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Outcomes of *Pemphigus* Treatments at the Royal Melbourne Hospital over 5 Years on Immune Suppressive Therapies used over this Time: A Retrospective Analysis

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Abstract

Background: Pemphigus is a rare, autoimmune blistering condition, resulting in significant morbidity and mortality. It warrants treatment by various immunosuppressive agents, which also contribute to significant morbidity and mortality. Newer treatment agents such as intravenous rituximab may be more effective or better tolerated. The aim of this study is to determine the patient responses to various Pemphigus treatments, and how these treatments have affected the patient's quality of life during their course of management.

Methods: All patients who have been treated for biopsy confirmed Pemphigus vulgaris at the Royal Melbourne Hospital qualified to have their medical records retrieved for the purposes of this quality assurance audit. The medical records of the entire cohort of 21 Pemphigus patients treated at the Royal Melbourne Hospital for Pemphigus vulgaris between May 2009 and May 2014 (inclusive) were retrieved for analysis. Relevant data pertaining to their particular Pemphigus treatment and how it affected their quality of life was extracted, as well as details regarding potential confounding factors, including medical co morbidities and concurrent medications. The PDAI (Pemphigus disease activity index) (Murrell et al. 2008) and the ABSIS (autoimmune bullous skin disorder intensity score) (Pfutze et al. 2007) were retrieved from each patient's record, with their scores being determined by the lesion extent and severity that was documented in the patient record template (Department of Dermatology, Royal Melbourne Hospital). PDAI and ABSIS values were recorded in Excel Database format as documented for each patient before their Pemphigus treatment was commenced, and upon their most current treatment review appointment. Both pre and post treatment ABSIS and PDAI scores were then analysed using SPSS (IBM, Armonk, NY, USA) statistical software.

Results: With the exception of 2 severe Pemphigus cases where treatment is ongoing, all of the Royal Melbourne Hospital patients have their Pemphigus treatments documented as significantly improving their overall quality of life. The relevant scoring of disease severity was markedly reduced across all subjects.

Conclusions: The treatment of Pemphigus vulgaris at The Royal Melbourne Hospital leads to significant improvement in the quality of life of its Pemphigus patients. Potential implications of this study may provide foundations for the development of a formal Pemphigus disease and treatment registry to enable adequate patient follow up and monitor their ongoing care. There is also potential for newer measures of Pemphigus treatment outcomes, which may be rigorously applied in dermatology clinics to allow a more objective measure of clinical treatment endpoints.

Keywords: *Pemphigus vulgaris*; Quality of life; Treatment; Autoimmune bullous disease

Abbreviations: ABSIS: Autoimmune Bullous Skin Disorder Intensity Score; ICC: Intra-class correlation coefficient; PDAI: Pemphigus Disease Activity Index; QOL: Quality of life; TABQOL: Treatment of Autoimmune Bullous Disease Quality of Life [Questionnaire]; TX: Treatment; DLQI: Dermatology Life Quality Index

Introduction

Pemphigus is a rare and blistering autoimmune skin dermatosis resulting in significant morbidity and mortality. The treatment of *Pemphigus* consists of various systemic immunosuppressive agents, which contribute to significant morbidity and mortality in their own regard. Ideally, the risks of immunosuppressive treatment should be outweighed by their benefits in improving and preventing mucocutaneous blistering and ulceration. However, adverse effects of systemic immunosuppression given for the treatment of *Pemphigus* may cause significant detriment to a patient's quality of life in addition to the distress caused by their *Pemphigus* in the first instance. The Department of Dermatology at the Royal Melbourne Hospital has continuously provided a tertiary treatment facility for the management of this rare, autoimmune blistering dermatosis. This study aims to evaluate the quality of care provided to *Pemphigus* patients at this treatment facility over the past 5 years, and evaluate how the treatments provided have affected the patient's quality of life.

