or orbital involvement were suspected, additional imaging and specialty consultation were requested. Oral propranolol was started at 0.5 mg/kg/day divided every 8 hours (hrs). If tolerated after 3 doses, the dose was escalated to 1 mg/kg/day divided every 8 hrs for 3 doses, then to 2 mg/kg/day divided every 8 hrs. Blood pressure and heart rate were serially measured by auscultation or cardiorespiratory monitoring every 2 hrs, irrespective of when propranolol was administered. Serum glucose was measured 1 hr post-dose for 2 doses with each dose escalation. Once discharged from the hospital, patients were followed every 4–8 weeks in the dermatology clinic for monitoring of treatment safety and efficacy.

In cases of treatment initiated in the outpatient setting for 2 older children during this study period, propranolol was started at 0.5 mg/kg/day divided every 8 hrs, and blood pressure and heart rate were measured 1 and 2 hrs after the first administered dose in the dermatology clinic. The dose was then slowly up-titrated in increments of 0.25–0.5 mg/kg/day over several weeks toward a goal of 1.5–2 mg/kg/day, with frequent follow-up by dermatology and the patient's primary care physician for monitoring of vital signs and adverse effects. When goal propranolol dose was achieved, follow-up visits were spaced every 1–2 mo.

Variables Measured

Data collected from patient medical records included patient demographics (age at onset of IH, gender, race, gestational age, birth weight), IH characteristics (primary IH^a anatomic site, size, configuration, depth, ulceration), prior treatments, and propranolol regimens (age at start and end of treatment, peak dose, concomitant treatments).

Our primary outcome was the safety evaluation of medication-related side effects. Hypotension was defined according to the Pediatric Advanced Life Support Guidelines (Systolic blood pressure <60 for 0–1 mo, <70 for 1 mo–1 yr, <70 + [2 × age in yrs] for 1–10 yrs).¹² Bradycardia was defined as a heart rate less than the 2nd percentile for age (Heart rate <90 for 0–1 mo, <105 for 1–6 mo, <110 for 6–12 mo, <90 for 1–3 yrs, <70 for 3–5 yrs, <65 for 5–8 yrs).¹³ A blood glucose of less than 70 mg/dL was used to signify hypoglycemia. The incidence of symptomatic hypoglycemia, hypotension or bradycardia (defined by signs of poor perfusion, respiratory distress, loss of consciousness, poor mentation, and/or poor feeding) was recorded. Moreover, we documented physician responses to adverse effects.

Our secondary outcome was the prevalence of clearance or near clearance of IH based on review of available photo-documentation. Photos were evaluated by a single investigator (L.C.S.) using a 5-point global assessment scale (1-no change, 2-minimal improvement, 3-

^aThe primary IH is that which prompts the consideration and use of propranolol for treatment.

moderate improvement, 4-almost clear, 5-clear). For patients with recrudescence of IH after completing propranolol therapy, we noted time to re-growth, duration of therapy, and age at discontinuation of propranolol.

Statistical Methods

As the study was intended to be purely descriptive, data on patient characteristics and safety and efficacy outcomes were summarized descriptively. Missing data were also described. Summary statistics were analyzed using Stata/IC10 (College Station, TX).

Results

Subject Characteristics

76 patients were included in our study (Table 1). The vast majority (97.4%, N=74) began propranolol therapy as inpatients during this period. The most common indication for propranolol was anatomic distortion, followed by risk or presence of visual compromise and ulceration. The median age at the start of treatment was 3 mo (interquartile range (IQR) 2–6 mo), and the median duration of treatment as of the last follow-up visit was 4 mo (IQR 2–7 mo). The median peak propranolol dose administered was 2 mg/kg/day (IQR 2–2 mg/kg/day). Patients often received concomitant treatments to facilitate IH involution, promote healing of ulcerations, or prevent or treat secondary infections. The most common medication given concurrently with propranolol was systemic corticosteroids (26.3%, N=20). Timolol gel, a topical beta-blocker, was occasionally used as a bridge to discontinuation of propranolol (9.2%, N=7).

