

Corticosteroid Use in Autoimmune Blistering Diseases

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KEYWORDS

- Pemphigus • Pemphigoid • Linear IgA dermatosis
- Autoimmune blistering diseases • Corticosteroids

Corticosteroids have been used in the management of autoimmune blistering diseases (AIBD) for more than 50 years, and are an essential component in the pharmacologic management of these conditions. While providing rapid remission and ongoing control of the symptoms of AIBD, they come with a variety of potentially serious acute and long-term side effects. The advent of immunomodulating and immunosuppressive therapies has complemented the use of corticosteroids but have not usurped its pivotal role. The advent of evidence-based medicine (EBM) has reevaluated the various types of corticosteroids and forms of corticosteroid delivery in AIBD to ascertain whether any advantages of specific delivery systems or regimens exist. With rare diseases such as those that comprise AIBD, large randomized controlled trials are difficult to coordinate and accomplish, meaning a paucity of high-level evidence exists as to the best methods of corticosteroid use in these conditions. Experience and evidence from cross-discipline use of corticosteroids shows that careful monitoring of patients and simple preventive measures are effective in minimizing the adverse outcomes associated with their use. This article attempts to outline the current level of evidence for corticosteroid use in a variety of AIBDs, and discusses appropriate investigations and interventions to minimize or prevent the associated adverse effects.

PHARMACOLOGY OF CORTICOSTEROIDS

Corticosteroids are based around the cyclopentano-penanthrene nucleus, a conjoined series of three 6-carbon rings and one 5-carbon ring, a base structure shared by cholesterol and sex hormones.¹ All corticosteroids exhibit a double bond between

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carbon atoms 4 and 5, as well as two ketone groups, attached to carbon atoms 3 and 20, which distinguish them from other cholesterol-based compounds. Different corticosteroids differ by their differing functional groups attached to the core ring structure as well as the oxidation state of the carbon atoms comprising the rings. General additions that increase corticosteroid potency include the insertion of a double bond between carbon atoms 1 and 2 (as in prednisone); the fluorination of carbon atoms 6 or 9 (as in clobetasol or dexamethasone); and the addition of a hydroxyl group at carbon atom 11 (as in clobetasol).¹

Corticosteroids act through binding to glucocorticoid-specific receptors and altering transcription factors as well as diffusing through the cell membrane and acting directly on the cell nucleus.² Inflammatory inhibition is mainly achieved through the interaction with and inhibition of nuclear factor κ B transcription factor, suppressing the production of chemokines and cytokines. Suppressed mediators include cyclooxygenases (COX), interleukins (IL) 1 through 6, tumor necrosis factor (TNF)- α , and macrophage colony stimulating factor. Although all of the exact mechanisms controlling the plethora of side effects of corticosteroids have not yet been elucidated, it is believed the majority of them are controlled through cyclic adenosine monophosphate-mediated pathways.² The end result is cytokine suppression, eosinopenia, lymphopenia, and monocytopenia. Neutrophilia is also observed. However, this is thought to be indirectly attributable to the decreased ability of neutrophils to migrate to the sites of inflammation due to cytokine suppression; neutrophil apoptosis is delayed as a result, contributing further to neutrophilia.²

Regarding the pharmacokinetics of corticosteroids, when prednisone is consumed orally it must be reduced enzymatically in the liver to prednisolone (the active product); this is done through reduction of a ketone group by the enzyme 11 β -hydroxysteroid dehydrogenase. Consequently, patients with hepatic dysfunction may have impaired conversion of prednisone to active prednisolone.³ In these circumstances, administration of prednisolone would be more beneficial than prednisone in achieving the desired serum concentrations necessary for treatment. In patients with otherwise normal hepatic function, prednisone and prednisolone are drugs of equivalency. A table of steroid equivalencies for those drugs used in AIBDs is presented in [Table 1](#).¹⁻⁴ With regard to conversion rates, serum concentrations for systemic steroids are roughly consistent. Measurements of equivalency for topical steroids have a much wider range than systemic steroids because, dependent on the site of measurement in the skin of the active ingredient, concentrations differ.³ The measurements presented in [Table 1](#) are taken from studies wherein concentrations were measured in the dermis or at the dermoepidermal junction—the site of activity of disease and immune suppression. Consequently, concentrations in the epidermis would be much higher for topical steroids.

