

Pre-infusion checklist for rituximab in pemphigus vulgaris patients: clinical audit

Farah Sagheer,¹ Maham Kayani,² Elma Khalil³

Abstract

Objective: To evaluate whether or not the pre-infusion checklist for rituximab was followed in patients of pemphigus vulgaris.

Method: The audit, intervention and re-audit was conducted at the Dermatology Department, Medical Teaching Institution-Lady Reading Hospital, Peshawar, Pakistan, and comprised in-patients of pemphigus vulgaris, confirmed by skin biopsy and immunofluorescence, who received rituximab between January 1 to March 31, 2022. The randomly picked cases were reviewed to check if the standard guidelines for rituximab prior to infusion had been followed. After completion of the first audit cycle, the medical team was give awareness about the latest pre-infusion rituximab guidelines, and they were also provided with a checklist and consent form to implement the change. Re-audit was performed from May to July, 2022, using the same method to see if improvements had been made. Data was analysed using SPSS 23.

Results: Of the 20 cases evaluated against 16 parameters, the first audit showed 7(43.5%) parameters to have been met across all cases. Re-audit comprised another set of 20 cases, and showed that 15(93.75%) parameters had been applied across the board Pneumococcal and influenza vaccine was the only element 1(6.25%) not touching universal application.

Conclusion: Re-audit showed major improvement in compliance with the standard guidelines.

Key Words: Pemphigus vulgaris, Rituximab, Clinical audit, Pre-infusion guidelines.

(JPMA 73: 1663; 2023) DOI: 10.47391/JPMA.7742

Submission completion date: 11-08-2022— **Acceptance date:** 15-04-2023

Introduction

Clinical audits form the basis of quality assurance in the healthcare system, coming under the category of clinical governance. Every audit is standardised in accordance with local and international guidelines to improve patient care¹. Pemphigus is a rare autoimmune disease with flaccid blisters, bullae and erosions of skin and mucous membranes². Pemphigus vulgaris (PV) has an incidence of 0.1-3.2 cases in 100,000 per annum globally³. Treatment of this condition and its variants still stand as a major challenge for dermatologists around the world. Many drugs have been tested and approved over the years, including systemic corticosteroids and immunosuppressive agents (ISAs), but unfortunately, dual therapy with steroids used in combination with ISAs failed to show promising results in the majority with severe disease⁴⁻⁶. Anti-cluster of differentiation-20 (CD20) monoclonal antibody, such as rituximab, has shown a major impact in the management of this disease and, hence, has been accepted by the Food and Drug

.....
¹Department of Dermatology, Medical Teaching Institute, Lady Reading Hospital, Peshawar, Pakistan, ^{2,3}Department of Internal Medicine, Medical Teaching Institute, Lady Reading Hospital, Peshawar, Pakistan

Correspondence: Elma Khalil. Email: elmasalahuddin5@gmail.com

ORCID ID. 0009-0002-8268-0662

Association (FDA) as one of the first-line treatment choices for moderate to severe PV in 2018.⁷

Before starting rituximab, patients should be briefed on the pros and cons of the medication, expected outcome and possible adverse effects, such as severe immunosuppression, reactivation of hepatitis B virus (HBV) and new infections.⁸⁻¹¹.

The current study was planned to assess whether or not the pre-infusion guidelines for rituximab were being followed in PV in-patients in a tertiary care setting.

Materials and Methods

The audit, intervention and re-audit was conducted at the Dermatology Department, Medical Teaching Institution-Lady Reading Hospital (MTI-LRH), Peshawar, Pakistan, and comprised data of in-patients with PV, confirmed by skin biopsy and immunofluorescence, who received rituximab between January 1 to March 31, 2022. The audit was based on local¹² and international¹³ guidelines. The type of audit was process, and the sample source was online medical records and hand-written notes for diagnosed PV cases. Data related to randomly picked cases was noted using a pre-designed audit proforma. Data was compared against the pre-infusion criteria before the initiation of rituximab which had 16 elements based on literature¹¹⁻¹⁸.