To date, no clinical audit undertaken at the Royal Melbourne Hospital has evaluated the patient's perspective regarding the standard of care specific to *Pemphigus* treatment. Other institutions which aim to achieve this have used their own derived measures which may not necessarily be applicable to the patient cohort at the Royal Melbourne, as its patients display wide variation in the magnitude of *Pemphigus* disease severity, with complex comorbidities [1].

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The earliest literature which aimed to evaluate the quality of life in response to the disease burden of *Pemphigus vulgaris* was published by Pfutze et al. [2], whereby the authors produced an Autoimmune Bullous Skin Disorder Intensity Score (ABSIS) aiming to ascertain both the extent of *Pemphigus* lesions, and the degree to which they impaired the subject's ability to eat certain textured foods. Murrell et al. [3] also formed an International Consensus Statement the following year, after which the *Pemphigus* Disease Activity Index (PDAI) was produced in attempt to quantify the severity of *Pemphigus* lesions. Despite the fact that numerous scoring tools exist to objectively quantify the *extent* of *Pemphigus* lesions, few studies evaluate or derive tools to measure the subjective impact of the disease and how its treatment has affected the patient's life. The resultant quality of life impact may not necessarily correlate with lesion resolution alone. Cosmesis, secondary infection, post inflammatory hyperpigmentation and adverse effects of specific treatment may all play a role in adversely affecting a patient's experience upon receiving treatment for *Pemphigus vulgaris*.

This study will use the values obtained by the PDAI and ABSIS located within each patient's record in attempt to objectively quantify the subjective treatment outcomes of *Pemphigus* patients at the Royal Melbourne Hospital. The PDAI and ABSIS have been independently validated in their own right with their reliability affirmed [4,5]. In particular, the PDAI has been found to closely correlate with the Physicians Global Assessment scale, thereby making it a useful tool to provide numerical data for the purposes of our study. In spite of the fact that neither the PDAI nor the ABSIS are specifically treatment related, their assessment both before and after the implementation of various treatment regimens is useful to determine the impact of treatment upon disease resolution and the ability for our patients to enjoy certain foods, which indirectly correlate with quality of life outcomes. It could be extrapolated that the magnitude of quality of life detriment would be greater the higher the patient's PDAI and ABSIS scores.

Study Aims and Objectives

This study will aim to identify whether quality of life has improved in response to treatments administered for patients with biopsy proven *Pemphigus vulgaris* at the Royal Melbourne Hospital Department of Dermatology over the past 5 years.

The clinical implications of the data analysis will be used to ensure that the highest level of patient care is upheld as current standard, whilst any detriment to the patient as a consequence of their treatment is kept to a minimum.

Clinical efficacy of each *Pemphigus* treatment regimen will also be taken into consideration, with optimal quality of life being the primary treatment outcome. The predominant treatment modalities for *Pemphigus vulgaris* at the Royal Melbourne Hospital have consisted of systemic prednisolone, with the addition of several steroid-sparing agents including azathioprine, cyclosporine, methotrexate, mycophenolate mofetil, and intravenous immunoglobulin (IVIG). More recently, intravenous rituximab has been used in the management of severe *Pemphigus vulgaris* refractory to former treatment. Each patient will have his or her tailored regimen recorded anonymously in order to determine if there are specific quality of life impairments that occur in response to a certain treatment, or if one treatment modality is superior to another as it may yield greater improvements in quality of life.

The total financial cost of treatment will be analysed from the raw data as a secondary treatment outcome, with the total length of treatment for each patient recorded anonymously in treatment days calculated as the total difference between their first and most recent visit to the Dermatology department at the Royal Melbourne Hospital.

Methods

This study was granted ethical approval by meeting the criteria for a Quality Assurance/Negligible Risk Research project as outlined by the Human Research Ethics Committee of the Royal Melbourne Hospital (QA project 2012132). Our study endeavoured to assess the impact of *Pemphigus* treatment on the quality of life of all patients at the Royal Melbourne Hospital who have received treatment for biopsy confirmed *Pemphigus vulgaris* between May 2009 and May 2014 (inclusive). The total sample of 21 Royal Melbourne Hospital patients with biopsy confirmed *Pemphigus vulgaris* on immunofluorescence had their medical records retrieved from the Health Information Services Department of the Royal Melbourne Hospital for the purposes of data collation regarding their *Pemphigus* treatment and clinical progress.

