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RESEARCH ARTICLE

EVALUATION OF CLINICAL OUTCOME AND ESTIMATION OF EFFECT OF SERUM CREATININE LEVELS IN PARKINSON'S PATIENTS WITH THE ADMINISTRATION OF ROPINIROLE.

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Abstract:
Parkinson's disease is a long term degenerative disorder of the central nervous system that mainly affects the motor system. Dopamine agonists are used in the treatment of parkinson's disease. Ropinirole is a dopamine agonist used in the treatment of parkinson's disease. Creatinine is a chemical waste molecule i.e. generated from muscle metabolism. Abnormally high levels of creatinine may indicate kidney damage or CKD. Few studies have been reported that the creatinine levels in parkinson's patients increase with ropinirole administration. This review is designed to investigate the rise in creatinine levels while taking ropinirole as an anti- parkinson's drug. The study is planned to conduct at Pushpagiri Medical College Hospital under the Neurology Department.

Key Words: Parkinson's disease, Creatinine, Ropinirole, Dopamine agonists.

Introduction:-

Parkinson's disease (**PD**) is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. The symptoms generally come on slowly over time. Early in the disease, the most obvious are shaking, rigidity, slowness of movement, and difficulty with walking(1). Thinking and behavioural problems may also occur. Dementia becomes common in the advanced stages of the disease.[1] Depression and anxiety are also common occurring in more than a third of people with PD. Other symptoms include sensory, sleep, and emotional problems. The main motor symptoms are collectively called "parkinsonism", or a "parkinsonian syndrome". The motor symptoms of the disease result from the death of cells in the substantia nigra, a region of the midbrain.

Ropinirole is a dopamine agonist prescribed for mainly Parkinson's disease, RLS and extrapyramidal symptoms. It can also reduce the side effects caused by selective serotonin reuptake inhibitors, including Parkinsonism syndrome as well as sexual dysfunction and erectile dysfunction caused by either SSRIs or antipsychotics.[4]Ropinirole acts as a D_2, D_3, and D_4 dopamine receptor agonist with highest affinity for D_2.(2)

For Parkinson's disease, the maximum recommended dose is 24 mg per day, taken in three separate doses spread throughout the day. The maximum dose recommendations of ropinirole for subjects with end stage renal disease (ESRD) should be reduced by 25% compared with those recommended for subjects with normal renal function. A 25% dose reduction represents a more straightforward dosage regimen in terms of available tablet strength, compared with a 30% dose reduction

- Creatinine is a chemical waste molecule that is generated from muscle metabolism.
- Creatinine is produced from creatine, a molecule of major importance for energy production in muscles.
- Approximately 2% of the body's creatine is converted to creatinine every day.
- Creatinine is transported through the bloodstream to the kidneys. The kidneys filter out most of the creatinine and dispose of it in the urine.
- Because the muscle mass in the body is relatively constant from day to day, the creatinine production normally remains essentially unchanged on a daily basis.[3][4]

Normal levels of creatinine in the blood are approximately 0.6 to 1.2 milligrams (mg) per deciliter (dL) in adult males and 0.5 to 1.1 milligrams per deciliter in adult females. (In the metric system, a milligram is a unit of weight equal to one-thousandth of a gram, and a deciliter is a unit of volume equal to one-tenth of a liter.)
The study involves the rise in serum creatinine levels while taking ropinirole as an anti Parkinson's drug. A rise in serum creatinine levels has been shown in some studies

Hanaa M. Roshdy[3]*et al* (2015) conducted a study on **"**Cytogenetic, Biochemical and Histopathological Effects of Ropinirole on Albino Male Mice".Ropinirole is a synthetic, nonergot derivative receptor agonist that has selective activity for the D2 class of dopamine receptors. Ropinirole is approved for the therapy of symptomatic Parkinson's disease and restless legs syndrome. The effects of ropinirole in doses equal and above the maximum recommended doses for human has not been adequately studied. dependent. The biochemical analysis were examined in the liver and kidney of treated males. The results showed that there were significant increases in the frequencies of MDA, ALT, AST, urea, uric acid and creatinine levels in all treated groups compared with the control males and these increase were dose-dependent. Moreover, the pathological analysis examined in the liver and kidney tissues of treated and control males showed that there were vascular degeneration of hepatocytes reduction of cellular in filtration and dilation of main blood vessels in liver tissue and intestinal hemorrhage and thickening of the parietal wall of Bowman capsule was observed in renal tissue and these effects were dose-dependent.