After the initial audit, a meeting was held in the department to educate the doctors and nursing staff regarding the audit findings, and to improve the implementation of the standard guidelines to improve deficiencies of the first cycle. A re-audit comprising another set of randomly picked cases was done from May 1 to July 31, 2022, using the same methods after explaining and providing the doctors with pre-infusion checklist proforma and written informed consent forms. Data was analysed using SPSS 23.

Results

Of the 20 cases evaluated against 16 parameters, the first audit showed 7(43.5%) parameters to have been met across all cases. Re-audit comprised another set of 20

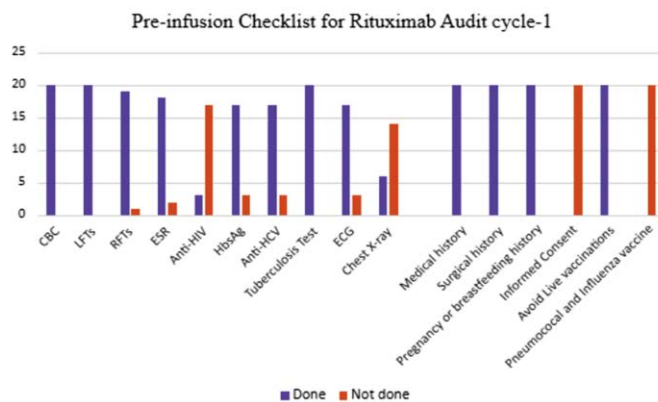


Figure-1: The first audit cycle.

CBC: Complete blood count, LFTs: Liver function tests, RFTs: Renal function tests, ESR: Erythrocyte sedimentation rate, HIV: Human immunodeficiency virus, HbsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, ECG: Electrocardiography.

Table: Percentages of each variable in audit and re-audit.

Parameters	Audit	Re-Audit
Complete blood count	100%	100%
Liver function tests	100%	100%
Renal function tests	95%	100%
ESR	90%	100%
Anti-HIV	15%	100%
HbsAg	85%	100%
Anti-HCV	85%	100%
Tuberculosis Test	100%	100%
ECG	85%	100%
Chest X-ray	30%	100%
Medical history	100%	100%
Surgical history	100%	100%
Pregnancy or breastfeeding history	100%	100%
Informed consent	0%	100%
Avoid live vaccinations	100%	100%
Pneumococcal and influenza vaccine	0%	75%

ESR: Erythrocyte sedimentation rate, HIV: Human immunodeficiency virus, HbsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, ECG: Electrocardiography

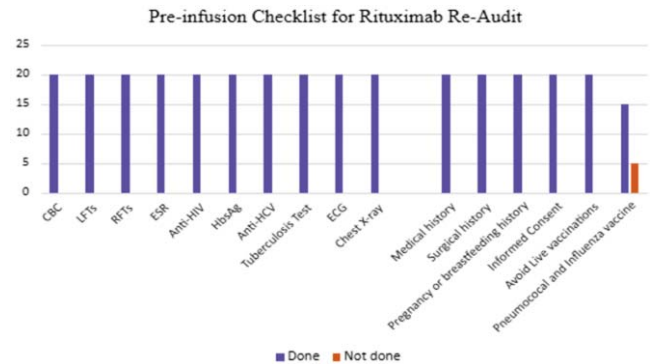


Figure-2: Post-intervention re-audit.

CBC: Complete blood count, LFTs: Liver function tests, RFTs: Renal function tests, ESR: Erythrocyte sedimentation rate, HIV: Human immunodeficiency virus, HbsAg: Hepatitis B surface antigen, HCV: Hepatitis C virus, ECG: Electrocardiography.

cases, and showed that 15(93.75%) parameters had been applied across the board. Pneumococcal and influenza vaccine was the only element 1(6.25%) not touching universal application (Table; Figures 1-2).

Discussion

A clinical audit forms an integral part of patient care by evaluating the healthcare system to improve overall outcome. Every hospital department should exercise conducting internal audits to enhance the quality of care¹⁹. Rituximab, a monoclonal antibody, was first developed with the intention of targeting cancer cells. Rituximab was later developed by the pharmaceutical sector and was approved by the Food and Drug Administration (FDA) in 1997 for treating non-Hodgkin's lymphoma after successful trials²⁰. In 2016, rituximab was ranked as the highest grossing anti-cancer therapy despite its lack of easy availability and high price. Since, rituximab has the ability to deplete normal and abnormal B-cells, it can be used to treat a range of autoimmune diseases and malignancies by immune suppression.

