Dermatology Practical & Conceptual

Treatment of Diabetes in Bullous Pemphigoid Patients: Where Do We Stand?

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Bullous pemphigoid (BP) affects predominantly elderly patients, and the disease incidence rises exponentially with age. A high prevalence of diabetes mellitus (DM) in patients with BP has been noticed, ranging from 20 to 30% [1].

The treatment of BP patients is challenging and should be carefully assessed bearing in mind their multiple comorbidities. Corticosteroids are the mainstay of treatment for BP. However, their systemic use is limited in diabetic patients by the risk of acute hyperglycemic complications. This is particularly concerning given the age group of BP patients and the chronicity of treatment. Adjunctive therapy with immunosuppressants such as azathioprine, mycophenolate mofetil or methotrexate may also be needed [2]. Also, novel targeted therapeutic approaches such as omalizumab and dupilumab have been reported as effective alternatives, but their use in BP is still off-label [3].

Several population-based studies supported an increased risk of developing BP in diabetic patients treated with dipeptidyl peptidase-4 inhibitors (DPP4i). A recent meta-analysis showed that the odds ratio (OR) for BP among patients receiving any DPP4i ranged from 1.27 to 3.45 [4]. The exact pathogenesis of how DPP4i might induce BP remains largely unclear and it is not known if the suspension of DPP4i can revert this immunological process. However, the clinical outcome appears to be better if DPP4i is discontinued.

A presumed association between BP and glucagon-like peptide-1 (GLP-1) receptor agonists has also been reported [5]. The underlying mechanism is unclear, however since DPP4i and GLP-1 receptor agonists both rely on enhancing the activity of the incretin hormone GLP-1, a common effect between these two classes of antidiabetic drugs should be sought. Although more robust studies are required, we suggest that this association is taken into account when selecting the most appropriate medication for BP patients.

Other widely used antidiabetic drugs like second-generation sulfonylureas and metformin seem safer options, but their use can be limited by the patient's comorbidities [6]. The sodium–glucose cotransporter (SGLT)2 inhibitors also seem like good alternatives. These drugs do not increase the risk of hypoglycemia, have low rates of adverse effects and may be continued in patients with moderate renal impairment. Overall, they can be used in selected BP patients.

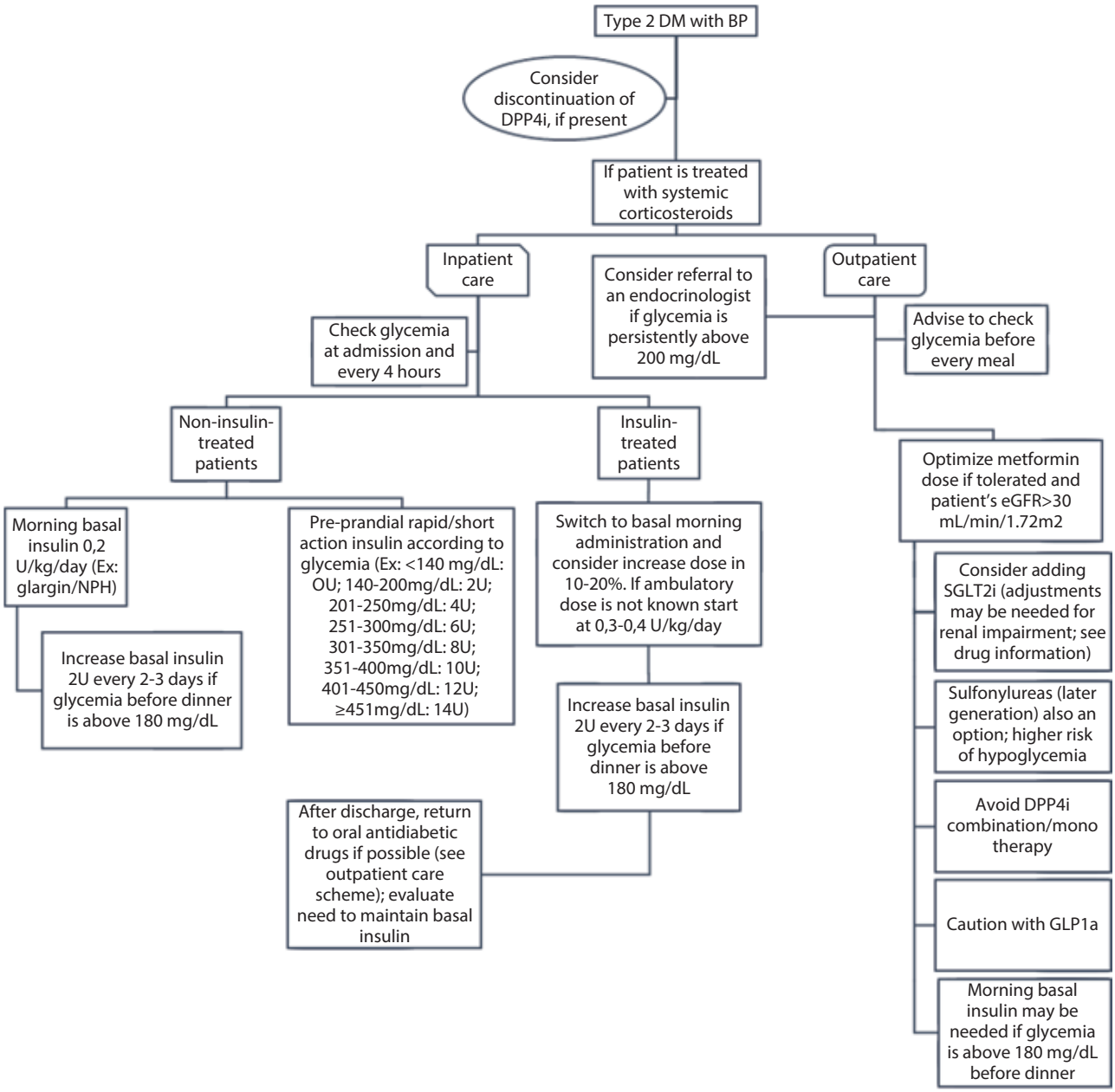

Figure 1. Proposed treatment algorithm for bullous pemphigoid patients with type 2 diabetes mellitus treated with corticosteroids. BP, bullous pemphigoid; DM, diabetes mellitus; DPP4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; GLP1a, glucagon-like peptide 1 receptor agonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

In many cases, insulin is the most suitable choice, particularly for inpatients on corticosteroids. Morning basal insulin may closely fit the glucose excursion induced by a single dose of morning corticosteroid. The initial dose and titration should take into account the patient's weight and dose of corticosteroid. Dairy adjustments are frequently necessary and often difficult to predict.

Based on the previous data, a treatment algorithm for BP patients with type 2 DM is proposed in Fig. 1.

In conclusion, it is decisive that we view BP patients beyond a single-disease framework and treat them in the context of multi-morbidities. Diabetes management in these patients can be particularly troublesome and, to date, there are no orienting guidelines on this matter. Endocrinologists should be aware of BP as a challenging problem in patients with DM and collaboration with dermatologists is essential for good outcomes.

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