Safety

22 patients (28.9%) had no documented adverse events while receiving propranolol. The remaining 54 subjects (71.1%; 95% CI 59.5–80.9%) each experienced at least one adverse event (Figure 1), resulting in a total of 102 adverse events. However, no patients suffered from serious adverse events, defined as life-threatening, resulting in significant or permanent damage, or death (hospitalization was not included as this was part of treatment protocol).

Among the adverse events reported, there were no cases of symptomatic hypoglycemia, hypotension, or bradycardia. 8 of 29 cases (27.6%; 95% CI 12.7–47.2%) with documented bradycardia prompted a change in propranolol dosing, although none were symptomatic. 9 of 22 patients (40.9%; 95% CI 20.7–63.6%) with documented hypotension received a change in their treatment regimen although again, none were symptomatic. Among all subjects with documented side effects, 53.7% (29) underwent no change in propranolol dose, 27.8% (15) had dose decreased, 11.1% (6) were unable to up-titrate to achieve goal dose or required slower up-titration (>24 hours) of dose during hospitalization, 3.7% (2) did not have dose adjusted to account for weight change, and 3.7% (2) had medication held temporarily. Side effects prompting a change in propranolol treatment regimen, in descending order, included documented hypotension (N=9), bradycardia (8), as well as symptoms independent of hypotension, bradycardia, and hypoglycemia such as cool extremities (6), sleep disturbance (4), color change in hands/feet (3), diarrhea (2), abdominal cramps (2), restlessness (2), poor appetite (1), emesis (1), and decreased activity (1).

A sizable proportion (26.3%, N=20) of our study population received concomitant corticosteroid therapy, with a mean overlap time of 3.2 mo. Hypotension was documented more commonly among the 40% (N=8) of patients who received concomitant corticosteroids, compared to only 25% (N=14) of patients who did not. None were symptomatic. Hypoglycemia occurred more often (30%, N=6) among patients who received concomitant corticosteroids than in those patients who did not (10.7%, N=6). None were symptomatic.

Treatment Efficacy

70 patients (92.1%) received at least 1 mo of propranolol therapy at the time of study completion, and of these, 41 patients (58.6%) had before and after treatment photographs available for analysis. 85.4% (95% CI 70.8–94.4%; N=35) achieved at least moderate improvement of their primary IH, with a median time to moderate improvement being 5 weeks (wks) (IQR 3–9 wks). 46.3% (95% CI 30.7–62.6%; N=19) achieved clearance or near clearance of IH, with a median time to near clearance being 15 wks (IQR 5–24 wks) (Figure 2). The median duration of propranolol therapy as of the last follow-up clinic visit was 6 mo (IQR 4–8 mo). The mean photo global assessment score achieved while on propranolol was 3.4 (standard deviation 0.9).

IH Recrudescence

At the time the study was performed, 12 subjects in the original 76 patient cohort had completed propranolol therapy, of which 7 (58.3%; 95% CI 27.7–84.8%) had documented recrudescence of IH off-treatment. An additional 9 patients with IH recurrence between August 2010 and December 2011 were examined. The median age at discontinuation of propranolol for those with IH recrudescence was 14 mo (IQR 10–15 mo) and the median duration of propranolol therapy for these patients was 9 mo (IQR 6–11 mo). The median time to first witnessed re-growth was 1 mo (IQR 10 days - 2 mo). The vast majority (87.5%) of patients with re-growth had facial hemangiomas, particularly of the nose and lip.

Discussion

Since the fortuitous discovery of the profound effects of beta-blocker therapy on IH, propranolol has become a first-line treatment for complicated IH, particularly ulcerated and airway IH. Propranolol induces regression of IH with greater consistency and to a greater extent than other therapeutic modalities. Hypotheses regarding its mechanism of action include vasoconstriction, decrease in vascular endothelial growth factor and angiogenesis, apoptosis of capillary endothelial cells, and down-regulation of the renin-angiotensin system.¹⁴ The perception of a milder side effect profile for propranolol in comparison to alternative agents makes it an attractive treatment option. However, propranolol must still be used with caution. Potential risks may include hypotension, bradycardia, hypoglycemia, bronchospasm, and feeding difficulties.¹⁵

None of the patients in our study experienced significant *symptomatic* adverse effects from propranolol use. At the same time, a large number of patients experienced at least one adverse effect as defined by our parameters, with the most common being bradycardia.

