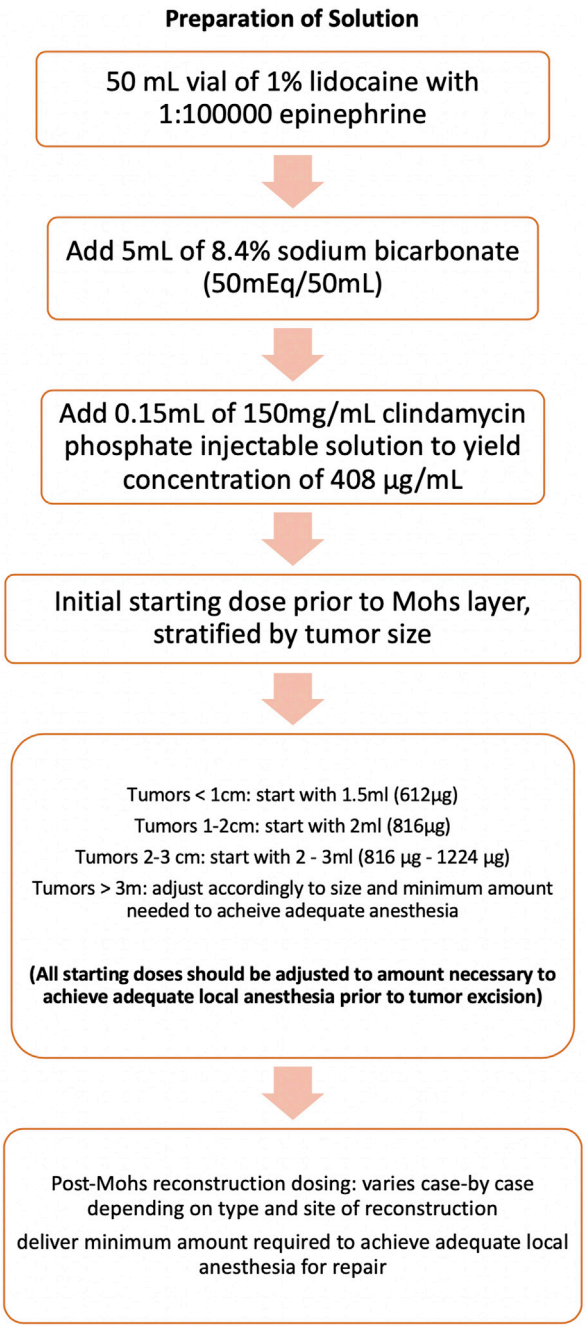

Fig 1. Intra-incisional clindamycin protocol algorithm for clinician use.

subcutis, negligible amounts enter systemic circulation; therefore, there is decreased potential for antibiotic resistance, systemic drug interactions, and disruption of the intestinal microbiome.[4]

One limitation of this study was the patient retention rate; approximately 18% did not return for routine postoperative follow-up. As such, it is plausible that the true surgical-site infection rate was higher. However, this is unlikely because we maintain close contact with our patients and referring providers for all surgical site complications.

In summary, this study demonstrates that preoperative, intra-incisional, prophylactic clindamycin is a safe and effective method to reduce postoperative surgical-site infections and may help to reduce systemic antibiotic overuse.

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The effectiveness of rituximab in pemphigus and the benefit of additional maintenance infusions: Daily practice data from a retrospective study

To the Editor: Rituximab in combination with short term prednisone or other immunosupressive therapy is recognized as the first-line therapy in pemphigus.[1] Additional maintenance infusions are often given on clinical indication, but evidence regarding these infusions is scarce. The aim of this study was to

Table I. Baseline characteristics of pemphigus patients treated with rituximab

Characteristics	Value
Male/female, n (%)	20 (38)/33 (62)
Mean age at start of rituximab, y, median (SD; range)	53.8 (14.3; 26-86)
PV/PF, n (%)	44 (83)/9 (17)
Mucosal PV, n (%)	17 (32)
Mucocutaneous PV, n (%)	27 (51)
Disease duration before rituximab, weeks, median (SD; range)	88 (192.8; 8-793)
Rituximab administered within 1 year after symptoms, n (%)	16 (30)
Rituximab naive/nonnaive,* n (%)	45 (85)/8 (15)
Time between prior and current cycle, weeks, median (SD; range)	149 (66.0; 84-248)
Received M6 and M12,† n (%)	25 (47)
Systematic‡	19 (36)
Nonsystematic§	6 (11)
Previous therapies, n (%)	
Prednisone	51 (96)
Azathioprine	36 (68)
Mycophenolate mofetil	12 (23)
Dapsone	6 (11)
Methotrexate	3 (6)
HIVIG	1 (2)
Number of previous therapies, median (SD; range)	2 (0.8; 0-4)
Adjuvant therapies to which rituximab was added, n (%)	
Prednisone	42 (79)
Mean cumulative dose, mg, median (SD; range)	1777 (1975.5; 0-7110)
Azathioprine	13 (25)
Mycophenolate mofetil	7 (13)
Dapsone	2 (4)
Methotrexate	2 (4)
HIVIG	2 (4)

HIVIG, Human intravenous immunoglobulin G; *M6*, month 6; *M12*, month 12; *PF*, pemphigus foliaceus; *PV*, pemphigus vulgaris; *SD*, standard deviation.

*Nonnaive patients previously received 2 infusions of 500 mg of rituximab.

†Patients who received 500 mg of rituximab at months 6 and 12.

‡Patients who received M6 and M12 infusions as the standard procedure.

