VOLUME - 9, ISSUE - 10, October - 2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Oncology

ROLE OF HORMONE THERAPY IN MEDICAL ONCOLOGY-

Awasthi, Chakrapani	Assistant professor Government Medical College Datia(MP).
Baig ,M.Q*	Associate professor MLB Medical College Jhansi. *Corresponding Author
Mahor Sachin	Associate Professor MLB Medical College Jhansi.

ABSTRACT First person was an Scottish surgeon Mr George beatson who removed ovary of breast cancer patient in1896 and found that tumor regressed but recurrence soon occurred resulted into disuse of procedure However 30 year later again in 1922 estrogen hormone was isolated people again thought of ovarian irradiation or surgical oopherectomy in breast cancer patients
in 1941 Huggins from usa reported favorable outcome of prostatic cancer while removing testis since that lots of work on hormone, treatment of breast cancer prostate cancer, thyroid cancer, endometrial cancer, Prostate has been done so far .

KEYWORDS : Ovarian cancer, Thyroid cancer, Prostate Cancer

DISCUSSION-

Hormone treatment of breast cancer patients
Locally advanced breast cancer
↓

Given 4 cycle of neo adjuvant chemotherapy ---- followed by response assessment
(Good response lesion become T1, T2, N0,N1, breast conservation therapy can be performed-----followed by radiotherapy-----maintenance treatment----hormone therapy)
(Poor response ---change type of chemotherapy---still no response
(Role of pre op radiotherapy)----Modified radical mastectomy----radiation therapy---maintenance chemotherapy----hormone treatment)

Breast function and development depends upon
Directly-----estrogen,progestrone,prolactin hormone
Indirectly----- corticosteroids, growth hormone, thyroid hormone estrogen responsible for ductal growth and progesterone responsible for alveolar growth

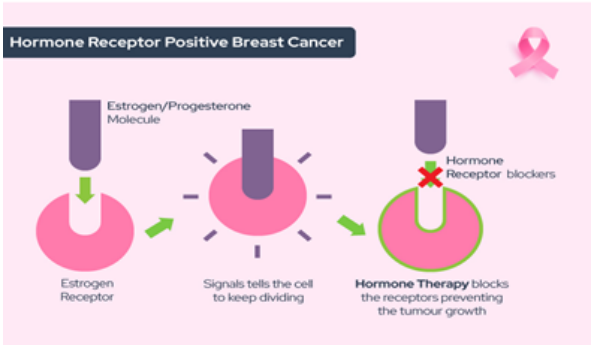

Figure -1

RECEPTOR STATUS

There are specific cytoplasm receptor known as estrogen and progesterone receptors present in breast tissue, this hormone present in tissue and stimulate cell growth by binding hormone receptors legend complex goes into nucleus attached to specific site of DNA and stimulate gene responsible for production of several growth factor

1- fibroblastic growth factor
2- transforming growth factor
3 -insulin like growth factor
4 -epidermal growth factor

Estrogen and progesterone receptor are cytosol protein that can be identified either on primary tumor tissue or metastatic tissue

Technique used are---Immuno histochemistry &fish technology
ER—positive & pr – positive – status in premenopausal women----45%
ER—positive & pr – positive – status in postmenopausal women----65%

Biopsy required for receptor status study not fnac
ER considered positive when> 10 fam mol/mg of breast tissue
PR considered positive when> 5 fam mol/mg of breast tissue
ER, PR Status evaluation must be done prior to chemotherapy or radiotherapy because adjuvant treatment might change the receptor status due to inherent tumor biology during surgery Cauterization must be avoided because these receptors are heat labile