However, this was most often transient sinus bradycardia while patients were asleep during hospitalization. Only 27.6% of these patients received a change in propranolol dosing, and with documented low blood pressures did not have sustained hypotension, and 40.9% of cases prompted a change in dosing solely for values out of expected ranges. At least 4 patients were noted to have had their blood pressures measured with an inappropriately large-sized cuff, thereby underestimating their true blood pressures. 12 patients had documented hypoglycemia, but none necessitated a change in treatment protocol as they were asymptomatic and blood glucose improved upon feeding or an immediate recheck of the blood sugar was noted to be normal. Given that no patients with documented bradycardia, hypotension or hypoglycemia were symptomatic, and that fewer than half of the subjects with adverse effects required changes in propranolol dosing, the majority of patients tolerated initiation and rapid up-titration of medication, both in hospital and during follow-up visits. Propranolol appears to be a safe treatment for IH when used under appropriate supervision.

Since the completion of our study, a consensus conference has been held in order to standardize protocols for initiating propranolol for the treatment of IH.¹⁶ Based on these consensus guidelines and other published reports, our group has transitioned to use of propranolol in the outpatient setting for most uncomplicated children with infantile hemangiomas over the age of 3 months. However, the presence of measurable changes in vital sign parameters in a sizeable minority of patients has prompted us to continue with an inpatient approach to initiation of propranolol when rapid up-titration is required for complicated IH such as airway and periorbital IH, or in those with significant prematurity. Intensive monitoring and resultant treatment alterations in this scenario may help to prevent clinically important or serious adverse events from occurring.

Based on photo assessments, at least half of the subjects achieved clearance or near clearance of IH. The high rate of IH clearance within the time frame of this study is a testament to the efficacy of propranolol for treatment of infantile hemangioma. We did, however, note that a substantial number of patients experienced recrudescence of IH. It is unclear what accounts for the propensity for recrudescence. IH re-growth tends to occur within 1 month of stopping propranolol. Of the 16 patients with rebound growth of IH, 37.5% had lip involvement, and 25% had nose involvement, the significance of which is unknown given our small sample size. Recrudescence can occur even after 11 months of therapy, and with discontinuing propranolol as late as 15 mo of age, suggesting that the IH has not entirely completed its proliferative phase. Based on these observations, patients with facial IH particularly of the nose and lip, may benefit from extending treatment to at least 15 mo of age to reduce the risk of recrudescence. This important aspect of propranolol therapy warrants further detailed study.

As with all studies, there are limitations to our exploratory study. Given the retrospective nature of this study, many patients had not received a prolonged duration of propranolol therapy, and therefore we were unable to capture longer-term safety and efficacy data. Arguably, it is during the initiation period that patients are most at risk for adverse events given the rapid up-titration of propranolol. However, even at steady dosages, precautions must still be taken to avoid adverse effects, such as temporarily discontinuing propranolol

during intercurrent illnesses and decreased oral intake to prevent hypoglycemia. Moreover, this study design likely underestimated the number of patients who would ultimately achieve clearance or near clearance of their IH. Secondly, without a control population in this study, it is difficult to attribute every adverse effect and positive treatment outcome to propranolol use. Many patients were using other medications concurrently, which could confound our results. It might also be argued that the subset of patients who received both systemic corticosteroids and propranolol may have had any potential adverse effects from beta-blocker therapy masked by concomitant use of the corticosteroid. It was surprising to note, however, that the prevalence of hypoglycemia and hypotension in our study were greater in the group of patients who received concomitant steroid therapy. This is difficult to interpret given the small sample size. Thirdly, this study lacked a standardized schedule for photo-documentation, resulting in a substantial percentage of patients for whom we could not accurately assess treatment outcome. In particular, it was challenging to determine time to IH clearance. Finally, the thresholds we used to define bradycardia in our study were derived from electrocardiogram data on infants and children who were awake, and therefore may overlap with the often lower resting heart rates that occur during sleep. To our knowledge, no large studies have been performed to establish reference ranges for normal heart rates in children who are sound asleep. As such, we may be overestimating the number of patients with a tendency to bradycardia while taking propranolol.

