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ORIGINAL RESEARCH

STUDY ON EVALUATION OF MET FOR MINVERSUSINSUL IN THERAPYINTHE MANAGEMENT OF GESTATIONAL DIABETES

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ABSTRACT

BACKGROUND: Gestational Diabetes mellitus (GDM) is defined as Glucose Intolerance, the valuesof plasma glucose falling in the range of Diabetes which is observed and detected for the first timeduringsecondorthirdtrimesterofpregnancy.GDMisquite oftenassociatedwithhighermaternalandneonatalmorbiditiesin theshort andlong-term andpredisposesbothwomen andchildto laterdevelopment of type 2 Diabetes **OBJECTIVE OF THE STUDY:** the objective of our study is tocomparematernalandneonataloutcomesinGDMpatientswhoareonmetforminandinsulin**.** **MATERIALS &METHODS:** the study on evaluation of metformin versus insulin therapy in themanagement of gestational diabetes was conducted in dept. of OBG Adesh Institute of MedicalSciences,Ambalaafterobtaininginstitutionalethicalcommitteeclearanceforaperiod ofoneyearfromJanuary 2021 to December 2021 in the age group of 26-35 years. Maternal and neonatal outcomesrecorded include: maternal: incidence of pre-eclampsia, PIH, neonatal outcomes include: macrosomia,birth weight, the incidence of small for gestational age, prematurity, Apgar score at the age of 5 min,hypoglycaemia. We also compared the mode of delivery (spontaneous, assisted or caesarean section)between the two groups. **RESULTS & CONCLUSIONS:** It is quite evident from in our study thattherewerenostatisticallysignificantdifferencesinboththegroupswithrespecttomaternalc omplications, mode of delivery and neonatal complications. In our study, we found that the oral antidiabetic medication metformin is equally effective as insulin in the treatment of GDM patients andwithout higher risks for maternal or neonatal complications. However, further randomized clinicalstudies with large number of patients and with long-term follow-up of children is needed to determinetheroleofMetforminasanalternativetreatmenttoinsulinin GDMpatients.

KEYWORDS:gestationaldiabetesmellitus,metformin,insulin,pre-eclampsia,hypoglycemia,macrosomiaand pre-maturity.

INTRODUCTION: GestationalDiabetesmellitus(GDM)isdefinedasGlucoseIntolerance,th evaluesof plasma glucose falling in the range of Diabetes which is observed and detected for the first timeduringsecondorthirdtrimesterofpregnancy.GDMisquiteoftenassociatedwithhighermat ernalandneonatalmorbiditiesin theshort andlong-term andpredisposesbothwomen

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andchildto laterdevelopmentoftype2Diabetes.[1-3]
The prevalence of GDM is rising globally and if left untreated, the condition is associated with anincreased risk of foetal and maternal complications such as preeclampsia and large-for-gestational age(LGA) infants. Screening followed by treatment of GDM reduces the risk of complications. AmericanDiabetes Association (ADA) and World Health Organization (WHO) recommend to screen for overtdiabetes at first prenatal visit, since these women have (untreated) a very high risk for pregnancycomplications and need treatment with insulin. Shortly after delivery, the glucose values generallynormalize, but women with GDM and their offspring are at increased risk to develop type 2 diabetes(T2DM) later in life.[4-7]Two large randomized controlled trials (RCTs) conducted in the past haveconfirmed that treatment of GDM between 24 and 28 weeks of pregnancy results in less perinatalcomplications,mainlyinthefrequencyofLGAandpreeclampsia.
However,controversyexistsregardingtheoptimalscreening anddiagnosticapproach forGDM.[3-5]
Therapeutic approach for GDM started with exercise and diet control, pharmacological interventionInsulin)isquiteneededtoachieveglycaemiccontrolfurthertopreventpregnancyassociatedcomplications.20%to60%ofGDMpatientsrequireadditionaltreatment.Multipleinjections,hypoglycemia and weight gain are disadvantage of insulin therapy. Hence there is a need for alternatepharmacological approach, one such anti-diabetic medication is Metformin.[6-10] Metformin reduceshepatic gluconeogenesis and improves peripheral glucose uptake without causing hypoglycemia andweight gain. Metformin in pregnancy is also used in patients with polycystic ovary syndrome (PCOS).Infertility secondary to PCOS is also treated with Metformin. It has no adverse effect on foetus as itcrossesplacenta.Reductioninspontaneousabortionbytreatmentwithmetforminisreportedinthefirsttrimester. There are few studies regarding usage and comparison of metformin versus insulin in theprogressive management of GDM. Hence we have undertaken this study to evaluate metformin versusinsulinin themanagementofGDM.[11-14]