RESPONSIVENESS OF AIBD TO CORTICOSTEROIDS

Pemphigus Vulgaris/Pemphigus Foliaceus

Steroids have been used as the cornerstone of pemphigus management for more than 50 years.⁵ The different types of corticosteroids used in pemphigus include oral prednisone/prednisolone as a continuous dosage for remission or maintenance therapy, and dexamethasone as used in oral pulsed dosage for remission and topical application for local or mucosal disease.⁶ [Table 2](#) presents the current recommendations and levels of evidence available for corticosteroid use in AIBD. A recent systematic review and meta-analysis⁵ examined a randomized controlled trial (RCT) of 22 participants comparing low-dose (45–60 mg/d) with high-dose (120–180 mg/d) oral prednisolone in a cohort of newly diagnosed pemphigus vulgaris (PV) and pemphigus foliaceus

Table 1
Equivalence table of different forms of corticosteroids used in AIBDs

Steroid Used		Converting To:					
		Prednisone/ Prednisolone ^a	Oral Dexamethasone	Intravenous Dexamethasone	Intravenous Hydrocortisone	Topical Betamethasone Valerate (0.1%) ^b	Topical Clobetasol Propionate (0.05%) ^b
Converting from:	Prednisone/ prednisolone ^a	Multiply by 1 mg/kg/d	Multiply by 0.12 mg/kg/d	Multiply by 0.196 mg/kg/d	Multiply by 16 mg/kg/d	Multiply by 0.48 mg/kg/d	Multiply by 360 mg/kg/d
	Oral dexamethasone	Divide by 0.12 mg/kg/d	Multiply by 1 mg/kg/d	Multiply by 0.61 mg/kg/d	Multiply by 133 mg/kg/d		
	Intravenous dexamethasone	Divide by 0.196 mg/kg/d	Divide by 0.61 mg/kg/d	Multiply by 1 mg/kg/d			
	Intravenous hydrocortisone	Divide by 16 mg/kg/d	Divide by 133.3 mg/kg/d		Multiply by 1 mg/kg/d		
	Topical betamethasone valerate (0.1%) ^b	Divide by 0.48 mg/kg/d				Multiply by 1 mg/kg/d	
	Topical clobetasol propionate (0.05%) ^b	Divide by 360 mg/kg/d					Multiply by 1 mg/kg/d

^a Prednisone and prednisolone are assumed to be equivalent.

^b Equivalence based on dermal concentrations.

Data from Refs. 1-4

Table 2

Recommendations and level of evidence for corticosteroid use in autoimmune blistering diseases

Type of Corticosteroid	Recommendations and Level of Evidence				
	Pemphigus	Bullous Pemphigoid	Mucous Membrane Pemphigoid	Linear IgA Dermatoses	Epidermolysis Bullosa Acquisita
Prednisone/ prednisolone (oral)	A (2–3) Basic pillar of therapy. Optimal regimen (high dose vs low dose) unknown with current evidence	C (1) Can be used if topical unfeasible (evidence of deleterious effect compared with topicals in severe disease)	C (3)	I (3)	C (3) Associated with increased mortality and adverse effects
Dexamethasone (intravenous pulsed)	C (2–2) No evidence supporting its use over oral corticosteroids. Experts recommend use in recalcitrant disease	N/A	N/A	N/A	C (3) Use in intractable or severe disease
Dexamethasone (Mouthwash)	N/A	N/A	B (3)	N/A	N/A
Clobetasol propionate (0.05%)	C (3) Localized or mild disease	A (1) Recommended for severe disease over systemic corticosteroids based on 12-mo mortality rates	C (3)	I (3)	N/A
Betamethasone (topical)	C (3)	N/A	I (3)	I (3)	N/A

Key to Recommendations and Level of Evidence**Recommendations:**

Level A: Good scientific evidence suggests that the benefits of the clinical service substantially outweigh the potential risks

Level B: At least fair scientific evidence suggests that the benefits of the clinical service outweigh the potential risks

Level C: At least fair scientific evidence suggests that there are benefits provided by the clinical service, but the balance between benefits and risks are too close for making general recommendations

Level D: At least fair scientific evidence suggests that the risks of the clinical service outweigh potential benefits

Level I: Scientific evidence is lacking, of poor quality, or conflicting, such that the risk-versus-benefit balance cannot be assessed

Levels of Evidence:

Level 1: Evidence obtained from at least one properly designed randomized controlled trial

Level 2-1: Evidence obtained from well-designed controlled trials without randomization

Level 2-2: Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one center or research group

Level 2-3: Evidence obtained from multiple time series with or without the intervention.

