ORIGINAL RESEARCH PAPER

Radiotherapy

FOR HIGH RISK GESTATIONAL TROPHOBLASTIC TUMORS, SHOULD WE REPLAC TRADIONAL CHEMOTHERAPY REGIMEN WITH NEW FRONTLINE BRD MC REGIME?

KEY WORDS: pelvis, sexual dimorphism, sciatic tubercle.

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ABSTRACT

Many researchers have emphasized the need for population specific data for methods which are based on measurements, as there are vast differences in body size in various populations. The pelvis is known to be the most sexually dimorphic part of the human body, the greater sciatic notch is the one of the most important discriminators between male and female and when we take the index value of greater sciatic notch ranging between 60.40 to 187.90 in male and the value of female hip bones ranging between 65.0 to 164.30. The purpose of this study was therefore to develop discriminant functions which can be used for sex determination on measurements of the pelvis.

Introduction – Gestational trophoblastic disease is basically group of disease which develops due to normal fertilization they are complete Hydatdiform mole, Partial Hydatdiform mole , Invasive mole, Choriocarcinoma, Placental site trophoblastic tumor, Above these group of disease occurs in reproductive age group of female and having high cure rate if treated early and comprehensively. That's why immediate and most effective form of Chemotherapy Regime must be offered to those young age females

Material and methods- Since traditional chemotherapy regimen used and their schedule is some how cumbersome as well as more over patients compliance is a problem.

So our aim is to find out simple straight form of new regimen of chemotherapy which is cost effective as well as have better compliance rate from patients side study will be aimed at following points.

a) Clinical Response rate
b) Toxicity profile

Study carried out on all High risk GTD patients registered in department of radiotherapy, BABA RAGHAVDAS MEDICAL COLLEGE, GORAKHPUR. All cases are diagnosed and histological proven as Gerntational trophoblastic disease with high serum HCG level. All the patients after taking their consent along with ethical committee approval taken up for study.

Inclusion criteria –
i) Previously untreated cases
ii) Minimum KPS 70 or more
iii) All cases having adequate bone marrow reserve WBC>4000/cm^3 Platelet count > lac/mm^3 Hqb> 10gm%.

Exclusion Criteria –
i) Patients having any concurrent illness along gestational trophoblastic disease.
ii) Patients who defaulted treatment during chemotherapy.
iii) Patients who have already received chemotherapy for the same disease.

Scheme of treatment –
All patients included in the study must be having serum HCG level more then 800 miu / ml.

All patients started with straight forward Cisplatin and Etoposide chemotherapy, with schedule dose adjusted according to their BSA(BODY SURFACE AREA) , Cisplatin given 45 mg./m^2 IV D_1 to D_2 and Etoposide 120 mg / m^2 D_1- D_3 with a name given as **BRD MC Regimen chemotherapy** and all patients Given adequate hydration before each cycle of chemotherapy on 3 weekly basis, All patients were giver 6 cycle of Cisplatin and Etoposide, chemotherapy, with every 3 cycle, Serum HCG estimation was done before each cycle of Chemotherapy and LFT, KFT, CBC was carried out .

Response Assessment and follow up –
Response assessed under three categories.

1)Complete response – Complete disappearance of symptoms USG pelvis (Radiologically) as well as normalization of HCG level.

2)Partial response - Only 50% reduction of size of tumor (Radiologically by USG pelvis) and 50% reduction of serum HCG level.

3)No response – Less than 50% response, Radiologically as well as Serologically will be

GTD PATIENT

S.No	Pt. Name	Registration No.	Age	Diagnosis	ßHCG level Pre Treatment	ßHCG level Post Treatment	HPE
1.	**A,K,**	176355	20 Ys.	GTD	31st March, 2017 31181.59 MIU/ML	6th July, 2017 13172.00 MIU/ML	Vasicular mole code no.3096 date 24-02-2017
2.	**NR,**	52605	23 Ys.	GTD	02-02-2017 225000 MIU / ML	19-04-2017 69900 MIU / ML	Decidua & chorionic villi with hydropic changes DH 276 /17 Dat
3.	**R,D,**	146601	22 Ys.	GTD	10-04-2016 144171.7 MIU / ML.		Gestational chorio carcinoma HP/ 13331/16 dt 06-04-2016
4.	**VD**	227271	28 Ys.	GTD	29-05-2015 3557.6 MIU / ML.	22-09-2017 5.58 MIU / ML.	Hysterectomy done indication bleeding PV
5.	**R.K.**	29559	22 Ys.	GTD	31-03-2015 105.7 MIU / ML.	25-01-2016 at BRD 42.95 MIU / ML. .	Feature consistent with product of conception and chronic non specific endometritis code B -15 /5212

6.	**RZ**	31563	40 Yr.	GTD	15-05-2010 58775. 822 MIU / ML.	26-04-2012 Less then 1.20 MIU /ML.	Hydatidiform mole complete type, Slide Nuber A 10.260 Dated 19-05-2010

Discussion

Although Gestational trophoblastic tumors found only less than 1% of all Gynecological malignancy but for oncologist its important to promote awareness of its life threatening potential with high curability if treated early

In India molar pregnancy occurs one among 400 normal pregnancies, GTD commonly occurs after molar pregnancy with risk of 5 fold greater among women older than 40years of age as well as women with very high risk those who are around 20 years of age.