Pauline Anderson[4]*et al* (2015) conducted a study on **"**Creatinine Study in Parkinson Disease Terminated early". Despite early promise and a great deal of interest in creatinine monohydrate as a possible treatment of Parkinson disease, a large new double-blind, placebo-controlled trial found that this treatment does not improve clinical outcomes in patients with this neurologic disorder. The new findings "do not support the use of creatinine" in patients with early Parkinson disease treated with background dopaminergic therapy, the study authors, with corresponding author Karl Kieburtz, MD, MPH, from the University of Rochester Center for Human Experimental Therapeutics, New York, conclude. The trial was terminated early for futility on the basis of an interim analysis of 955 participants who had completed 5 years of follow-up.

Kulisevysky. J[5]*et al*(2010) conducted a study on "Tolerability and Safety of Ropinirole versus Other Dopamine Agonists and Levodopa in the Treatment of Parkinson's Disease".The present study evaluated the tolerability and safety of ropinirole against those of other dopamine agonists (bromocriptine, cabergoline, pramipexole, rotigotine, pergolide) and placebo in monotherapy and adjuvant therapy with levodopa in the treatment of Parkinson's disease, as reported in the peer reviewed medical literature. A systematic review of the medical literature was carried out for relevant English language articles in the MEDLINE database and Cochrane Library from January 1975 to November 2008. The searches were limited to either double-blind clinical trials or randomized clinical trials that included both patients with early Parkinson's disease receiving dopamine agonist monotherapy, and patients at a later stage on combined treatment with levodopa. In all the included studies, dopamine agonists, including ropinirole, exhibited a higher incidence of adverse events than placebo. Ropinirole showed an adverse event profile similar to other dopamine agonists. Consideration of the clinical characteristics of each patient and the differences in the incidence of adverse events related to each dopamine agonist, may help to optimize the dopamine agonist therapy.

Stephane Thobois[6]*et al* (2006) . conducted a study on **"**Proposed dose equivalence for rapid switch between dopamine receptor agonists in Parkinson's disease".Progressive reduction of the dose of one dopamine receptor agonist and simultaneous, progressive dose escalation of another is a
frequently used strategy for controlling motor symptoms of Parkinson's disease (PD) or avoiding specific adverse events. Rapid switch has been proposed as an alternative that might reduce the need for such major limitations as the possible exacerbation of symptoms and the need to monitor patients for several weeks. However, the equivalence of doses of dopamine receptor agonists before and after switching drugs remains empirical because few clinical trials have addressed this issue. Six studies comparing 2 dopamine agonists and 4 studies analyzing the switch between dopamine agonists were selected. The proposed conversion factors were 1:6 for bromocriptine to piribedil, 1:6 for pergolide to ropinirole, 10:6 for bromocriptine to ropinirole, 10:1 for bromocriptine to pergolide, and 10:1 to 10:1.5 for bromocriptine to pramipexole.

