Review Article

Corticosteroid Pulse Therapy

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ABSTRACT:

Pulse therapy is the intermittent delivery of suprapharamacologic dosages of medications to improve therapeutic benefit and reduce side effects.. There are several drugs used in the treatment of pulse therapy which includes corticosteroids, antibiotics, immunosuppresants, antifungals and antivirals. The article focuses on various regimens employed in corticosteroids pulse treatment indications, adverse effects, contraindications and newer modifications.

Keywords: Corticosteroids, pulse therapy, dexamethasone

INTRODUCTION:

Pulse therapy is a process of administering suprapharmacologic doses of drugs in an alternating ,manner to reduce side effects and enhance therapeutic effect.[1]

In 1969, Kountz and Cohn were first to put the concept of Pulse therapy after renal transplant to immediately achieve graft survival.[2]

In India, Dr. J.S. Pasricha in 1981 first used pulse therapy to subside pain of patient suffering from Reiter's disease.[3]

However a lot of people around the world are suffering from various autoimmune and inflammatory diseases. Increasing awareness about oral diseases in public has lead to an increase in number of medically compromised patients visiting oral physicians. Hence, there are different groups of drugs available to enhance the treatment.[3]

Corticosteroids are class of drugs occurring naturally drug**.** PT was found to be effective in management of widespread immune mediated disorders where effective disease control is achieved through rapid infusion of the drug in comparison to conventional. The main aim of pulsing is to attain effective and rapid control of disease. Oral dosage of drug reduces long-term continuance of corticosteroid drugs along with the complications.[4]

VARIOUS TYPES OF DRUGS EMPLOYED IN PULSE TREATMENT :

i) Corticosteroids
ii) Antibiotics
iii) Immunosuppressives
iv) Antibiotics
v) Antifungals

The efficacy of synthetic corticosteroids are based on the rate of absorption and

concentration necessary to get maximum effects, increase potency with half life that range between half hour to 4.5 hours. The drug is metabolized in liver and 95% is excreted by kidneys. Agents with high bioavailability are methylprednisolone and dexamethasone as they primarily bound to serum albumin.[5]

INDICATIONS:[6]

1) Systemic lupus erythematosus
2) Systemic sclerosis
3) Pemphigus vulgaris
4) Lichen planus
5) Toxic epidermal necrolysis
6) Steven johnson syndrome

CONTRAINDICATIONS:[6]

1) Pregnant and lactating patients
2) Hypersensitivity to steroid preparation
3) Systemic infections which includes uncontrolled hypertension and fungal sepsis.

Corticosteroid medication:[6]

- Dexamethasone methotrexate
- Dexamethasone cyclophosphamide
- Dexamethasone azathioprene
  - Oral mini pulse corticoteroid therapy
  - Cyclophosphamide
  - Methyl prednisolone
  - Topical corticoteroid
  - Kountz and Cohn were first to successfully use pulse administration of corticosteroids for treatment renal graft rejection. Pulse therapy using a combination of corticosteroids for a blistering disorder in pemphigus vulgaris was first introduced by Pasricha et al and Kanwar in India. Since then pulse therapy has been used to treat various other diseases.[2]

- **DEXAMETHASONE CYCLOPHOSPHAMIDE PULSETHERAPY:**

Cyclophosphamide is a different type of immunosuppresant. The medications appear to cause cell death as soon as division takes place and are mostly damaging to quickly growing tissues. DCP refers to the intravenous infusion of high concentrations of cyclophosphamide and corticosteroids, often dexamethasone 100mg or 500mg of methylprednisolone daily, with one dosage of 500mg cyclophosphamide administered once a month.[7]

Dexamethasone Cyclophosphamide is divided in to four stages[8]

Stage I:.comprises a gradual loading dose of 100mg dexamethasone mixed in 5% Dextrose of 500 ml over two hours for three days, as well as a 500mg infusion of cyclophosphamide on one of the days forms single DCP.
The drug is continued till 28 days till the lesion resolves and no new lesion appears between pulsing. Orally,50 mg of cyclophosphamide is administered. During this time, the patient may experience clinical lesion recurrences in between. To achieve a faster clinical recovery, standard doses of oral corticosteroids should be given
Stage II: creates a DCP schedule given a fixed period of 9 months.
Stage III: Daily single dose of 50mg cyclophosphamide orally is given for 1 year
Stage IV:Follow up is performed after withdrawal of all medications.

