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Trends in the development of novel approaches to cure benign prostatic hyperplasia: Hormones to 5α-Reeducates inhibitors

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Benign prostatic hyperplasia (BPH) a common condition of aging men is characterized by nonmalignant enlargement of the prostate gland, and clinically manifested as lower urinary tract symptoms (LUTS). Past experience reveals that with the advent of profound knowledge of the pathogenesis, the natural history, and risk of the progression and new generation of experiments powered by technological breakthroughs, the concept of management has undergone many changes with time. The specific approach used to treat benign prostatic hyperplasia depends upon number of factors like age, prostrate size, weight, prostate specific antigen level and severity of the symptoms. Quest spanning over hundred years to find out the novel approaches for the potentially progressive condition (BPH) of aging men has resulted in the discovery of the Finasteride and Dutasteride as 5α-Reeducates Inhibitors in 2002, starting from the discovery of the first stillbesterol in the early 1937. Research outcome from our laboratories has also resulted in some novel steroidal derivatives as 5α-Reeducates Inhibitors and found to be more potent than Finasteride. These new agents can be used for the design of future targets and development of new drugs in the treatment of BPH. Yet one cannot be certain that the quest has ended and the discovery of this number of active leads may also help in developing new safe and effective drugs.

Personalized medicine is an approach to medical care that tailors therapy to the individual characteristics of each patient. With advances in genomic analysis and the ability to develop biomarker assays and targeted therapeutics using small molecules, personalized medicine can more accurately diagnose disease, prognosticate those at risk of developing more aggressive disease, and identify who will likely respond to a medication to help direct the optimal course of management while minimizing morbidity and potential side effects from ineffective therapies. This approach can also improve efficiency and lessen the financial burden on the current healthcare system.

Lower urinary tract symptoms (LUTS) negatively impact quality of life for millions of patients and cost the US healthcare system over $4 billion each year. These symptoms include voiding or obstructive symptoms such as weak stream, hesitancy, and sensation of incomplete emptying, and storage or irritative symptoms such as urgency, frequency, and nocturia. The etiology of LUTS includes urological, neurological and comorbid conditions. While the hallmark of symptomatic benign prostatic hypertrophy (BPH) involves bladder outlet obstruction, other causes of LUTS include bladder cancer, prostate cancer, urinary tract infection, overactive bladder, urethral stricture, cerebrovascular accident or other neurologic injury, Parkinson's disease, diabetes mellitus, congestive heart failure, and obesity.For personalized medicine to succeed in the treatment of LUTS, it should identify the specific disease which is the cause of the LUTS. Our goal in this review is to focus on the application of personalized medicine for management of bladder outlet obstruction secondary to BPH, which as mentioned above, is one of many causes of LUTS.

BPH appears to be associated with a state of hyperplasia of both the stromal and epithelial compartments, with the enzyme 5α reductase Type 2 (5AR2) playing a key role in driving organ growth. The mainstays of medical therapy include 5α reductase inhibitors (5ARIs) and alpha-adrenergic blockers. However, at least 25–30% of patients do not respond to this therapy.Understanding specific mechanisms and differential gene expression amongst individuals will allow for a better targeted approach to medical therapy.

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