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APALUTAMIDE :
OPTION FOR THE TREATMENT OF NON-METASTATIC CASTRACTION RESISTANT PROSTATIC CARCINOMA

INTRODUCTION

Most prostate cancers are slow growing; however, some grow relatively quickly. The cancer cells may spread from the prostate to other area of the body, particularly the bones and lymph nodes. It may initially cause no symptoms. In later stages, it can lead to difficulty urinating, blood in the urine or pain in the pelvis, back, or when urinating. Factors that increase the risk of prostate cancer include older age, a family history of the disease, and race. About 99% of cases occur in males over the age of 50. Having a first degree relative with the disease increases the risk two to threefold.

APALUTAMIDE

Apalutamide is a nonsteroidal antiandrogen (NSAA) medication which is used in the treatment of prostate cancer. It is specifically indicated for use in conjunction with castration in the treatment of non - metastaticcastration-resistant prostate cancer (NM-CRPC). It is taken by mouth.

PHARMACOLOGY

Pharmacodynamics

Apalutamide acts as a selective competitive silent antagonist of the androgen receptor (AR) of the androgen receptor, via the ligand-binding domain, and hence is an antiandrogen. It is similar both structurally and pharmacologically to the second-generation NSAA [Non-steroidal antiandrogen] enzalutamide, but shows some advantages, including higher antiandrogenic activity as well as several-fold following 4 weeks of administration, with an approximate 5-fold reduced central nervous system distribution. The latter difference may reduce its comparative risk of seizures and other central side effects. Apalutamide has 5- to 10-fold greater affinity for the AR than bicalutamide, a first-generation NSAA. The acquired F876L mutation of the AR identified in advanced prostate cancer cells has been found to confer resistance to both enzalutamide and apalutamide. A newer NSAA, darolutamide, is not affected by this mutation, nor has it been found to be affected by any other tested/well - known AR mutations.

Pharmacokinetics

The oral bioavailability of apalutamide is 100%. Mean peak levels of apalutamide occur 2 hours following administration, with a range of 1 to 5 hours. Food delays the median time to peak levels of apalutamide by approximately 2 hours, with no significant changes in the peak levels themselves or in area-under-curve levels. Steady-state levels of apalutamide are achieved accumulation. Peak concentrations for 160mg/day apalutamide at steady-state are 6.0µg/mL (12. 5µmol/L), relative to pea levels of 16.6µg/mL (35.7µmol/L) for160mg/day enzalutamide and mean (R)-bicalutamide levels of 21.6µg/mL (50.2µmol/L) for 150mg/day bicalutamide.The mean volume of distribution of apalutamide at steady-state is approximately 276 L. The plasma protein binding of apalutamide is 96%, while that of its major metabolite. N-desmethylapalutamide is 95%, both irrespective of concentration. Apalutamide is metabolized in the liver by CYP2C8 and CYP3A4. A major active metabolite, N-desmethyla palutamide, is formed by these enzymes, with similar contribution of each of these enzymes to its formation at steady-state.

Following a single oral dose of 200 mg apalutamide, apalutamide represented 45% and N-desmethylapalutamide 44% of total area-under-curve levels. The mean elimination half-life of apalutamide at steady-state is 3 to 4 days. After a single dose of apalutamide, its clearance rate (CL/F) was 1.3L/h, while its clearance rate increased to 2.0 L/h at steady-state. This change is considered to be likely due to CYP3A4 auto-induction. Approximately 65% of apalutamide is excreted in urine (1.2% as unchanged apalutamide and 2.7% as N-desmethylapalutamide) while 24% is excreted in feces (1.5% as unchanged apalutmaide and 2% as N-desmethylapalutamide).

Side effects

Hot flushes, joint pain, tiredness, nausea, decreased appetite, weight loss, decreased sexual ability, increased blood pressure, underactive thyroid,seizure, rashes, itching, dizziness.

CONCLUSION

Aplatumide is a better option for the treatment of castration resistant non-metastatic prostatic carcinoma in adult. It is better option than other Anti-androgen or 5-alpha reductase inhibitors. Aplatumide possess less side effects as comparison to other anti-androgens or 5-alpha reductase inhibitors.

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A RETROSPECTIVE STUDY ON EPIDEMIOLOGICAL PATTERN AND PROTOCOL FOR THE MANAGEMENT OF SNAKE BITE CASES FOLLOWED BY AWARENESS ON PREVENTIVE STRATEGIES AND FIRST AID MEASURES FOR THE COMMUNTIY

Snake bite is an important and serious problem in many parts of the world, especially in South Asian countries. The estimated number of snakebites worldwide has been put as 5.4 million resulting in 2.5 million envenomations and 125,000 deaths.
It is estimated that there are over 1,000,000 snakebites in India alone leading to between 45,000 and 50,000 deaths annually. Of the estimated deaths due to venomous snakebite worldwide, half occur in India. In the state of Tamilnadu, nearly 30,000 cases are reported per annum and the death rate is about 1%.

BACKGROUND

Snake bite is an acute life threatening time limiting medical emergency. It is a preventable public health hazard often faced by rural population in tropical and subtropical countries with heavy rainfall and humid climate [44]. Snake bite is a well-known occupational hazard amongst farmers, plantation workers and other outdoor workers and result in much morbidity and mortality throughout the world. This occupational hazard is no more an issue restricted to a particular part of the world, it has become a global issue.

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PROTOCOL FOR SNAKEBITE

Step 1: Detailed History, Physical Examination, Basic Laboratory Investigations, H/o Allergy &Asthma (Atopy)

Step 2: Determine poisonous / non-poisonous snake bite. If poisonous determine, neurotoxic / cytotoxic or both

Step 3: Assessment of type of poisoning: Neurotoxic or Haemotoxic

Step 4 : Treatment Protocol:
General: Assess Airway, Breathing and Circulation Start TWO IV lines with wide bore needles, Ventilate (if necessary) Injection T.T. (if not documented earlier) Anti-Snake Venom administration

Step 5: Repeat Dose of ASV

RESULT

COMPARISON OF NO: OF CASES BEFORE AND AFTER AWARENESS

S.No	AWARENESS	No.S	%
1.	BEFORE	43	57.33
2.	AFTER	25	33.33

COMPARISON OF CLINICAL OUTCOME BEFORE AND AFTER AWARENESS

S.No	AWARENESS	No.S	%
1.	BEFORE	6	8
2.	AFTER	3	4

CONCLUSION

Educating the rural people about hazards of snake bite, early referral and treatment is very important Poison information center should be created for better access to the public on poison management.

Most of the snakebites were preventable as they were associated with occupation and absence of footwear. Health education measures should be intensified about the use of gumboots to protect rural farmers from snakebite.

Training of the rural MOs regarding snakebite management is required because snakebite can be managed at Primary Health Centre level only.

Proper storage of Anti venom is vital to prevent Adverse reactions to Anti venom. Adequate preparedness of the rural health centers regarding snakebite management specially during rainy season is very crucial. Emphasis on early reporting of any snakebite to the local hospitals is recommended.

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WORLD AIDS DAY AWARENESS PROGRAMME HAS BEEN CONDUCTED BY OUR FACULTY MEMBERS & STUDENTS IN PERIYAMPATTI ON 03.12.2018

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