Therapy with DCP has a number of goals**.** These are as follows**:**[9]

- Improve the drug's efficacy and speed of reaction.
- To eliminate the necessity for long-term steroid use
- To get a steroid-free effect

Mode of action:

Cyclophosphamide is an alkylating agent. It is able to form strong electrophiles that form covalent linkages to electron rich groups of DNA. The active metabolite is phosphoramide mustard, which further undergoes cyclization to the reactive aziridium intermediate which in turn alkalizes the DNA that further result in irreparable DNA damage and apoptosis of the cell. Cyclophosphamide is highly toxic to rapidly proliferating cells.[10]

Adverse Effects of DCP therapy :

It occurs due to constituents in pulse itself

Due to cyclophosphamide:

- Carcinogenesis
- Leucopenia
- Diffuse hyper- pigmentation of skin.
- Gonadal damage
- Thrombocytopenia
- Diffuse loss of hair

Due to corticosteroids:

- Hyperacidity
- Hypertension
- Diabetes mellitus
- Demineralization of bone
- Viral, fungal, and bacterial infections.

Due to pulse therapy:

- Hair loss
- Sleep disturbances
- Weakness
- Metallic taste
- Muscle and bone pain
- Loss of taste
- Headache
- Menstrual irregularities
- Palpitations
- Generalized swelling
- Diarrhoea
- Congestive heart failure

MODIFICATIONS: - Pasricha JS[5]

I. Rao et al. made only minor alterations to the DCP therapy procedure.Few changes were made in the DCP therapy protocol by Rao et al.

i. Substitution of cyclophosphamide methotrexate or azathioprine in some patients.
ii. Treatment of intercurrent infections with conventional steroid therapy.
iii. When cyclophosphamide 500mg was administered, a 500ml container of dextrose was added to avoid urinary problems..
iv. Supportive drugs were included during first three phases. for example oral calcium 500mg daily and Injectable vitamin D3 one lakh

v. unit once a month during first two phases.

I. Three modifications were instituted by Pasricha et al. in the DCP regimen.

i. Even though the lesion was present, thorough washing of the oral cavity, scalp and skin was required.

ii. Superadded infections were prevented by the use of anti-candida drugs and oral antibiotics.

iii. Use of oral corticoteroids in doses to control disease activity results in rapid healing of the lesions improves psychological benefit to the patient.

TREATMENT WITH DEXAMETHASONE AZATHIOPRENE (DAP)

Cyclophosphamide is replaced with azathioprine 50 mg.Patients who aren't married or who are married but aren't happycyclophosphamide is used to treat those who haven't finished their family. As cyclophosphamide, 50 mg azathioprine was substitutedis known to cause amenorrhoea and oligospermia.Bone marrow suppression, including leukopenia and thrombocytopenia, is a side effect of azathioprine. Anemia, increased susceptibility to infections (particularly varicella and herpes simplex viruses), hepatotoxicity, alopecia, GI toxicity, and pancreatitis are only a few of the side effects. Furthermore, infection rates and lymphoproliferative disorders may be linked.[11]

DEXAMETHASONE METHOTREXATE PULSE THERAPY (DMP)

During the first three stages of pulse therapy, cyclophosphamide is replaced by 7.5 mg methotrexate, given orally in three doses of 2.5 mg at 12 hourly intervals weekly, along with dexamethasone pulses in the first two phases. DMP is used in individuals who have not been able to complete stage 1 despite receiving 12 DCP or DAP pulses. The regimen was the most effective.

PULSE THERAPY WITH METHYL PREDNISOLONE

Methyl prednisolone is a strong anti-inflammatory drug with an intermediate action. Despite the presence of the lesion, thorough cleansing of the scalp, skin, and mouth cavity was necessary. Methylprednisolone is given in doses ranging from 20 to 30 mg/kg every pulse, with a maximum dose of 1 g. Lupus nephritis, non-renal lupus, minimum change nephrotic syndrome, rheumatoid arthritis, sclerosis, polymyositis, and polyarthritis nodosa were all treated with MPPT.[11]

ORAL MINIPULSE TREATMENT:

Patients on corticosteroid pulse therapy are given high doses of medications intravenously. As a result, patients must be monitored in a hospital setting. Oral micro pulse therapy can prevent this in patients with oral lesions without skin involvement (OMP). It offers the benefit of pulsing and allows for lower dosages to be administered orally. This results in better patient compliance and a lower risk of corticosteroid-related short- and long-term side effects.[19]

The OMP routine was developed primarily to treat quickly or widespread vitiligo, with the goal of attaining similar therapeutic benefits to pulse therapy while having fewer side effects. It is now being tested for the treatment of lichen planus,

particularly in refractory instances. A ten milligramme dosage.[3]

CORTICOSTEROID PULSE THERAPY ON THE SKIN

The application of superpotent corticosteroids on a regular basis.It entails the use of superpotent corticosteroids on an as-needed basis. Clobetasol propionate (0.05%) is a topical psoriasis medication that is applied three times a week at 12-hour intervals..[3]

CONCLUSION

Owing to the well established adverse effects of corticosteroids, pulse therapy appeared as a novel option which permit their use and also limit their unwarranted effects which ultimately lead to benefit the patient as patients with autoimmune disorders are left with minimal options.

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