NEW DRUG

Pidotimod: An Immunity Booster

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ABSTRACT

Pidotimod is a synthetic dipeptide, which has immunomodulatory property. It is used in recurrent upper respiratory tract infections, where there is nonspecific immune deficiency, especially in children who are more prone to recurrent respiratory infections. This article discusses its structure, pharmacokinetics including mechanism of action and clinical uses. A brief review of literature has been carried out. Possible future application is suggested.

Keywords: Immunomodulators, immunity, immunoglobulin

Acute respiratory infections (ARIs) are the most common infections encountered in pediatric settings and pose a major challenge to the health system in developing countries because of the associated high morbidity and mortality.[1,2] Recurrent respiratory infections (RRIs) present a demanding challenge for pediatricians.[3] ARIs are the infections of any segment of respiratory tract or its accessory structures including paranasal sinuses, middle ear and pleural cavity.[4] But they may not remain confined to respiratory tract and may have systemic effects, due to possible extension of infection or microbial toxins, inflammation and reduced lung function.[5] RRIs can lead to complications such as recurrent otitis media, recurrent infectious rhinitis, recurrent pharyngitis or tonsillitis.[1] RRIs have been generally defined as 3 or more separate episodes of respiratory illnesses or more than 15 days of respiratory symptoms in the past 3 months.[6]

India, Bangladesh, Indonesia and Nepal together account for 40% of the global ARI mortality.[2] In India, 6% of children younger than 5 years of age had symptoms of ARI, i.e., cough, short and rapid breathing and 69% of them availed health care services.[4] ARIs accounted for 30% to 50% of health care visits and 20% to 40% of hospitalizations.[7] An adult has 2 to 4 episodes of ARI/year and a child has 6 to 8 episodes/year. In India, at least 300 million episodes of ARI are estimated to occur every year, out of which 30 to 60 million are moderate to severe ARIs.[4]

Pidotimod is a biological response modifier; chemically it is 3-L-pyroglutamyl-L-thiazolidine-4-carboxylic acid and is unrelated to other immunomodulating agents.[3] Its potential for immunostimulation has been evaluated in conditions with underlying suppressed cell-mediated immunity such as chronic bronchitis and RRIs in children. It is indicated as adjuvant therapy in prophylaxis and management of RRIs including rhinitis, sinusitis, otitis, pharyngitis and tonsillitis. It is also useful in acute exacerbations of chronic bronchitis.

MECHANISM OF ACTION

Pidotimod is a synthetic dipeptide molecule, which exhibits immunomodulatory properties. It exerts its immunomodulating activity by acting on both acquired as well as innate immunity.[3] It affects cell-mediated immune responses by stimulating interleukin (IL)-2 production. Pidotimod increases polymorphonuclear neutrophil chemotaxis and phagocytosis. It also enhances T-cell blastogenesis, anti-CD3 activity and activity of natural killer cells. It also induces maturation and activation of dendritic cells, activation of toll-like receptor (TLR) and release of interferon-gamma (IFN-γ). RRIs have been associated with immunodeficiency conditions like deficiency of immunoglobulin A (IgA), deficiency in cell-mediated immunity (such as total T-lymphocytes, response to mitogens, rosette-forming activity) and decreased neutrophil chemotactic activity and interferon production. It improves or optimizes the impaired T-helper/T-suppressor ratio in children with RRIs.

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ABSORPTION AND DISTRIBUTION

Pidotimod is available in vial, sachets and tablets. The time to peak drug concentration (T_{max}) of pidotimod is 1.5 hours (range 1.3-1.8 hours). After single oral dose of 200 mg, 400 mg and 800 mg in healthy individuals, the mean peak serum concentrations of pidotimod were found to be 2.8, 4.8 and 10.3 μg/mL, respectively. When pidotimod is administered with food, its oral bioavailability is decreased up to 50% and peak serum levels is achieved up to 2 hours later compared to administration in fasting state. Pidotimod should be given 2 hours before or 2 hours after meals to optimize absorption.

It has low protein binding of 4% with a volume of distribution of 30 liters.[8]

METABOLISM AND ELIMINATION

Pidotimod undergoes minimal hepatic metabolism. Approximately 45% of an oral dose (200-800 mg) of pidotimod is excreted unchanged in urine within 24 hours of administration. The total plasma clearance of pidotimod after oral administration is approximately 11 L/hour.

