Bangladesh Crit Care J September 2014; 2 (2): 51-52

From the Desk of the Editor

Use of Corticosteroid in Critically Ill : Cautions and Precautions

Hossain Shahid Ferdous

The role of corticosteroids in critical illness has long been a discussion among critical care investigators and clinicians. Systemic inflammation is the hallmark mechanism in sepsis, septic shock, and acute respiratory distress syndrome (ARDS). Given the effective anti-inflammatory properties of drugs and the relative functional adrenal insufficiency in critically ill-patients, it would be a logical choice in the treatment of sepsis and ARDS. However, despite several decades of clinical studies exploring their role in both sepsis and treatment of ARDS, their use remains controversial.

Owing to stress and inflammatory response on the hypothalamic pituitary axis, corticosteroid levels are often relatively high in sepsis. However, other aspects of critical illness may also affect the corticosteroid metabolism in its effect. Reduced enzymatic breakdown in the liver and kidney[1], prolonged half life due to renal dysfunction, and lower concentration of corticosteroid binding globulin with a higher percentage of free and active cortisol may indeed increase cortisol disposal[2]. In addition, inflammatory cytokines may increase peripheral conversion of precursor to cortisol[3]. However, the optimum level of cortisol in critical illness remains unclear. Absolute adrenal insufficiency is rare, but suboptimal levels are more common and are associated with worse outcome. These patients typically have an exaggerated pro-inflammatory response and a relative functional corticosteroid insufficiency. This has given rise to a somewhat controversial syndrome, the so-called "critical illness related corticosteroid insufficiency" (CIRCI), defined as an inadequate corticoid activity with regard to the severity of the illness[4]. Besides inadequate levels-related to illness, corticosteroid tissue resistance at the target tissue level is proposed as a mechanism of suboptimal activity[5]. Identifying CIRCI-patients remains difficult as we lack reliable tests that quantify corticosteroid activity at the tissue level, and so the diagnosis of CIRCI remains elusive[4].

Based on the available evidence, the Surviving Sepsis Campaign (SSC) international guidelines[6] recommend to use intravenous hydrocortisone only in septic shock refractory to vasopressor therapy and fluid resuscitation (Grade 2c), not to use steroids in the absence of shock (Grade 1c), to use Hydrocortisone 200 mg/day (Grade 2c) in continuous infusion (Grade 2d) as repetitive bolus can lead to a sudden increase in blood glucose levels, and to taper the dosage when vasopressors are no longer necessary (Grade 2c).The SSC guidelines also indicate that adrenocorticotropic hormone stimulation test is not useful in identifying the subset of a patient who should receive hydrocortisone. There is also no recommendation on the optimal duration of steroid therapy in SSC guidelines.

The development of ARDS is an immune-mediated pulmonary injury, caused by an initial specific insult (sepsis, trauma etc), leading to loss of the alveolar-capillary barrier, injury to the alveolar epithelium, and an influx of neutrophils, macrophages and fibrin.

On basis of results of various trials, we can come to conclusion that, systemic glucocorticosteriods clearly have a role in early ARDS in situations where it has been precipitated by a steroid-responsive process such as eosinophilic pneumonia, pneumocystis pneumonia, auto-immune systemic disease. However, in other causes of ARDS, the benefit on mortality is not proven strong enough. It can be used in selected patients with high probability of fibroproliferation, but should not be initiated after day 14 of ARDS onset. Certain clinical conditions may prompt intensivists to almost always prescribe systemic steroids and reduce equipoise for future placebo-controlled trials. Moreover, one survey[8] shows that in selected academic centers a majority of intensivists do not prescribe corticosteroids for pneumonia, ALI and ARDS.

Corticosteroids are extensively used in Palliative Medicine[6]. Examples include conditions like spinal cord compression, raised intracranial pressure, superior vena caval obstruction, obstruction of hollow viscus, Lymphangitis, carcinomatosis etc. Steroid is also used to relieve pain in nerve compression, liver capsular pain, metastatic arthralgia etc.

Dexamethasone provides a relative high corticosteroid dose for fewer tablets and has less mineralocorticoid effects than prednisolone, methylprednisolone and hydrocortisone, and so causes less fluid retention and biochemical disturbance. Dexamethasone is therefore the most commonly used corticosteroid in Palliative Medicine.

Standard doses for the different indications of steroid usage are not established[7]. It has been suggested that steroids should be prescribed for a trial period of one week before review, except where the intention of treatment is tumor control. It is unlikely that a greater response to treatment will occur after one week. It is safe to stop steroids abruptly after one week (dose equivalent to 40mg/day of prednisolone or 6mg/day of dexamethasone), if there has been no benefit. If larger doses are used or smaller doses are used for a longer period of time, doses must be reduced cautiously e.g. decrease by a third of the total daily dose every 5 days.

Steroid can weaken patients' immune system, making it easier for him to get an infection. So patients on steroids or on any other immune compromising drug should be in reverse isolation[8].