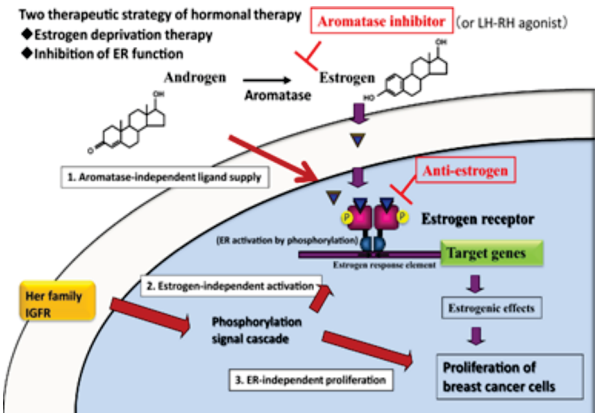

Figure-2

Response status with hormone treatment

RECEPTOR –ER Positive ,PR Positive= 78%
ER+, PR - =35%
ER-, PR-=10%
ER-,PR+ =45%

Why ER-ve,PR-ve tumor still have 10%response reacts with hormone treatment because it is a quantitative assessment , Tamoxifen anti estrogenic drug but has a week agonist action on endometrium, it blocks the estrogen hormone action on estrogen receptor, henceforth it blocks the production of several growth factor responsible for tumor growth

tamoxifen dose recommended is 10 mg bd or 20 mg od, it can be used as primary modality of treatment in very old lady not suitable for surgery or radition therapy

SIDE EFFECT OF TAMOXIFEN

Hot flushes (SSRI)-40% most common, vaginal dryness, fluid retention, irregular menstruation, thromboembolism,2%,risk of endometrial hyperplasia---endometrial cancer
Some patient does not response to hormone therapy?

What is tamoxifen resistance?

Tamoxifen have both antiestrogenic effect as well as weak estrogenic effect some breast cancer cells shows cellular hyper sensitization to the week estrogenic effect of tamoxifen leading to tamoxifen resistance

Aromatase inhibitor

we know post menopausal women major source of estrogen is from adrenal gland , it produces Androestrodian which gets converted in peripheral adipose tissue into estrogen by help of aromatase enzyme, thus aromatase inhibitor can be use as anti estrogenic drug dose 1 letrazal 2.5 mg od 2 Anstrazol 1 mg od

Indication of aromatase inhibitor over tamoxifen

1) post menopausal women
2) women h/o tamoxifen response
3) women with h/o dvt
4) women with her 2+ve status

Side effect of Aromatase inhibitor

Hot flushes (can be treated by SSRI (example Venlaflaxin), vaginal dryness, musculoskeletal pain, high rate of osteoporosis compare to tamoxifen ,headache, duration of treatment still unanswered.

OTHER OPTIONS FOR HARMONAL MANIPULATION

LHRH agonist—Goserline (zoldex) 33.6 mg s/c 4 weekly
Leuprolide 3.75 mg s/c 4 weekly or ovarian ablation with radiotherapy 15 Gy /5#
Progesterone –Medroxyprogesterone (provera) 400-500 mg po daily or i.m injection 500 mg weekly
pure antiestrogen (fulvestrant) 250 mg Im monthly

HORMONE TREATMENT OF PROSTATE CANCER INDICATION

1) Giving adjuvant treatment before and after radition increases survival
2) Single treatment with hormone is not sufficient combine treatment with orchidectomy & hormone therapy is required
3) Men who are osteopenic /osteoporotic should be strongly considered for Bisphosphonate treatment (zolindronic acid)

HISTORICAL BACKGROUND—

Almost a century ago androgen dependency of the prostate was shown by white, who treated malignant prostatic enlargement by orchidectomy without hormone treatment in localized diseases failure rate 10%, Without hormone treatment in extra capsular diseases failure rate 25% , Without hormone treatment in seminal vesicle involvement failure rate 75%, Hormone treatment is a sheet anchor for advanced prostatic cancer treatment

MODES OF HORMONE MANUPULATION

1) ESTROGEN
2) ORCIDECTOMY
3) LHRH AGONIST
4) NON STEROIDAL ANTIESTROGEN

ESTROGEN -Act by supporting LHRH and LH release thus taking away stimulus for testosterone production Major disadvantage- (cardiovascular effect)