Rascol[7]*et al* (2000) conducted a study on"Ropinirole as Compared with Levodopa inParkinson's Disease"**.** The studysummarize the results of their study by stating that Parkinson's disease is best managed with ropinirole alone as the initial treatment, with levodopa used as a supplemental, second step if necessary. This recommendation is based on their finding that the risk of dyskinesias (medication-induced chorea) is lower with ropinirole.If a reduced risk of

dyskinesia is to be the basis for making a recommendation with such broad implications, then the magnitude of the problem must warrant this concern. They reviewed the medical records of 350 randomly chosen patients with Parkinson's disease who were seen in the past year at our clinic, all of whom were receiving carbidopa–levodopa as primary treatment. Eighty-three of the patients (24 percent) had dyskinesias rated as moderate or severe (a score of 2 or higher on items 32 and 33 of the Unified Parkinson's Disease Rating Scale [UPDRS]). Of the patients who had been treated for 5 years or less, only 7 percent had clinically significant dyskinesias, and of the 246 patients who had been treated for up to 10 years, only 12 percent had clinically significant dyskinesias. ,Parkinson's disease can be managed well with levodopa therapy, without the use of adjunctive agonist therapy, over a five-year period. Our experience suggests that the risk of dyskinesias is a weak basis for a treatment recommendation with such broad clinical and financial implications. Although early use of an agonist makes sense in patients with early-onset Parkinson's disease, for patients in their 60s, 70s, or 80s, carbidopa–levodopa remains the best treatment.

Sethi KD[8] ***et al*** (1998) conducted a study on "Ropinirole for the treatment of early Parkinson disease: a 12-month experience".The objective of the study was to evaluate ropinirole hydrochloride as dopaminergic monotherapy in patients with early Parkinson disease. A 6-month extension of a double-blind, placebo-controlled study. Patients who successfully completed the initial 6-month study could enter the 6-month extension study (ropinirole, n = 70; placebo, n = 77).The efficacy variables were the number of patients who successfully completed the 12-month study and did not require supplemental levodopa, the number of patients requiring supplemental levodopa, and the proportion of patients having an insufficient therapeutic response. The result of the study shows that ropinirole was effective and well tolerated as monotherapy for 12 months in patients with early Parkinson disease

Conclusion:-

The current review shows the study to be conducted in order to study the rise in creatinine levels with the administration of ropinirole in parkinson's patients by conducting a prospective experimental study. The sudy is a control based study.

References:-

1. Com3ella CL, Stebbins GT, Brown-Tom SN, Goetz CG. Physical therapy and Parkinson's disease: a controlled clinical trial. Neurology, 44, 1994, 376-378.
2. Lida M, Miyazaki I, Tanaka K, Kabuto H, Iwata-Ichikawa E, Ogawa N: Dopamine D2 receptor-mediated antioxidant and neuroprotective effects of ropinirole, a dopamine agonist. Brain research, Volume 838, Issues 1–2, 14 August
3. Hanaa M. Roshdya, Mahrousa M. Hassananea, Salwa M. Kassema, Nermeen M. Shaffieb. Cytogenetic, Biochemical and Histopathological Effects of Ropinirole on Albino Male Mice'. Int. J. Pharm. Sci. Rev. Res., 30(1), January – February 2015; Article No. 29, Pages: 160-168
4. Pauline Anderson, Laurie Barclay, MD. Creatinine Study in Parkinson Disease Terminated Early. CME/CE Released: 5/5/2015; Valid for credit through 5/5/2016
5. Jaime Kulisevsky, Javier Pagonabarraga. Tolerability and Safety of Ropinirole versus Other Dopamine Agonists and Levodopa in the Treatment of Parkinson's Disease Meta-Analysis of Randomized Controlled Trials. February 2010, Volume 33, Issue 2, pp 147–161
6. ThoboisS.Proposed dose equivalence for rapid switch between dopamine receptor agonists in Parkinson's disease: a review of the literature. ClinTher. 2006 Jan;28(1):1-12.
7. Rascol et al. (May 18 issue. Ropinirole as Compared with Levodopa in Parkinson's Disease.Engl J Med 2000; 343:884-885September 21, 2000DOI: 10.1056/NEJM200009213431211 the new England journal of medicine
8. Sethi KD[1], O'Brien CF, Hammerstad JP, Adler CH, Davis TL, Taylor RL, Sanchez-Ramos J, Bertoni JM, Hauser RA. Ropinirole for the treatment of early Parkinson disease: a 12-month experience. Ropinirole Study Group. 1998 Sep; 55(9):1211-6.