Women having blood group A when gets married with a men whose blood group is O at high risk of developing molar pregnancy.

Due to wide spread use of USG use in early pregnancy, prenatal diagnosis of molar pregnancy being made up even as early as 9 to 10 weeks of pregnancy.

Gestational trophoblastic tumors metastatic potential is 8.8 % cases having (most commonly in Invasive mole, Choriocarcinoma)

Prognostic Scoring

Table-1

	Score			
	0	1	2	4
Age	-	>39y	-	>39y
Antecedent Pregnancy	Mole	Abortion	Term	-
Interval from Pregnancy (MO)	>4	4-6	7-12	>12
Serum Human chorionic gonadotropin	>103 IU/L	103-104 IU/L	104-105 IU/L	>105 IU/L
Largest tumor	>3cm	3-5 cm	>5cm	-
Metastatic sites	Lung	Spleen, kidney	Gastrointestinal tract, liver	Brain
Number of metastases	-	1-3	4-8	>8
Prior Chemotherapy	-	-	One Drug	Two or more drugs
(From Bagshawe KD. Treatment o high-risk choriocarcinoma. J Reprod Med 1384;29:813, with permission)				

Score system apply,
0 to 6 considered as low risk group,
score ≥ 7 considered in high risk group

For high risk group combination chemotherapy is a treatment of choice after evacuation (D & C Procedure) EMA-CO Regime most commonly used which consist of agents , Etoposide, vincristine, Cyclophosphamide ,Dactinomycin ,Leucovarine,

Problems with above regime is the schedule of its treatment so patients compliance is one of the problem, second fertility preservation since most communal happens among women around 20 years of age its important to preserve fertility .

Knowing the fact EMA-CO Regime having response rate of 80 to 85 % for all high risk cases of molar pregnancy

Its that Cisplatin and Etoposide regime is not being used earlier but certainly not used as front line chemotherapy for all high risk cases of GTD tumors rather, Cisplatin and Etoposide being used as salvaged chemotherapy regime

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Drug Regimens for Gestational Trophoblastic Disease!!

LOW RISK (SINGLE AGENTS)

Methotrexale": 30-50mg/m^2 IM weekly; 0.4mg/kg IM or IV daily for 5 d (Repeat in 2 wk); or 1 mg/kg IM or IV on d I, 3.5, and 7 (repeat in 2 wk) plus folinic acid (leucovorin), o.1 mg/kg or Iv ON D 2,4,6 AND 8

Dactinomycin: 1.25 mg/m^2 IV (repeat in 2 wk), or 10ug/kg (up to 0.5 mg) IV daily for 5 d (repeat in 2 wk)

HIGH RISK (DRUG COMBINATION)

EMA-CO consists of alternating cycles of EMA (d 1 and 2) and CO (d 8)

Day 1: EMA *Etoposide,* 100 mg/m^2 IV; *dactinomycin,* 0.5mg IV; and *metho- trexte,* 100 mg IV push followed by 200 Mg/m^2 12-h IV

Day 2 : EMA : *Etoposide,* 100 mg/m^2 IV;*dactnomycin,* 0.5 mg IV; and *folinic* and 15 mg IV or PO every 12 h x 4,24 h after start of methotrexate

Day 8: CO: *vincristine,* 1 mg/ m^2 IV; and *cyclophosphamide*, 600 mg/ m^2 IV MEA consists of alternating cycles of methortexate (d 1) with EA (d9-11).
Repeated every 19 d.

Day 1: methotrexate, 300 mg/ m^2 IV; folinic acid, 15 mg every 6h to com- Mence 24 h after chemotherapy for 8 does (first 4 doses to given IV). 7 - d break.

Days 9-11: Etoposide, 100 mg/m^2 IV daily; dactinomycin, 0.5 mg IV daily.
7-d breaks and repeats methotrexate.

SALVAGE REGIMENS

VIP: etoposide, ifosfamide, and Cisplatin (doses as per germ cell regimen)
EMA-EP: Etoposide, methotrexate, actinomycin D-etoposide, Cisplatin 25

EP: Etoposide, Cisplatin (doses as per germ cell regimen)

Single agents: taxanes, platinum, and vinca analogue; topoisomerase I Inhibitors; ifosfamide; gemcitabine

Table-2

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