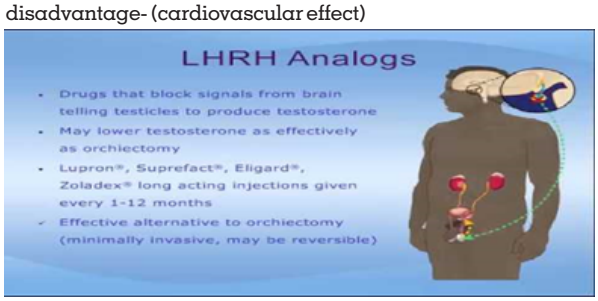

Figure -3

ORCHIDECTOMY—Bilateral orchidectomy is a gold slandered which rapidly brings down the serum testosterone to 1/10 th pre treatment value, Disadvantage—physical trauma to emasculation, loss of libido, erectile impotency, LHRH agonist- LHRH naturally secreted by hypothalamus, however if larger dose of LHRH agonist build up thus pituitary became refractory to LHRH stimulus thus stop secreting LH hormone thus decreases production of testosterone, however initially during LHRH agonist treatment these increases in testosterone production might leads to increase in symptom called flare phenomena, this can be effectively blocked by combining LHRH agonist treatment initially with anti androgenic drug like flutamide 250 mg tds.

NON STEROIDAL ANTI ESTROGENIC DRUGS-

Flutamide and Biclutamide, They are androgen receptor antagonist. They act inhibiting binding of testosterone and dihydrotestisteron to androgen receptor in target tissue.Doses fultamide 250mg tds and calutide 50 mg od

SIDE EFFECTS OF NONSTEROIDAL ANTI ESTROGENIC DRUG ARE

1. Gynecomastia
2. Gastrointestinal side effect
3. Derange Liver function tests

Advantage of treatment with non steroidal anti androgenic drugs, No cardiovascular side effects, Maintaining the sexual potency, Treatment with flutamide and orchidectomy leads to significant improvement in overall survival metastatic prostatic cancer

Hormone treatment in thyroid cancer - Differentiated thyroid cancer patients after surgery &radio iodine treatment patient developed hypothyroidism, to aim of giving external thyroxin treatment life long,

1) after surgery to avoid deficiency of t3/t4 hormone
2) after surgery left over malignant cells might repopulate under influence of TSH thus to decreases TSH level be give T3 T4 hormone treatment

REFERENCES-

1- Hersh AL, Stefanick ML, Stafford RS (2004) National use of postmenopausal hormone therapy: annual trends and response to recent evidence. JAMA 291:47–53
2- Writing Group for the Women's Health Initiative I (2002) Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the women's health initiative randomized controlled trial. JAMA 288:321–333
3- Cogliano V, Grosse Y, Baan R, Straif K, Secretan B, El Ghissassi F (2005) Carcinogenicity of combined oestrogen-progestagen contraceptives and menopausal treatment. Lancet Oncology 6:552–553
4- Cook LS, Weiss NS, Doherty JA, Chen C (2006) Endometrial cancer. In: Schottenfeld D, Fraumeni JF (eds), Cancer epidemiology and prevention. Oxford, Oxford Press
5. Beatson CT. On treatment of inoperable cases of carcinoma of the mamma: suggestions for a new method of treatment with illustrative cases. Lancet. 1896;148(3803):162–165.
6. Feinlieb M. Breast cancer and artificial menopause: a cohort study. J Natl Cancer Inst. 1968;41(2):315–329.
7. MacMahon B, Cole P, Lin M, et al. Age at first birth and breast cancer risk. Bull

World Health Organ. 1970;43(2):209–221.
8. McGuire WL, Chamness GC. Studies on the estrogen receptor in breast cancer. Adv Exp Med Biol. 1973;36(0):113–136.
9. Hoover R, LA Gray Sr, Cole P, MacMahon B. Menopausal estrogens and breast cancer. N Engl J Med. 1976;295(8):401–405.
10. Ross RK, Paganini-Hill A, Gerkins VR, et al. A case-control study of menopausal estrogen therapy and breast cancer. JAMA. 1980;243(16): 1635–1639.