Conclusion

This study provides descriptive information that indicates that initiation and rapid up-titration of propranolol in the inpatient setting is safe for the treatment of IH, as no study patients experienced significant symptomatic adverse effects at the peak doses established by our institutional protocol, and the majority required no alterations in treatment regimen. However, given that changes in vital signs were detected, we recommend that patients be hospitalized for initiation of propranolol when rapid up-titration is necessary. In less urgent cases where slower up-titration of propranolol is reasonable, outpatient initiation is a feasible, rational, and cost-efficient option. Propranolol also appears to be effective in the treatment of complicated IH, though recrudescence can occur off treatment. Extending treatment to at least 15 mo of age may help to minimize IH re-growth. These observations will hopefully continue to add to the body of information available for those prescribing beta-blocker therapy for management of complicated IH.

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References

1. Kilcline C, Frieden IJ. Infantile Hemangiomas: How Common Are They? A Systematic Review of the Medical Literature. *Pediatric Dermatology*. 2008 Mar; 25(2):168–173. [PubMed: 18429772]
2. Luu M, Frieden IJ. Haemangioma: clinical course, complications and management. *British Journal of Dermatology*. 2013 Jul; 169(1):20–30. [PubMed: 23701395]

3. Bauland CG, Lüning TH, Smit JM, Zeebregts CJ, Spauwen PHM. Untreated hemangiomas: growth pattern and residual lesions. *Plast Reconstr Surg*. 2011 Apr; 127(4):1643–1648. [PubMed: 21460670]
4. Bennett ML, Fleischer AB Jr, Chamlin SL, Frieden IJ. Oral corticosteroid use is effective for cutaneous hemangiomas: an evidence-based evaluation. *Arch Dermatol*. 2001 Sep; 137(9):1208–1213. [PubMed: 11559219]
5. Al Buainian H, Verhaeghe E, Dierckxsens L, Naeyaert JM. Early treatment of hemangiomas with lasers. A review. *Dermatology (Basel)*. 2003; 206(4):370–373. [PubMed: 12771489]
6. Jiang C, Hu X, Ma G, Chen D, Jin Y, Chen H, et al. A Prospective Self-Controlled Phase II Study of Imiquimod 5% Cream in the Treatment of Infantile Hemangioma: Jiang et al. *Pediatric Dermatology*. 2011 May; 28(3):259–266. [PubMed: 21615472]
7. Brandling-Bennett HA, Metry DW, Baselga E, Lucky AW, Adams DM, Cordisco MR, et al. Infantile hemangiomas with unusually prolonged growth phase: a case series. *Arch Dermatol*. 2008 Dec; 144(12):1632–1637. [PubMed: 19075148]
8. Chang E, Boyd A, Nelson CC, Crowley D, Law T, Keough KM, et al. Successful treatment of infantile hemangiomas with interferon-alpha-2b. *J Pediatr Hematol Oncol*. 1997 Jun; 19(3):237–244. [PubMed: 9201147]
9. Wilson MW, Hoehn ME, Haik BG, Rieman M, Reiss U. Low-dose cyclophosphamide and interferon alfa 2a for the treatment of capillary hemangioma of the orbit. *Ophthalmology*. 2007 May; 114(5):1007–1011. [PubMed: 17337066]
10. Greenberger S, Yuan S, Walsh LA, Boscolo E, Kang K-T, Matthews B, et al. Rapamycin suppresses self-renewal and vasculogenic potential of stem cells isolated from infantile hemangioma. *J Invest Dermatol*. 2011 Dec; 131(12):2467–2476. [PubMed: 21938011]
11. Léauté-Labrèze C, Dumas de la Roque E, Hubiche T, Boralevi F, Thambo J-B, Taïeb A. Propranolol for severe hemangiomas of infancy. *N Engl J Med*. 2008 Jun 12; 358(24):2649–2651. [PubMed: 18550886]
12. Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 10: pediatric advanced life support. The American Heart Association in collaboration with the International Liaison Committee on Resuscitation. *Circulation*. 2000 Aug 22; 102(8 Suppl):I291–342. [PubMed: 10966679]
13. Moss, AJ.; Adams, FH.; Emmanouilides, GC. Moss and Adams heart disease in infants, children, and adolescents: including the fetus and young adult. Baltimore: Williams & Wilkins; 1995.
14. Shah S, Frieden IJ. Treatment of infantile hemangiomas with Beta-blockers: a review. *Skin Therapy Lett*. 2013 Oct; 18(6):5–7. [PubMed: 24305730]
15. Lawley LP, Siegfried E, Todd JL. Propranolol treatment for hemangioma of infancy: risks and recommendations. *Pediatr Dermatol*. 2009 Oct; 26(5):610–614. [PubMed: 19840322]
16. Drolet BA, Frommelt PC, Chamlin SL, Haggstrom A, Bauman NM, Chiu YE, et al. Initiation and use of propranolol for infantile hemangioma: report of a consensus conference. *Pediatrics*. 2013 Jan; 131(1):128–140. [PubMed: 23266923]