Dramatic results in uncontrolled trials might also be regarded as this type of evidence

Level 3: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Abbreviation: N/A, data not available.

(PF) patients.⁷ Although the low number of participants made the study underpowered, no significant difference in the time to disease control was demonstrated.⁷ All patients achieved remission in a time ranging from 5 to 42 days for the high-dose steroids and 7 to 42 days for the low-dose steroids. Rates of remission as recorded over a 5-year period were also not statistically significant ($P = .30$).⁷

Regarding pulsed corticosteroid use, an RCT of 22 participants⁸ compared the efficacy of adjuvant pulsed oral dexamethasone (300 mg/d for 3 consecutive days, monthly) versus placebo in newly diagnosed patients concurrently treated with prednisolone and azathioprine. Although the small number of patients in the cohort contributed to the poor power of the study, no significant differences in the rates of remission or relapse were identified. Of importance, the rates of adverse outcomes or side effects were significantly higher among the pulsed-corticosteroid cohort when compared with the continuous-dosage cohort ($P < .01$).⁸ It must be noted, however, that the patients enrolled in this particular study did not have severe or refractory disease, and that pulsed corticosteroids may have a useful role in those particular subgroups of patients.⁶ At present no double-blinded placebo-controlled RCTs are available that evaluate pulsed corticosteroids in severe or refractory pemphigus, so the evidence supporting this stems from expert recommendation.⁶ As the power of the study by Mentink and colleagues⁸ was low, there is no evidence supporting the use of one intervention (dexamethasone or the control regimen) over the other. The study also commented that pulsed dexamethasone was associated with higher rates of corticosteroid-associated adverse effects.⁸ These findings again highlight the importance of a dynamic corticosteroid regimen individualized for each patient depending on their individual disease severity, treatment response, and degree of adverse effects from therapy.

Topical corticosteroid use in PV and PF has been documented in several case reports,^{9,10} and expert recommendations state that it may be useful in localized or mild disease.⁶ No controlled trials exist to formally evaluate its efficacy, but strong corticosteroids such as betamethasone or clobetasol are typically used. For mucosal lesions, topical clobetasol propionate is typically used in mild disease, although mostly as an adjunct to systemic treatment.^{6,11}

Bullous Pemphigoid

Corticosteroids, both oral and topical, are used widely in the management of bullous pemphigoid (BP), with topical preparations of high-potency steroids (such as clobetasol propionate) being used for mild to moderate disease and systemic corticosteroids used for more severe disease.¹² As BP is a disease of the elderly, mortality of those diagnosed with BP is relatively high, and despite the introduction of corticosteroids and other immunosuppressive and immunomodulating agents has not improved since the 1950s.^{12,13} Debate is ongoing as to whether this is indicative of the underlying comorbidities inherent in the patient population and if the role of treatment actually improves mortality rates. Recent research by Parker and MacKelfresh¹³ indicates that as the natural history of the disease is usually self limiting and the majority of patients succumb to causes unrelated to their BP, adverse effects primarily from systemic corticosteroids may actually increase the risk of mortality.¹³

A recent Cochrane systematic review and meta-analysis¹² examined an RCT of 26 participants comparing high-dose (1.25 mg/kg) and low-dose (0.75 mg/kg) oral prednisolone in patients with newly diagnosed BP.¹⁴ Fifty-one percent of patients in the low-dose cohort patients achieved remission by day 21 compared with 64% of high-dose cohort patients. Power was limited by the small sample size of the study, and no significant difference between time to remission or overall mortality was revealed. A second study comparing oral prednisolone with methylprednisolone

comprised 57 participants, monitored for 10 days. No significant difference in rates of remission or decrease in the number of bullous lesions was seen between the two treatment groups.¹⁵ Self-reported pruritus scores were found to be significantly more improved in the methylprednisolone cohort than in the prednisolone cohort.¹⁵ Examination of the methodology of the study shows that randomization and blinding were adequate, although the degree of allocation concealment is questionable, thus querying the reliability of this result.