In order to evaluate their quality of life as it pertained to their *Pemphigus* treatment, the PDAI and ABSIS scoring systems were used as an indirect clinical measure of patient quality of life. At present, these clinical measures are the most relevant tools that possess the ability to provide numerical values that may directly correlate with the degree of quality of life disturbance. The PDAI was used with the assumption that a greater extent of *Pemphigus* lesion distribution and post inflammatory damage correlates directly with more detrimental quality of life impact with respect to cosmetic appearance. The ABSIS was applied with the inference that a higher score is indicative of greater cutaneous and intraoral involvement and hence quality of life impairment has occurred due to the patient's inability to enjoy certain foods.

Reliability and convergent validity of the PDAI and ABSIS has been evaluated by Rosenbach and colleagues in which they reported the intra-class correlation coefficient (ICC) with 95% confidence interval to be 0.98 (0.96-1.0) for the PDAI, and 0.80 (0.65-0.96) for the ABSIS, inferring a high degree of accuracy in the physician's agreement between their initial test scoring and re- rating of the same subject [6]. The authors also concluded the validity of each scoring system in relation to the physician's global assessment scale (PGA), where the PDAI was reported to have a correlation of 0.60 (0.49-0.71), and the ABSIS having a correlation of 0.43 (0.30-0.55).

The PDAI and ABSIS scores as they had been noted in the patient records were obtained both before the patient's treatment was commenced, and after their treatment had been weaned. If the patient in question was still receiving ongoing treatment during the end of the 5 year analysis period, then their most current PDAI and ABSIS values were recorded as their clinical endpoint achieved as of May 2014. The resulting PDAI and ABSIS values were grouped into pre-treatment and current PDAI and ABSIS values within a Microsoft Excel Spreadsheet, along with total treatment duration (days). The pre and post PDAI and ABSIS values were later exported into the statistical program IBM SPSS Statistics Version 22 (IBM, Armonk, NY, USA) and a standardised *T-test for paired samples* was performed, due to the fact that the same sample of *Pemphigus* patients were scored at 2 separate intervals by each of the PDAI and ABSIS systems, and the raw data for each of the pre-treatment scores was evenly distributed.

Secondary outcomes were also extracted anonymously for each patient from the raw data, including any outlying adverse treatment outcomes additional to the common treatments adversely affecting

quality of life, total duration of treatment (recorded as total treatment days) for each patient, and the magnitude of difference between pre-treatment and post treatment PDAI and ABSIS scores. Confounding factors were also recorded, including any associated patient co morbidities and corresponding treatments that may additionally detract from quality of life, despite the fact that such treatments were unrelated to the patient's treatment for *Pemphigus vulgaris*.

Results

The *Paired Samples T-test* was conducted as all of the 21 patients were scored by the same PDAI and ABSIS systems both before and after their *Pemphigus* treatment was administered. The *T-test* was also implemented due to the fact that the raw pre and post treatment scores were evenly distributed, making the resultant data relatively symmetrical.

In the case of the PDAI scores, the mean "most recent" PDAI was 7.333, which was significantly lower than the mean pre- treatment PDAI of 47.762. The mean *difference* between the pre and post treatment PDAI scores was found to be 40.4286, with the calculated p *value* (Sig.) markedly less than 0.05 (Sig .000), making this a significant reduction in PDAI score in response to *Pemphigus* treatment.

Similarly, the most recent ABSIS score had a mean value of 6.952, which was also markedly lower than the mean pre- treatment ABSIS score of 63.6976. The mean difference between pre and post ABSIS scores was calculated to be 56.74524, making it statistically significant (with a p value <0.05). In addition, the mean difference between pre and post treatment ABSIS scores (56.74524) was greater than that obtained by the paired difference in the PDAI scores (40.4286), which could infer that despite the persistence of erosive lesions and post inflammatory hyper pigmentation, the overall impairment to quality of life was still reduced overall.