Use of rituximab for autoimmune disorders, such as rheumatoid arthritis (RA), was approved by the FDA in 2006. Due to its promising results, it has been rendered as one of the important treatment lines for controlling RA symptoms over the years. Furthermore, similar achievements have been obtained in cutaneous immunological disorders like PV²¹.

Pemphigus is an uncommon category of autoimmune diseases consisting of fluid-filled blisters on skin and mucous membranes. It can involve any part of the body, including mouth, eye, nose, throat and genitals. Among its many types, PV is the most common one. Traditionally, steroids and immunosuppressants are the mainstay of treatment and maintenance in PV cases.

Rituximab was licensed for PV management after a successful randomised controlled study in 2017, proving that there was a two-fold decrease in relapse rate and a three-fold higher remission rate in comparison to steroids⁸. As any medication, rituximab holds its fair share of pros and cons with side effects ranging from mild drug reaction to severe infections leading to death. These include infusion-related reactions, severe cutaneous manifestations, reactivation of HBV and progressive multifocal leukoencephalopathy. Therefore, keeping these potentially dangerous side effects in mind the American College of Rheumatology (ACR) has set down guidelines for the safe use of rituximab¹³.

The current study, done to assess compliance with the guideline, showed that important documentation like written informed consent was being taken lightly, and consent was being taken verbally instead. After explaining and providing the medical staff with the printout of consent forms, a 100% improvement was seen in the re-audit.

Rituximab, due to its immunosuppressive nature, has the power to make one prone to infections as simple as common cold to as deadly as pneumocystis jiroveci pneumonia (PJP), tuberculosis and hepatitis. Its immune-weakening phenomenon is also linked to reactivation of serious viral infections, like HBV and sometimes HCV. Moreover, a reduction in B cell count can be very dangerous for individuals positive for human immunodeficiency virus (HIV) as it makes them vulnerable to life-threatening infections. Initially, only 85% and 15% subjects were tested against hepatitis and anti-HIV, respectively, which improved to 100% by giving the medical team a checklist to avoid missing out on such important blood tests.

According to the ACR guidelines¹³, vaccination prior to rituximab prevents infections caused by bacterial (pneumococcal) and viral (influenza) organisms, like meningitis, pneumonia, sepsis and flu-like illness. The first cycle represented 0% practice for vaccination prior to infusion, but in the post-intervention re-audit, it rose up to 75%. However, all patients could not be vaccinated due to unavailability of the vaccination at the hospital pharmacy, its high cost, certain social beliefs, and inaccessibility at local stores. Comparing the findings of the audit and re-audit cycles, a major change from 43.5% to 93.8% was attained. Therefore, the aim now is to provide the pre-infusion vaccination free of cost at the hospital.