The 2002 RCT by Joly and colleagues¹⁶ comparing topical clobetasol propionate (0.05%) with oral prednisone demonstrated a significant advantage of topical clobetasol propionate (0.05%, 40 g/d) over oral prednisone (1 mg/kg/d) in individuals with severe BP (defined as more than 10 new blisters per day) in regard of overall mortality within 1 year of initiation of treatment. The significance of this finding increased when multiple regression analysis took into account age and functional status. Of importance, this study¹⁶ also had adequate power to detect a decrease in the 1-year mortality rate in both severe and moderate disease groups. This result lends credence to the suggestion that in severe BP, systemic corticosteroids may have a deleterious effect on mortality rates when compared with topical high-potency corticosteroids. A follow-on study with 309 participants¹⁷ found that lower doses of clobetasol propionate (0.05%, 10–30 g/d) had noninferior mortality rates than the standard regimen of 40 g/d in both severe and moderate disease. When adjusted for age and functional status, the investigators concluded that the lower doses were more beneficial to patients with both moderate and severe disease, with lower rates of mortality or life-threatening adverse effects (including sepsis and diabetes mellitus) than the original 2002 study.^{12,17} Although the evidence may suggest that twice-daily topical corticosteroids more beneficial than oral dosing, the practicalities of application by elderly patients with multiple comorbidities is a significant barrier to the implementation of these recommendations.

Mucous Membrane Pemphigoid

Therapies for AIBD that involve mucous membranes are targeted at topical applications as well as the consideration of systemic corticosteroids in severe disease.

There is a paucity of evidence from RCTs regarding treatments for mucous membrane pemphigoid (MMP), cicatricial pemphigoid (CP), and other subtypes of AIBD that contain mucous membrane involvement. Expert recommendations cite topical therapies such as clobetasol propionate, betamethasone valerate, and dexamethasone mouthwashes.^{18,19} A Cochrane review confirmed that the only RCT evidence related to MMP regarded the treatment of ocular involvement with dapsone or cyclophosphamide, dependent on disease severity.¹⁹ There were no RCTs of steroid use in either MMP or epidermolysis bullosa acquisita (EBA). Furthermore, to date no reliable evidence sources (such as RCTs) have been found to further elucidate the efficacy of these topical treatments in these conditions.

Linear IgA Disease

Steroid use in linear IgA disease can be separated into topical and systemic regimens. While potent topical steroids such as clobetasol propionate 0.05% has been recommended for mild disease, it can also have a role in symptom control while the offending stimulant is removed in drug-induced disease.²⁰ No RCTs have been identified to date regarding the efficacy of corticosteroids in linear IgA disease, and expert recommendation quotes dapsone as a first-line agent,^{20,21} with other immunosuppressive and immunomodulating agents such as mycophenolate mofetil (MMF) also having reports of successful treatment.²⁰ In this regard, systemic corticosteroids are only considered

a useful adjunctive treatment in the setting of other therapies, and to this end evidence of its usefulness is lacking.

Epidermolysis Bullosa Acquisita

EBA is a recalcitrant AIBD in which treatment is known to be difficult. A recent Cochrane review found no RCTs of treatment modalities in EBA, although a handful of nonrandomized studies were found involving a wide variety of immunosuppressive and immunomodulating therapies.^{22,23} Due to the adverse outcomes of the high-dose steroids needed to successfully control EBA, other management strategies such as intravenous immunoglobulins (IVIG) and anti-CD20 monoclonal antibodies (rituximab) have come to the fore as the mainstay of treatment in EBA.²² While prednisone/prednisolone, 0.5 to 1.0 mg/kg/d is still included in the initial treatment regimen for EBA, recalcitrant or severe disease management concentrates on other immunomodulating therapies such as cyclosporine, plasmapheresis, and colchicine for maintenance therapy. Ishii and colleagues²³ state that pulsed corticosteroids may also be useful in severe disease, although these recommendations have not been borne out in randomized trials. Again, the rarity of the conditions comprising AIBD makes such evidence difficult to compile.

Pemphigoid Gestationis

Although there are no RCTs available assessing the effect of corticosteroids in this condition, as prednisone is relatively safe during the later stages of pregnancy and during breastfeeding as compared with many other systemic immunosuppressants, oral corticosteroids such as prednisone tend to be used.²⁴

MINIMIZING THE ADVERSE EFFECTS OF CORTICOSTEROID USE

The side effects or adverse outcomes of corticosteroid use are both acute and chronic.