Many patients received multiple systemic therapies throughout the course of their treatment. The adverse effects in response to each treatment regimen were also recorded retrospectively as they were documented within the patient's record (Table 1). There was significant morbidity and consequent quality of life impairment in response to azathioprine and systemic prednisolone in particular. Mycophenolate mofetil was found to have a markedly fewer incidences of side effects, in comparison to systemic prednisolone. In contrast, no adverse events or detrimental treatment related quality of life impairment was noted in response to intravenous rituximab, with the dosing regimen documented for each patient (Figures 1 and 2).

Discussion

Statistical analyses of the differences in PDAI and ABSIS before and after treatment are consistent with a vast improvement in both resolution of clinically apparent disease and a high magnitude of quality of life benefit due to the administration of multiple pharmacotherapies.

19 of the 21 *Pemphigus* patient cohort reported immense satisfaction and gratitude with respect to their *Pemphigus* treatment, quoting that it had led to a significant quality of life benefit since treatment of their *Pemphigus* had commenced at the Royal Melbourne Hospital. Six of the seven eligible patients on rituximab therapy had attained PDAI and ABSIS scores that were either 0 (corresponding to complete disease resolution) or very low, with scores ranging from 1-7, which represented post inflammatory hyper pigmentation of resolved lesions. The only other patient (Table 2) receiving rituximab is currently mid treatment, awaiting clinical lesion re epithelialisation at the time of publication. The post-treatment ABSIS score for this patient remained elevated due to the oropharyngeal distribution of their remaining lesions, resulting in difficulty with drinking and eating textured food, and hence a greatly diminished quality of life. Although these subjective measures can be a crude means of scoring, the PDAI and ABSIS scores were used in combination in attempt to objectively quantify quality of life benefit. The importance of using such scoring systems has been reinforced in prior literature, namely through the work of Murrell et al. [7] in which the necessity to score bullous diseases clinically is advocated.

Adverse treatment effects	Prednisolone (systemic)	MMF	IVIG	Rituximab	Azathioprine	Total Patient Cases
Sleep Disturbance	3					3
Increased appetite	4					4
Weight gain	3					3
Increased BSLs	2					2
Lethargy	3	1				4
Agitation/irritability	2					2
Osteopaenia/osteoporosis	9					9
Lymphopaenia	1				**1***	2
Oral candidiasis	7					7
Spontaneous Ecchymoses	2					2
Gastric upset (nausea/vomiting/diarrhoea)	3	4				7
Flare of infection (orchitis, CMV, HSV)	4	4			1	9
Flare of Acne	1					1
LFT derangement		2				2
Shortness of Breath	1	1				2
Cushingoidfacies	5					5
Post inflammatory hyperpigmentation	3	4		1		8
Patient perceived effects (discomfort/distress)	2	2				4
Unaffordability				1		1
Total side effect cases for each treatment	55	20		2		77
Total patients (receiving treatment for pemphigus vulgaris)	21 (n)	17	2	7		
n=total sample of patients with biopsy proven pemphigus vulgaris						
*severe life threatening lymphopaenia (<0.2) with reduced T-cell subsets (CD4 and CD8 counts) for single case of MMF tx						

Table 1: Distribution of adverse treatment effects encountered on most common systemic therapies for the management of Pemphigus Vulgaris.