Steroids must be reduced gradually especially in patients whose symptoms may recur and those who have recently received repeated courses (particularly if >3 weeks) or who have received >40mg prednisolone or equivalent. In other conditions where there are other potential causes of adrenal suppression steroids should be tapered gradually.

Critical care physicians need to keep in mind many unpleasant side effects of steroids. The risk of side effects depends on the dose and length of treatment.

Psychiatric disturbances are common and include depression, mania, psychosis delirium and insomnia. Proximal myopathy, osteoporosis, avascular bone necrosis are common musculoskeletal problems. Diabetic patients receiving steroids have uncontrolled blood sugar, worsening hypertension. They are more susceptible to get pancreatitis. If patients complain of insomnia steroids should be prescribed in morning after food so as to prevent insomnia. Diabetic patients with uncontrolled blood sugar from steroid may need to increase the dose of insulin. If there is a history of peptic ulcer disease caution must be taken if patient complains of dyspepsia.

Patients commenced on steroids who are already on NSAIDs, Aspirin or Warfarin must be prescribed a proton pump inhibitor such as Lansoprazole. The use of steroids in combination with these drugs should be avoided where possible.

Critical care physicians should remember drug interaction between some important drugs used in ICUs along with steroids. Antiepileptics like Carbamazepine, Phenytoin, Phenobarbitone accelerate the metabolism of steroids, which means that the steroids have less effect. Patients on anti-epileptics may require higher doses of steroids. Steroids can alter the metabolism of Warfarin. On commencing steroids the INR must be monitored regularly for patients on Warfarin.

It is essential that steroid doses are monitored regularly. Careful monitoring helps to achieve maximum symptom benefit from the smallest possible dose of steroids. It is often a question of finding the balance between the problems and the benefits. The most common cause of steroid-related problems is failure to review the patient.

So the take home message for general clinicians who are prescribing steroids in the inpatient units are the following. This is also applicable for ICU patients. Patients treated with systemic steroids for more than 3 weeks should be given steroid treatment card at the onset of treatment and encouraged to carry it with them. Steroids must be prescribed before midday to prevent insomnia, can be given as a single dose. A proton pump inhibitor must be prescribed when steroids used alongside NSAIDS, Aspirin or Warfarin. The patient and caregivers must be informed of the reason for steroid use. When commenced on steroids the patient must be assessed within the first one to two weeks to identify whether or not the treatment has helped. If there is no improvement in symptoms the steroids must be stopped. If the patient has been on steroids for a week or less the steroids can be stopped abruptly. If an improvement in symptoms is reported, the dose should be reduced by approximately one third every 4-7 days until a dose is reached below which symptoms recur. If the patient has been on a high dose of steroids for several weeks/ months the dose should be reduced cautiously at lower dose intervals and over a longer period of time, by the use of 0.5 mg tablets (provided dexamethasone is used) and if necessary switching the patient to prednisolone. All patients being discharged from an in-patient unit must be given clear instructions on the reducing dose of the steroids and informed of a review date if they are to continue on a maintenance dose. All discharge letters for patients on steroids must clearly state the reason for steroid use, the regime for dose reduction and plan for future review.

Hossain Shahid Ferdous

MBBS, DEN, Fellow of Endocrinology (Aus), FACP, FACE

Senior Consultant, Department of Endocrinology,

BIRDEM General Hospital. Shahbagh, Dhaka.

E Mail: dr_hsferdous@hotmail.com

Reference:

1. Boonen E, Vervenne H, Meersseman P, Andrew R, Mortier L, Declercq PE, et al. Reduced cortisol metabolism during critical illness. N Engl J Med 2013;368:1477-88. [PUBMED]
2. Cooper MS, Stewart PM. Corticosteroid insufficiency in acutely ill patients. N Engl J Med 2003;348:727-34.
3. Marik PE. Critical illness-related corticosteroid insufficiency. Chest 2009;135:181-93. [PUBMED]
4. Marik PE, Pastores SM, Annane D, Meduri GU, Sprung CL, Arlt W, et al. Recommendations for the diagnosis and management of corticosteroid insufficiency in critically ill adult patients: Consensus statements from an international task force by the American College of Critical Care Medicine. Crit Care Med 2008;36:1937-49.
5. Effect of high-dose glucocorticoid therapy on mortality in patients with clinical signs of systemic sepsis. The Veterans Administration Systemic Sepsis Cooperative Study Group. N Engl J Med 1987;317:659-65. [PUBMED]
6. Annane D, Sébille V, Charpentier C, Bollaert PE, François B, Korach JM, et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. JAMA 2002;288:862-71.
7. Sprung CL, Annane D, Keh D, Moreno R, Singer M, Freivogel K, et al. Hydrocortisone therapy for patients with septic shock. N Engl J Med 2008;358:111-24.
8. Annane D, Bellissant E, Bollaert PE, Briegel J, Confalonieri M, De Gaudio R, et al. Corticosteroids in the treatment of severe sepsis and septic shock in adults: A systematic review. JAMA 2009;301:2362-75.