As outlined in **Table 3**, the adverse effects of corticosteroids range from weight gain and insulin resistance to acute psychopathology. Prevention strategies, ongoing management, and appropriate treatment of adverse effects that do arise are essential aspects of patient care in individuals with AIBD on systemic as well as widespread potent topical corticosteroids.² Evidence from studies in pemphigus have suggested that cumulative corticosteroid dose has a significant influence over the rate of adverse effects, again emphasizing the need for titration of steroid use according to individual patient responses.²

Metabolic Effects

The most common metabolic effects of corticosteroids include an increase of appetite and salt retention, leading to an increase in eating and drinking with consequent weight gain, hyperglycemia, and insulin resistance, along with hyperlipidemia. Base-line lipids (cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, liver function tests) are advised prior to long-term glucocorticoids, with regular monitoring every 4 to 6 weeks, particularly when in combination with hepatotoxic drugs such as methotrexate.² Monitoring of weight and blood glucose should also be undertaken alongside lipids, especially in patients with preexisting diabetes or insulin resistance, as well as monitoring for hypertension. The effect of corticosteroids on blood glucose and lipids takes weeks to occur after starting therapy and a similar timeframe to return to normal after cessation of therapy.²

Table 3 Adverse outcomes from corticosteroid use in AIBDs and relevant strategies to prevent and alleviate effects			
Adverse Effect	Timeframe of Onset	Prevention Strategies	Treatment Strategies
Weight gain	Weeks to months	Dose minimization	Dose minimization Diuretic therapy
Hyperglycemia/ insulin resistance	Weeks	Dose minimization	Endocrinology review Hypoglycemic therapy, insulin therapy
Osteoporosis	Years	Dose minimization Calcium and vitamin D supplementation Bisphosphonates	Calcium and vitamin D supplementation Bisphosphonates Acute management of fracture events
Osteonecrosis	Years	Dose minimization	
Myopathy	Weeks to years	Dose minimization Exercise, physiotherapy	Dose minimization Exercise, physiotherapy
Cataracts	Months	Dose minimization	Ophthalmology review Cataract removal
Glaucoma	Days to weeks	Dose minimization	Ophthalmology review
Psychopathology (Ranging from anxiety to acute psychosis)	Days-Weeks	Dose minimization	Neuropsychiatric review Antipsychotic medications
Hyperlipidemia	Weeks	Dose minimization Dietary modifications	Dietary modifications Statin therapy
Hypertension	Weeks	Dose minimization Dietary modifications (low sodium)	Dietary modifications (low sodium)
Infection/sepsis	Weeks	Dose minimization Prophylactic antibiotics Prophylactic antifungals Prophylactic antivirals	Acute medical management (intravenous antibiotics and supportive care)
Nausea/reflux	Days	Dose minimization Prophylactic proton pump inhibitors	Proton pump inhibitors Histamine-2 receptor antagonists

Data from Refs. ^{2,25–35}

Musculoskeletal Effects

One of the most common long-term effects of corticosteroid use is steroid-induced osteoporosis. With the greatest rate of bone mineral density loss occurring in the first 12 months of corticosteroid therapy, assessment and therapy before initiation of therapy or as soon as possible after initiation of therapy is vital.^{25–27} Baseline bone mineral density (BMD) testing, along with serum calcium, magnesium, and vitamin D levels are necessary. The test considered most beneficial for BMD is dual x-ray absorption spectrometry (DEXA), due to a combination of its low radiation levels and reproducibility.^{25,26} Yearly BMD testing along with ensuring adequate supplementation of calcium (recommended 1500 mg/d) and vitamin D (recommended 800 IU/d) can help minimize osteoporosis.^{25,26} Other prophylactic pharmacologic therapies include bisphosphonates such as alendronate and risendronate.^{27,28} Rheumatologic

guidelines recommend administration of bisphosphonates to all men and postmenopausal women on long-term corticosteroid therapy of greater than 5 mg prednisone per day.²⁶ Nonpharmacologic methods aimed at maintaining bone mineral density in the setting of long-term corticosteroid use include a low sodium diet (to help prevent calcium loss from the renal tubules) and minimizing caffeine and alcohol intake.^{25,26} Muscle atrophy and weakness is a delayed complication of systemic steroids, with little that can be done to prevent it; gentle exercise can help to keep the muscles as strong as possible.