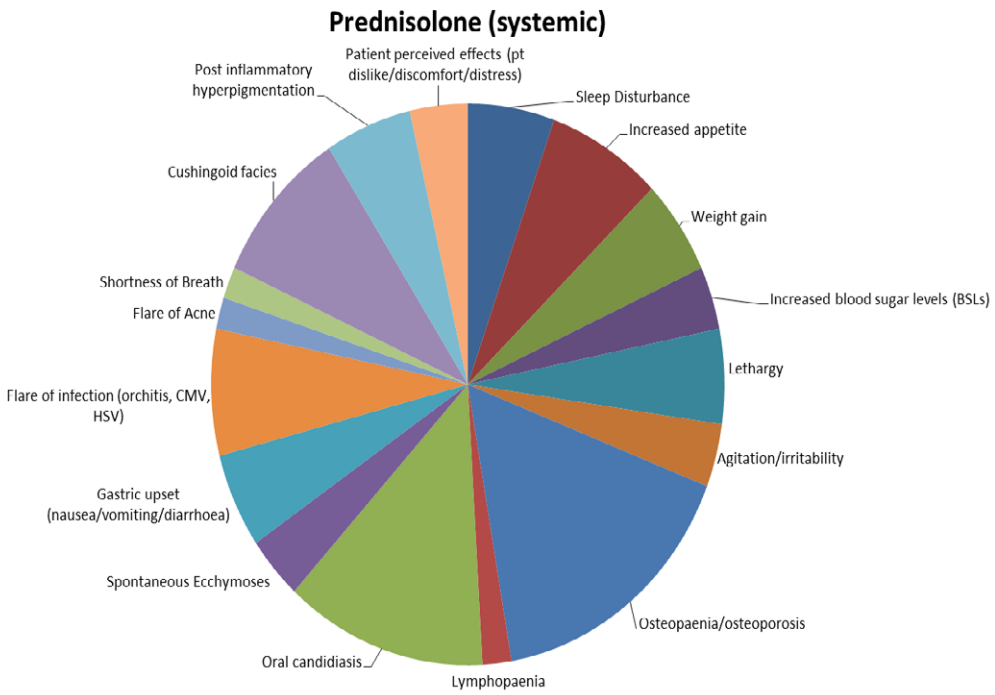

Figure 1: Treatment related effects of systemic prednisolone.

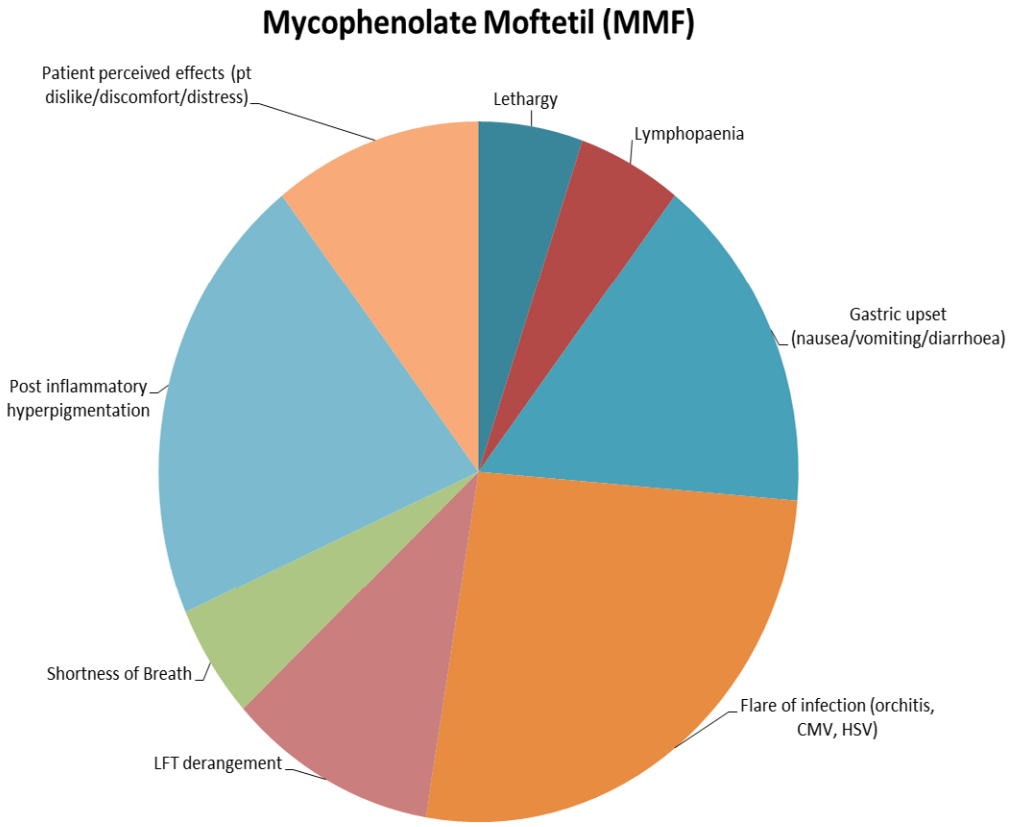

Figure 2: Treatment related effects of mycophenolatemofetil.