Conclusion

The audit showed 43.5% compliance with the set

parameters, but post-intervention re-audit registered 93.8% compliance over a span of 3 months.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Dilnawaz M, Iftikhar N. Departmental case notes audit: A quality assurance measure in a changing organizational climate. *J Pak Assoc Dermatol* 2018;27:279-81.
2. J Joly P, Horvath B, Patsatsi A, Uzun S, Bech R, Beissert S, et al. Updated S2K guidelines on the management of pemphigus vulgaris and foliaceus initiated by the european academy of dermatology and venereology (EADV). *J Eur Acad Dermatol Venereol* 2020;34:1900-13. doi: 10.1111/jdv.16752..
3. Yeh SW, Sami N, Ahmed RA. Treatment of pemphigus vulgaris: current and emerging options. *Am J Clin Dermatol* 2005;6:327-42. doi: 10.2165/00128071-200506050-00006.
4. Darling MR, Daley T. Blistering mucocutaneous diseases of the oral mucosa—a review: part 2. Pemphigus vulgaris. *J Can Dent Assoc* 2006;72:63-6.
5. Kasperkiewicz M, Schmidt E. Current treatment of autoimmune blistering diseases. *Curr Drug Discov Technol* 2009;6:270-80. doi: 10.2174/157016309789869065.
6. Tóth GG, Jonkman MF. Therapy of pemphigus. *Clin Dermatol* 2001;19:761-7. doi: 10.1016/s0738-081x(00)00190-5.
7. Business Wire. FDA Approves Genentech's Rituxan (rituximab) For Pemphigus Vulgaris. [Online] 2018 [Cited 2022 August 15]. Available from URL: <https://www.businesswire.com/news/home/20180607006256/en/FDA>.
8. Frampton JE. Rituximab: A Review in Pemphigus Vulgaris. *Am J Clin Dermatol* 2020;21:149-56. doi: 10.1007/s40257-019-00497-9.
9. Aksoy S, Harputluoglu H, Kilickap S, Dede DS, Dizdar O, Altundag K, et al. Rituximab-related viral infections in lymphoma patients. *Leuk Lymphoma* 2007;48:1307-12. doi: 10.1080/10428190701411441
10. Smalls DJ, Kiger RE, Norris LB, Bennett CL, Love BL. Hepatitis B Virus Reactivation: Risk Factors and Current Management Strategies. *Pharmacotherapy* 2019;39:1190-203. doi: 10.1002/phar.2340.
11. British Association of Dermatologists (BAD). Rituximab. [Online] 2019 [Cited 2022 August 15]. Available from URL: <https://www.bad.org.uk/pils/rituximab/>.
12. Burns DA, Breathnach SM, Cox N, Griffiths CEM. In: Burns T, Breathnach S, Cox N, Griffiths C, eds. *Rook's Textbook of Dermatology*, 8th ed. West Sussex, UK: Wiley Blackwell; 2010.
13. American College of Rheumatology (ACR). Medication Guide: Rituximab (Rituxan). [Online] 2022 [Cited 2022 August 15]. Available from URL: <https://www.rheumatology.org/learning-center/medication-guides/medication-guide-rituximab-rituxan>.
14. Buch MH, Smolen JS, Betteridge N, Breedveld FC, Burmester G, Dörner T, et al. Updated consensus statement on the use of rituximab in patients with rheumatoid arthritis. *Ann Rheum Dis* 2011;70:909-20. doi: 10.1136/ard.2010.144998.
15. Noormohammadpour P, Ehsani A, Mortazavi H, Daneshpazhooh M, Balighi K, Mofidi M, et al. Rituximab therapy improves recalcitrant Pemphigus vulgaris. *EXCLI J* 2015;14:109-16. doi: 10.17179/excli2014-603.
16. Leonardi CL, Heffernan MP, Gill JG. Rituximab and future biological therapies. In: Wolverton SE, eds. *Comprehensive Dermatologic Drug Therapy*, 3rd ed. Philadelphia, PA: Elsevier Inc, 2013; pp 333-341.e3. doi: 10.1016/B978-1-4377-2003-7.00027-3

17. American College of Rheumatology (ACR). Medication Guides. [Online] 2022 [Cited 2022 October 20]. Available from URL: <https://www.rheumatology.org/Learning-Center/Medication-Guides>.
 18. Ajithkumar K, Johny S, Salim P, Asokan N. Rituximab in pemphigus vulgaris-Standard operating procedure. *J Skin Sex Transm Dis* 2022;4:236-9. Doi: 10.25259/JSSTD_66_2020.
 19. Allen B. Internal audits can safeguard hospital revenue. *Healthc Financ Manage* 2013;67:106-8, 110, 112.
 20. Maloney DG, Liles TM, Czerwinski DK, Waldichuk C, Rosenberg J, Grillo-Lopez A, et al. Phase I clinical trial using escalating single-dose infusion of chimeric anti-CD20 monoclonal antibody (IDEC-C2B8) in patients with recurrent B-cell lymphoma. *Blood* 1994;84:2457-66.
 21. Pierpont TM, Limper CB, Richards KL. Past, Present, and Future of Rituximab-The World's First Oncology Monoclonal Antibody Therapy. *Front Oncol* 2018;8:163. doi: 10.3389/fonc.2018.00163.
-