Neuropsychiatric Effects

Central nervous system effects of high-dose corticosteroids can include disturbing psychiatric symptoms, which can have rapid onset of several days after initiation of therapy. Affective disturbances including depression and hypomania can be seen at moderate doses, but psychosis and mania are almost exclusively seen at doses above 20 mg/d.²⁹ One retrospective analysis in patients with multiple sclerosis taking steroids was able to identify individuals at risk by previous episodes of major depression prior to the onset of disease.²⁹ Factor analysis in a cohort of systemic lupus erythematosus (SLE) patients on systemic glucocorticoids showed that hypoalbuminemia was a significant predisposing factor to corticosteroid-induced psychosis in that patient population.³⁰ Insomnia is a common complaint present at low doses, and in elderly populations cognitive impairment, particularly memory loss, may manifest.³¹ While preventive measures encompass monitoring and education as well as appropriate dosing regimens, treatment of psychosis with various antipsychotic medications has been documented as effective.³⁰

Cardiovascular Effects

The risk of ischemic heart disease and cardiac failure is increased in individuals on long-term corticosteroid therapy greater than 7.5 mg of prednisone per day, as per the result of a case-control study of more than 50,000 individuals.³² The risk as measured by odds ratios was greater for current users of systemic glucocorticoids than for previous users. Although the risk was not as great for cerebrovascular disease as with cardiovascular disease, the results have not been verified in RCTs and, hence, general recommendations on prevention or monitoring of patients on systemic corticosteroids are currently inappropriate.

Gastrointestinal Effects

Corticosteroids have been reported to be associated with an increased risk of peptic ulcer disease, gastritis, and gastroesophageal reflux disease. Several studies have quantified the increased risk as marginally significant for glucocorticoids alone, although in combination with nonsteroidal anti-inflammatory drugs (NSAIDs), a significant elevation in the risk for gastroenterological complications above the level attributable to NSAIDs alone is detectable within the first 3 months of use.³³ Current expert recommendations in other fields do not recommend prophylaxis with proton pump inhibitors (PPIs) in the setting of glucocorticoids alone, but it can be considered for those individuals taking both glucocorticoids and NSAIDs.³³ It is the authors' practice, and that of other dermatologists in the field, to prescribe PPIs to AIBD patients on chronic, high-dose corticosteroids. No information is available as to the effect of COX-2-specific NSAIDs combined with systemic corticosteroids.

Ophthalmologic Effects

Posterior subcapsular cataracts are a well-documented adverse effect of prolonged corticosteroid use. These bilateral, slowly developing cataracts can usually be distinguished clinically from senile cataracts. Findings from rheumatologic research suggests that younger patients, particularly children, are more susceptible to the formation of cataracts, and that doses equivalent to less than 10 mg prednisolone per day can still cause significant increases in the rates of cataract formation when compared with matched controls.³⁴ Anecdotally, several of the authors' pemphigus patients have had to undergo cataract surgery. Increased intraocular pressure can also occur within months of systemic corticosteroid use, mimicking open-angle glaucoma, although it is much more commonly a risk with ocular use of corticosteroids.² Patients with preexisting glaucoma have an increased sensitivity to corticosteroids and risk of disease progression, and regular ophthalmologic reviews are a necessary part of monitoring side effects in these patients.³⁵

Risk of Infection

The risk for potentially serious infection in AIBD patients, particularly those on long-term corticosteroid therapy combined with other immunosuppressive therapy, is high. Expert recommendations suggest the consideration of prophylaxis for *Candida* and/or *Pneumocystis* infections in patients with high-dose MMP.² Although no clear consensus guidelines are available concerning infectious prophylaxis in AIBD, Williams and Nesbitt² state that trimethoprim-sulfamethoxazole or dapsone are acceptable options for bacterial prophylaxis, with dapsone having additional anti-inflammatory properties. Valacyclovir can be used for viral prophylaxis for herpes simplex, and chlorhexidine/miconazole mouthwashes are appropriate for oral candidiasis prophylaxis.² Concerns over tuberculosis reactivation with individuals on immunosuppressive regimens have led rheumatologic authorities to suggest baseline chest radiographs and tuberculin skin testing prior to long-term immunosuppressive therapies. Opinions vary as to the appropriateness of these investigations in those on glucocorticoids alone, as most concern centers around the use of TNF- α inhibitors, such as infliximab and rituximab.² Drugs such as rituximab are being used as first-line treatment for pemphigus patients who have significant contraindications to high-dose corticosteroids.¹⁶ Cost-benefit analyses in the short term may find that oral corticosteroids are cheaper than topical alternatives and biological therapies, but the longer term costs of the sequelae of high-dose steroids, listed above, have yet to be properly evaluated.

EXPERT RECOMMENDATIONS

Corticosteroids are a central tenet in the management of AIBD, and it is unlikely that any ethics committee would permit RCTs of placebos versus systemic steroids in the acute phases of these diseases, because the mortality decreased so dramatically when steroids were introduced for pemphigus. The focus is to minimize side effects with the lowest doses of corticosteroids or an alternative mode of application that is possible for efficacy.

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