Pt No.	Rituximab Dose	Date Administered	Other Pv Medications	Pre Tx Pdai	Pre Tx Absis	Post Tx Pdai	Post Tx Absis	Total Tx Days
1	500 mg infusion (375 mg/m^2)	3/03/2014	IVIG 2 g/kg, MMF 1 gBD, Prednisolone 50 mg (weaned to 12.5), Valgancyclovir 450 mg BD, azathioprine 100 mg ceased (2012-2014)	36	55.65	29	48	112
	500 mg infusion (375 mg/m^2)	17/03/2014						
2	500 mg infusion (375 mg/m^2)	28/11/2012	MMF 1 g BD, Prednisolone 75 mg	57	122	0	0	674
	500 mg infusion (375 mg/m^2)	12/12/2012						
3*	500 mg infusion (375 mg/m^2)	12/04/2012	Azathioprine (ceased), Prednisolone 3 g/d, MMF 1.5 g BD	31	45	0	0	728
	500 mg infusion (375 mg/m^2)	26/04/2012						
	500 mg infusion (375 mg/m^2)	1/09/2013	***Patient qualified for second rituximab treatment course due to recurrence of clinically active disease**					
	500 mg infusion (375 mg/m^2)	15/09/2013						
4	500 mg infusion (375 mg/m^2)	30/11/2012	Prednisolone 25 mg→4 mg/d, MMF 3.5 g/d (4x tabs mane, 3 tabs nocte)	80	56	2	2	511
	500 mg infusion (375 mg/m^2)	14/12/2013						
5*	500 mg infusion (375 mg/m^2)	21/09/2012	Azathioprine (contraindicated due to ↑↑ALP and GGT), Prednisolone 25 mg/d, MMF 1 g BD	84	62.5	7 (due to PIHP ONLY)	0	702
	500 mg infusion (375 mg/m^2)	6/10/2012						
	750 mg IV infusion	25/04/2013	***Patient qualified for second rituximab treatment course due to recurrence of clinically active disease**					
	750 mg IV infusion	10/05/2013						
6	500 mg infusion (375 mg/m^2)	29/09/2011	MMF 500 mg BD	10	47	2	1	792
	500 mg infusion (375 mg/m^2)	14/10/2011						
7	500 mg infusion (375 mg/m^2)	13/10/2011	MMF 1 g mane, 500 mg nocte, Prednisolone. Azathioprine (contraindicated due to lymphopaenia)	47	69	4	2	910
	500 mg infusion (375 mg/m^2)	27/10/2011						

Table 2: Pemphigus Vulgaris Patients managed with Rituximab at the Royal Melbourne Hospital.

14 of our 21 patients had a final ABSIS score of 5 or lower, which may be due to the fact that there is minimal quality of life impairment from their treated *Pemphigus*, or that their disease has completely resolved in the absence of post inflammatory hyperpigmentation. The remaining 7 patients are still on low dose immunosuppressive therapies warranted for ongoing *Pemphigus*, either intra-orally or in aesthetic sites of the face, neck and scalp. Their corresponding doses of agents including prednisolone and MMF have been titrated such that the patient's quality of life is minimally affected, or not affected at all. In 2 cases, patients reported their preference to remain on low dose MMF therapy prophylactically as there is no impairment to their quality of life, and the decreased likelihood of a *Pemphigus* flare is reassuring [8].