§Patients who received M6 and M12 infusions on clinical indication.

analyze the effectiveness of rituximab with and without maintenance infusions. Retrospective data were obtained from patients with pemphigus vulgaris and pemphigus foliaceus treated with rituximab between 2012 and 2017. Two infusions of 1000 mg were administered with an interval of 2 weeks (month [M] 0 and M1/2). From 2014, patients received additional maintenance infusions of 500 mg at M6 and M12 as the standard protocol (systematic infusions). Before 2014, M6 and M12 infusions were administered on clinical indication (nonsystematic infusions). The primary outcome was the relapse rate during the first 3 years after initial rituximab infusion, comparing patients with and without M6 and M12. Secondary outcomes were disease control, partial remission (PR), and complete remission on/off therapy[2] and adverse events according to the Common Terminology Criteria for Adverse Events grading system.

Fifty-three patients received M0 and M1/2 infusions, of whom 25 received additional M6 and M12 infusions. Table I summarizes the baseline characteristics. A total of 30 (57%) patients developed a relapse within the first 3 years after the M0 infusion, with a median time of 42 weeks (standard deviation, 41.6; range, 9-149 weeks). The relapse rate was significantly lower in the group with M6 and M12 infusions compared to the group without these infusions (n = 10 [40%] vs n = 20 [71%]; $P = .024$). Table II summarizes the clinical response, relapses, and prednisone dose per subgroup. No significant difference in relapse rate was seen between the group with systematic and nonsystematic infusions (Table II). In multivariate logistic regression, maintenance infusions at M6 and M12 were associated with a significantly lower relapse rate corrected for the following variables: pemphigus subtype, rituximab naive versus non-naive patients, disease duration before rituximab administration, and mean cumulative dose of prednisone (odds ratio, 0.126; 95% confidence interval, 0.024-0.667; $P = .015$) (Supplemental Table I; available via Mendeley at https://doi.org/10.17632/byrr3vppdm.1). All patients achieved disease control, of whom 12 (23%) patients achieved PR and 41 (77%) patients achieved CR. PR off therapy was achieved by 4 (8%) patients and CR off therapy by 30 (57%) patients. No significant differences in clinical response were seen between the pemphigus subtypes (Table II). Overall, 78% of the reported adverse events were mild, 15% were moderate, and 7% were severe, but none were life-threatening (Supplemental Table II; available via Mendeley at https://doi.org/10.17632/byrr3vppdm.1). No deaths occurred during follow-up.

In this study, additional maintenance infusions at M6 and M12 showed a beneficial effect in preventing relapses. Our study was limited by the heterogeneity of the study population and the absence of Pemphigus Disease Area Index scores. However, after correction for other variables related to disease severity, maintenance infusions were still associated with a significantly lower relapse rate.

Table II. Clinical endpoints and cumulative dose of concomitant prednisone in subgroups of patients with pemphigus treated with rituximab

Subgroups	DC, n (%)	PR, n (%)	PR off therapy, n (%)	CR, n (%)	CR off therapy, n (%)	TTR, weeks, median (SD; range)	Relapse, n (%)	Mean cumulative dose of prednisone, mg
PV	44 (100)	12 (27)	4 (9)	32 (73)	21 (48)	39 (25.6; 5-106)	27 (61)	1997
Mucocutaneous PV	27 (100)	6 (22)	2 (7)	21 (78)	14 (52)	33 (24.9; 12-106)	14 (52)	2103
Mucosal PV	17 (100)	6 (35)	2 (12)	11 (65)	7 (41)	45 (27.4; 5-92)	13 (76)	1852
PF	9 (100)	0 (0)	0 (0)	9 (100)	9 (100)	62 (48.8; 49-170)	3 (33)	970
M6 and M12 yes*	25 (100)	4 (16)	1 (4)	21 (84)	16 (64)	55 (36.8; 7-168)	10 (40)§	2625‖
M6 and M12 no*	28 (100)	8 (29)	3 (11)	20 (71)	14 (50)	39 (32.1; 5-170)	20 (71)§	928‖
Systematic M6 and M12†	19 (100)	1 (5)	1 (5)	18 (95)	13 (68)	49 (27.5; 17-109)	6 (32)	2326
Nonsystematic M6 and M12‡	6 (100)	3 (50)	0 (0)	3 (50)	3 (50)	69 (58.5; 7-168)	4 (67)	2045

CR, Complete remission; *DC*, disease control; *M*, month; *PF*, pemphigus foliaceus; *PR*, partial remission; *PV*, pemphigus vulgaris; *SD*, standard deviation; *TTR*, time to remission.
*Patients who received 500 mg of rituximab at both M6 and M12.
†Patients who received both M6 and M12 infusions as the standard procedure.
‡Patients who received both M6 and M12 infusions on clinical indication.
§$P = .024$. Denotes significant differences between patients who received M6 and M12 infusions versus patients without these infusions. All other variables did not show a significant difference between the subgroups.
‖$P = .023$. Denotes significant differences between patients who received M6 and M12 infusions versus patients without these infusions. All other variables did not show a significant difference between the subgroups.

Other studies[3-5] indirectly support the importance of maintenance infusions by reporting high relapse rates varying between 50% and 100% after treatment with rituximab without additional infusions. All patients in our study achieved remission, with the majority achieving CR, proving that rituximab is an effective treatment for pemphigus. In addition, only minimal severe adverse events were reported. These findings imply that maintenance treatment should be administered in all patients with pemphigus to prevent relapses.

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