Figure 1.
Documented Adverse Events (N=76)

Figure 2.
Cheek IH (pre and post-propranolol). A large, red plaque involving the left cheek and left lower eyelid is significantly flattened with reduced erythema and only residual telangiectasias 5 months after propranolol initiation.

Table 1

Baseline characteristics of patients and infantile hemangiomas (IH) (N=76)

Patient Characteristics	Proportion, N (%)
Gender	
Male	18 (23.7%)
Female	58 (76.3%)
Race	
Caucasian	58 (76.3%)
African American	8 (10.5%)
Hispanic	3 (3.9%)
Asian	2 (2.6%)
Missing	5 (6.6%)
Gestational Age	
37weeks	50 (65.8%)
<37weeks	24 (31.6%)
Missing	2 (2.6%)
Birth Weight	
<1kg	2 (2.6%)
1 and <2kg	7 (9.2%)
2 and <3kg	14 (18.4%)
3 and <4kg	27 (35.5%)
4kg	7 (9.2%)
Missing	19 (25.0%)
Age at Onset of IH	
<1wk	24 (31.6%)
1 and <4wk	31 (40.8%)
4 and <8wk	8 (10.5%)
8	6 (7.9%)
Missing	7 (9.2%)
Number of IH	
Single	49 (64.5%)
Multiple	27 (35.5%)
Anatomic Site of Primary IH	
Head and Neck	60 (78.9%)
Periorbital	26 (34.2%)
Lip	3 (3.9%)
Ear	3 (3.9%)
Nose (other than tip)	5 (6.6%)
Nasal tip	2 (2.6%)

Patient Characteristics	Proportion, N (%)
Cheek	10 (13.2%)
Parotid	3 (3.9%)
Forehead/Glabella	4 (5.3%)
Scalp	1 (1.3%)
Neck	2 (2.6%)
Hemifacial	1 (1.3%)
Airway	8 (10.5%)
Visceral	2 (2.6%)
Buttock	3 (3.9%)
Extremities	2 (2.6%)
Back	1 (1.3%)
IH Configuration	
Localized	48 (63.2%)
Segmental	15 (19.7%)
Unclassified	10 (13.2%)
Indeterminate	3 (3.9%)
IH Depth	
Mixed	50 (65.8%)
Deep	15 (19.7%)
Superficial	1 (1.3%)
Unclassified	10 (13.2%)
Presence of Ulceration	
Yes ^a	58 (76.3%)
No	18 (23.7%)
Prior Treatment of IH	
Systemic Steroids	24 (31.6%)
Topical Steroids	1 (1.3%)
Topical Timolol	6 (7.9%)
Laser	5 (6.6%)
Surgery	1 (1.3%)
Topical Antibiotics	10 (13.2%)
Systemic Antibiotics	6 (7.9%)
Concomitant Treatment of IH	
Systemic Steroids	20 (26.3%)
Topical Steroids	0 (0%)
Topical Timolol	7 (9.2%)
Laser	7 (9.2%)
Surgery	0 (0%)
Topical Antibiotics	13 (17.1%)

Patient Characteristics	Proportion, N (%)
Systemic Antibiotics	3 (3.9%)

^aSites of ulceration (in descending order of frequency): Buttock, cheek, lip, extremity, ear, nose, scalp, back