The use of the PDAI and ABSIS as quality of life evaluation tools within this study is justified by the data in support of their reliability and convergent validity as reported by Rosenbach et al. [6] Validity and reliability of the PDAI and ABSIS measures used within this study was also investigated by Rahbar et al. [9], in which they compared the inter-raterreliabilities and convergent validity between the PDAI, ABSIS and *Pemphigus vulgaris* Activity Score (PVAS) upon cross sectional evaluation of 100 patients. The authors concluded that the PDAI and ABSIS displayed the highest inter- rater reliability. They confirmed that the PDAI had the highest validity of the three measures, and recommended the PDAI for use in multicentre studies for rare diseases, such as *Pemphigus vulgaris*.

Given that *Pemphigus* is a rare autoimmune disease with a relatively small incidence in the Victorian population, the patient cohort under review in this study does not provide a large enough sample size from which *statistically* powerful data could be derived. Despite this, the *clinical* significance obtained from studying the management outcomes of this 21-patient cohort provides an insightful representation of the clinical endpoints achieved at the Royal Melbourne Hospital's Department of Dermatology.

In spite of a finite catchment period for this retrospective study, the total treatment durations differed for every patient. Many of the adverse impacts of *Pemphigus* treatment are duration dependent; as the patient had a greater likelihood of developing adverse effects the longer they were on immunosuppressive therapies. A longer duration of treatment also had increased likelihood of negative impaction on the patient's quality of life due to increased financial strains. There was also

increased financial burden on the hospital system whereby rituximab was administered intravenously, and hospital admission required accordingly.

Numerous confounding factors were also present as they may have undermined the relevance of using the PDAI and ABSIS as quality of life measurement tools. In particular, the fact that several patients did *not* initially present with *oral Pemphigus* lesions rendered the "Severity" section of the ABSIS redundant in estimating the detriment to their quality of life.

Additional sources of confounding could also have arisen due to some patients having oral lesions that may have been erroneously mistaken for *Pemphigus vulgaris*. One patient displayed concurrent oral lichen planus on their buccal mucosa, another suffered from recurrent oral apthuous ulcers and herpes simplex stomatitis. Such oral pathologies may have falsely elevated the scores recorded in their PDAI and ABSIS by contributing to higher oral pain and lesion distribution scores; hence quality of life would still remain adversely affected although the reason for this was not the patient's *Pemphigus* lesions. Scoring error may also be due to other medications prescribed for patients for other comorbidities [10]. Systemic prednisolone was prescribed for 3 of the 21 patients in order to symptomatically manage inflammatory arthropathies, and resulted in greater incidence of adverse effects and significant morbidity and mortality despite the fact that these treatments were not initially prescribed for the treatment of the patient's *Pemphigus vulgaris*.

Few outlying cases existed within our patient cohort in which treatment responses showed significant variation from the mean PDAI and ABSIS values. Such cases included a rare but potentially lethal adverse effect in which administration of azathioprine resulted in severe lymphopaenia in which T- lymphocyte subset counts decreased to <0.2 ($\times 10^9$/L). Subsequently, the systemic azathioprine was ceased and replaced with mycophenolatemofetil.

The clinical safety of mycophenolatemofetil as it used in the treatment of dermatoses and the resultant patient quality of life has been an ongoing issue of contention documented throughout prior literature. A review article published in the Journal of Dermatological Treatment by Doukaki et al. [11] noted the prinicpal adverse effects of MMF consisted of gastrointenstinal toxicity, lymphopaenia and neutropaenia, and increased rates of specific infections. They concluded that MMF in combination with steroids was effective and safe in the medium term; however they also suggested "larger studies need to be performed to establish appropriate therapeutic dosages in *Pemphigus* patients." When combined with the findings of Doukaki et al. our study attempts to provide further insight with respect to the adverse treatment effects and quality of life impact related to mycophenolatemofetil in the management of *Pemphigus*, in combination with other immunomodulatory therapies.

A previous systematic review published in the Cochrane Library by Martin et al. [12] agreed that mycophenolate is a promising steroid sparing agent in the treatment of *Pemphigus* , however its use requires further evaluation since its effect on relapse of flares, severity scores, and quality of life has not been assessed.

