COMMENTARY

New Aspects of β_2-Adrenergic Agonists

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ABSTRACT:
β_2-adrenergic receptor agonists is a class of medications that act on the β_2-adrenergic receptors. They are mostly used to treat asthma and other respiratory problems at present. However, the newer research have highlighted that they can be utilized in numerous other disorders like Congenital Myasthenic Syndrome, Down syndrome, Amyotrophic lateral sclerosis, Idiopathic Stuttering Priapism & Dyslipidemia etc.
Keywords: β_2-adrenergic receptors, β_2-adrenergic receptor agonists, Indications, New aspects

INTRODUCTION:

β_2-adrenergic agonists are medications that act on β_2-adrenergic receptors. These receptors are present on smooth muscles of uterus, gastrointestinal tract, detrusor muscle of urinary bladder, seminal tract, bronchi, blood vessels and pancreas. They cause relaxation of bronchial smooth muscles, vasodilation in muscle and liver, relaxation of uterine muscle release of insulin etc. These drugs are classified into various types based on their duration of action.

- Short acting drugs like Salbutamol, Levosalbutamol, Terbutaline,Pirbuterol,Procaterol,Clenbuterol, Meta-proterenol, Fenoterol, Bitolterol mesylate, Ritodrine etc.
- Long-acting drugs like Salmeterol,Formoterol, Bambuterol,Clenbuterol,Olodaterol,Vilanterol etc.
- Ultra long acting drugs like Isoprenaline[1].

β_2-adrenergi cagonists as mentioned earlier are , familiar for the treatment of pulmonary disorders[2] but have created a new identity in medicine by the ongoing advance researches.With this background, a five year literature searching was done on Google scholar and Pakmedinet.com from 2011 to 2015 by using the key words β_2-adrenergic receptors, β_2-adrenergic agonists and new aspect of β_2-adrenergic agonists. A total of 22 studies were found related to β_2-adrenergic agonists. Refining the search by using the phrase new aspect of β_2-adrenergic agonists, curtailed the available number of articles to 5 that is 2011(0), 2012(0),2013(1),2014(2), 2015(2).This piece of information is enough for provision of insight into this particular class of drugs. A beneficial use of β_2-adrenergic agonist is found to be in congenital myasthenic syndrome.This is a rare disorder resulting from mutations in genes encoding for presynaptic, synaptic, and postsynaptic proteins that are involved in the signal transmission of the neuromuscular junction. The disease is characterized by fatigable weakness of the skeletal muscles with symptom onset from birth to early childhood[3].A study conducted on children 13 to 16 years of age were given salbutamol.

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They have documented that oral salbutamol treatment essentially improves symptoms in inherent myasthenic disorder in children[4].

Van danga in 2014 found that formoterol which is a long acting β_2-adrenergic agonist caused significant improvement in cognitive function in mice by improving dendritic complexity. Considering its widespread use in humans and positive effects on cognition in mice, formoterol or similar β_2 adrenergic receptor agonists with ability to cross the blood brain barrier might be attractive candidate for clinical trials to improve cognitive function in individuals with down syndrome[5].Down syndrome is characterized by decrease in intellectual capacity due to degeneration of locus coeruleus, a noteworthy player in logical learning. Sean in 2014 have found that formoterol might instigate mitochondrial biogenesis, restore the expression and capacity of mitochondrial proteins and expand the duplicate number of numerous qualities included in the mitochondrial electron transport chain, apparently through actuation of down-stream interpretation pathways[6].

It is also documented that β_2-adrenoceptor agonistsslow down the progression of ALS (Amyotrophic lateral sclerosis) by effectively treating its symptoms. Amyotrophic lateral sclerosis (ALS; also known as Lou Gehrig's disease) is a neuromuscular disorder in which there occursa gradual loss of function and eventual death of motor neurons in the spinal cord and brain, as well as significant atrophy of the muscles[7].Clinically, it is characterized by stiff and/or twitching muscles and significant muscle weakness due to gradual muscle wasting, resulting in difficulty in ambulating, speaking, swallowing, and eventually breathing. Bartusa et al have found in 2015 that orally-dynamic β_2-agonists might give a novel and helpful intends to diminish the side effects of ALS and potentially postpone illness movement[8].

β_2-adrenergic agonists can also be used in idiopathic stuttering priapism. According to the findings of newer case report study which showed that Idiopathic stuttering priapism can be treated with salbutamol orally. Recurrent ischaemic priapism also known as stuttering priapism is an uncommon form of ischaemic priapism, and its treatment is not yet clearly defined. If left untreated, it may evolve into classic form of acute ischaemic priapism and lead to erectile dysfunction due to fibrosis of corpora cavernosa. Hormonal therapy such as cyproterone acetate, oestrogen, bicalutamide or Lh-Rh agonist are often effective but can cause side effects such as hypogonadal state and infertility. Other medical options are 5-alpha-

reductase and phosphodiesterase-5 inhibitors, ketoconazole, baclofen, digoxin, gabapentin and ß2-adrenergic agonist terbutaline.This study reported the first case of stuttering priapism treated with ß2-adrenergic agonist salbutamol.This study proved that beta-2-agonist salbutamol is effective for the treatment of stuttering priapism[9].

Another advance role of ß2-agonist drugs has been found in Dyslipidemia.Makiin 1996[10] found that albuterol administration was associated with favorable changes in the serum lipid profile with significant lowering of LDL-c and increases in HDL-c in a small human trial without marked impairment of glucose tolerance or its physiologic determinants. His finding have been encoded by Yanrui in 2015.[11] He has documented that selective β_2-agonist, bambuterol also significantly lowered LDL-c in a relatively small healthy volunteer population.It is due to the fact that β_2-adrenergic agonism stimulates intracellular cAMP, which regulates a number of pathways involved in lipid and glucose metabolism. Sterol regulatory element-binding proteins (SREBPs) are major transcription factors regulating the biosynthesis of cholesterol, fatty acids and triglycerides[12].SREBP is controlled by cAMP, which may explain why β_2-agonism may affect LDL-c, HDL-c and triglycerides[13].

Thus working on newer aspects of older or conventional drugs is an open venture for future years. Already available or older drugs enjoy the confidence of experience and safety with their pharmacokinetics, pharmacodynamics and chemical properties discernible at present to all along with endorsement and approval by the standard regulatory authorities. Their by they provide good opportunity to begin with utilization of less resources than a totally new start altogether for discovery of a new drug.

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