The elimination half-life of pidotimod is 4 hours.[8]

DRUG INTERACTIONS AND ADVERSE EFFECTS

Concurrent or recent use of some drugs like other immunomodulatory drugs, corticosteroids and viral vaccinations may interfere with immunologic actions of pidotimod. It is a generally well-tolerated drug but some very rare side effects such as flushing, rash, pruritus, nausea, vomiting, abdominal pain, diarrhea, headache and drowsiness have been reported.

PRECAUTIONS

Pidotimod should be used with caution in patients with renal failure, diabetes and children below 2 years. It is contraindicated in patients with known hypersensitivity to the components of the formulation. In children aged 2 to 8 years, pidotimod has been used for treatment of acute episodes of RRIs in a dose of 400 mg orally twice daily for 15 to 20 days, in combination with standard antibiotic therapy. A maintenance dose of 400 mg/day, without additional antibiotics has also been used for 60 days, following the acute treatment phase. For prophylaxis of RRIs in children of 2 to 13 years of age, pidotimod is usually given orally at dose of 400 mg once-daily before breakfast for 60 days. A twice-daily regimen of pidotimod 400 mg for 15 days, followed by once-daily maintenance dose, has been used to rapidly improve immune response.

USE IN SPECIFIC POPULATIONS

In adult patients with renal impairment having serum creatinine 2 to 5 mg/dL, the elimination half-life of pidotimod is prolonged up to 8 hours and its clearance reduced (mean 1.6 L/hour) following intravenous administration. Considering the usual dose interval of oral therapy (once or twice daily), it may not be necessary to reduce dose in these patients. However, additional repeat dose studies with oral dosage forms in patients with varying degrees of renal insufficiency are needed to confirm this recommendation. Pidotimod may prevent RRIs in children.[9] Immunomodulatory activity of pidotimod administered with standard antibiotic therapy in children hospitalized for community-acquired pneumonia has been observed.[10] Pidotimod may prevent ARIs in healthy children entering into daycare.[11]

POSSIBLE FUTURE APPLICATIONS

Pidotimod has shown improvement in symptoms; hence, it may be considered for use in ambulatory adult COVID-19 patients without pneumonia to prevent worsening of symptoms. However, more studies are needed to confirm these observations.[12]

CONCLUSION

Pidotimod has immunomodulatory action. It has been shown to be effective in reducing ARIs and reducing their severity among children who suffer from RRIs. It may also be beneficial in preventing ARIs in healthy children attending daycare centers. In hospitalized patients with acquired pneumonia, pidotimod is associated with favorable and persistent immunomodulatory effect when used along with standard antibiotic therapy. Overall, pidotimod is safe and has good tolerability.

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Women are at Higher Risk of Lung Cancer Than Men

In recent years, pollution and other factors in India have led to a troubling trend of greater lung cancer rates in women than men. The findings further showed that smoking rates remained stable even when the percentage of female lung cancer patients grew. The All India Institute of Medical Sciences (AIIMS) in Delhi hosted the study, which spanned 10 years from January 2008 to March 2018.

Historically, lung cancer has been more common in men than in women. Still, the pattern seems to be shifting in numerous regions of the world in recent years, according to Dr Anant Mohan, Head of the Department of Pulmonary Medicine at AIIMS. The causes were alteration in smoking behaviors, exposure to environmental toxins and biomass, particularly in rural women. But the improved access to health care facilities had encouraged more women to seek medical attention Dr Anant stressed.

The recently unpublished study by the pulmonary department showed that non-tobacco exposures such as indoor air pollution, poor environmental quality or urban air quality might have a role in women's rising trend of lung cancer. The study found that squamous cell carcinoma (SCC) increased from 25.4% to 30.6%, while adenocarcinoma (ADC) increased from 9.5% to 35.9%. Better survival rates were found among the nonsmokers, those who were younger, primarily women and more educated. They also had a higher prevalence of ADC, epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) mutations.

(*Source: https://health.economictimes.indiatimes.com/news/industry/lung-cancer-rates-higher-in-women-than-men-study/94772766*)