Treatment of *Pemphigus* with rituximab infusions appeared to significantly improve quality of life within the cohort of this study, provided it was used in refractory cases of *Pemphigus vulgaris* that were resistant to other immunosuppressive therapies. No significant adverse effects specific to rituximab use were reported amongst the seven patients receiving rituximab therapy [13,14].

The clinical efficacy of rituximab has been documented extensively within prior literature. A retrospective cohort study of 47 *Pemphigus* patients conducted by Leshem et al. [15] reported immediate post-infusion *Pemphigus* exacerbations in four cases, and severe infusion reactions reported in two cases. The patients within their cohort had received higher doses of rituximab therapy which consisted of two 1000g infusions on days 1 and 15, in addition to their concurrent immunosuppressive medications, which is significantly greater than those used in our patient cohort [16].

None of the seven patients within our study reported such effects, possibly due to the fact that our rituximab treatment protocol included dosages far lower than those reported in prior studies. Our treatment protocol is consistent with that reported by Horváth et al. [17] in which our patients with *Pemphigus* are treated with a single course of two infusions of rituximab (500 mg each, or 375mg/m^2) at an interval of 14 days between each rituximab infusion. Horváth et al. [17] concluded such a protocol to be effective and safe in the treatment of *Pemphigus*. Despite the infrequent cases of relapse in clinical disease, we believe our *Pemphigus vulgaris* rituximab protocol is justified on the basis of optimising our patient's quality of life and cost effectiveness of treatment, which is in accordance with the clinical endpoints achieved in their standard of care.

This study is supportive of a multimodal approach to immune modulatory therapy for the management of *Pemphigus vulgaris* in order to optimise patient quality of life. Significantly fewer adverse effects occurred in response to treatment with mycophenolate mofetilin comparison to prednisolone. Fewer adverse effects were associated with rituximab, rendering it the most favourable steroid sparing agent from the perspective of patient quality of life [18,19]. The only detrimental effect of rituximab within our cohort was the residual post inflammatory hyper pigmentation after the infusions of rituximab had ceased. This however would be more likely a consequence of the initial magnitude of severity of the *Pemphigus* disease process itself, rather than an adverse effect of the intravenous rituximab infusion.

Future Implications

This study is the first of its kind to provide clinically significant insights into how treatment regimens have affected the quality of life of the Royal Melbourne Hospital's cohort of patients with biopsy proven *Pemphigus vulgaris*.

In view of the limitations of the PDAI and ABSIS that have been found throughout the undertaking of this study, there exist strong clinical indications for a more concise and patient friendly quality of life measure to be derived for routine application within the Department of Special Dermatology at the Royal Melbourne Hospital. Collation and analysis of medical record derived data for these patients could potentially lead to the formulation of a *Pemphigus* disease registry in the State of Victoria. This would be vital to ensure uniform and clinically superior standards of patient care are achieved with respect to the assessment and management of this rare disease.

Future cost-benefit analyses of the data derived from the patient registry could allow for the establishment of state wide hospital protocols specific to the treatment of *Pemphigus*. This would ensure the lowest possible, yet most effective medication dosages are administered, especially in the case of newer agents including rituximab.

Conclusion

The responses to the treatment of biopsy proven *Pemphigus vulgaris*

at the Royal Melbourne Hospital have been extremely favourable, with the majority of the *Pemphigus* patients reporting significant improvement in their quality of life and overall satisfaction with their level of tailored care on multiple immune modulatory therapies. Furthermore, there appears to be a significant reduction in clinical scores which directly correlate with disease severityand quality of life impairment, as a result of the treatment regimens administered at the Royal Melbourne Hospital for the management of this debilitating dermatosis.

Consequently, various adverse effects of treatment have been monitored and appropriately documented as part of a *Pemphigus* patient registry. As a result, these adverse effects may be anticipated and minimised in future treatment cases in order to augment the levels of care and quality of life for future *Pemphigus* patients.

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