OBJECTIVE OF THE STUDY: The objective of our study is to compare maternal and neonataloutcomesin GDM patientswho areonmetformin and insulin**.**

MATERIALS AND METHODS:the study on evaluation of metformin versus insulin therapy in themanagement of gestational diabetes was conducted in dept. of OBG Adesh Institute of MedicalSciences,AmbalaafterobtaininginstitutionalethicalcommitteeclearanceforaperiodofoneyearfromJanuary2021 to December2021 in theagegroup of26-35 years.
After taking voluntary consent from all the patients enrolled in the study, we included age matched,BMImatchedGDMpatientswhowerediagnosedbasedonstandard2hour75gramsOGTTperformedat 11-32 weeks because of high risk duration. The diagnosis of GDM was confirmed based on atleasttwooutofthreeabnormallyhighglucose(intherangeofDiabetes)aslaiddownbyWHO,thatisfasting>120mg/dL,1hours>180mg/dland2hours>160mg/dlfollowingoral75gramsofglucosedissolvedin 300 mL of water.All patients were evaluated on OPD basis. Dietary and exercise counselling weredone. Self-monitoring of plasma glucose was thought to all the patients.We included a total of 100patientsdiagnosedwithGDMandwerandomlydividedsubjectsintotwogroupsGroup1patientsweregiven tab Metformin 500 mg to 1000 mg OD or BD. Group 2 were given regular insulin TID. Weexcluded type 1 diabetes patients, multiple gestations,

gestational age > 20 weeks, known foetal andchromosomal defects, contraindications to metformin use, on insulin at the start of pregnancy, andHbA1c> 9%.Maternal andneonataloutcomesrecordedinclude:maternal:incidenceofpre-eclampsia(elevatedBP>140/90 mmHg and proteinuria >0.3 gr/24 hours of urine), PIH (pregnancy induced hypertension:elevated blood pressure detected for the first time during pregnancy without proteinuria), neonataloutcomes include: macrosomia (birth weight > 4500 g and/or >2 SD), birth weight (grams and SD forgestational weeks), the incidence of small for gestational age (SGA; birth weight <2 SD), prematurity(birth < 37 weeks of gestation), Apgar score at the age of 5 min, hypoglycaemia (serum glucose<45mg/dL measured during the first two hours postpartum). We also compared the mode of delivery(spontaneous,assisted orcaesarean section)betweenthetwo groups.[15] Allthedatawasenteredintheexcelsheetandthestatisticalanalysiswasdoneusing SPSSsoftwareforthecomparisonbetween thegroups using student‘t’testand pvalue.

RESULTS AND DISCUSSION: We included a total of 100 GDM patients in our study, divided intotwo groups. Group 1 patients were given tablet metformin and Group 2 were given regular insulintherapy. The mean age in years and BMI in group 1 and group 2 were 29.62 ± 6 years, 32.45 ± 6.3kg/m^2 and 29.58 ± 6.1 years, 32.23 ± 6.89 kg/m^2 respectively. There were no statistically significantdifferencesin ageandBMIbetween thetwogroups. Thepvaluewas notsignificant.

Table1:Showstheincidence ofMaternalComplicationsandmodeofdeliveryin allpatients

	Group1 (number50)	Group2(number50)	P value
PIH	0 (0%)	0 (0%)	NS
Pre-eclampsia	2 (4%)	1 (2%)	NS
Inductionoflabor	25 (50%)	29 (58%)	NS
Spontaneousdelivery	29 (58%)	31 (62%)	NS
Assisteddelivery	6 (12%)	5 (10%)	NS
Caesareansection	15 (30%)	14 (28%)	NS

Itisquiteevidentfromtheabovetablethattherewerenostatisticallysignificantdifferencesinboththegroupswith respectto maternalcomplications and modeofdelivery.

Table2:ShowstheincidenceofNeonatalComplications

	Group1 (number50)	Group2 (number50)	P value
Birthweight	2832 ±400	2900 ±389	NS
APGARat5minutes	8.8 ±0.3	8.4 ±0.7	NS
Macrosomia	10 (20%)	12 (24%)	NS
Hypoglycemia	14 (28%)	24 (48%)	NS
Pre-mature	6 (12%)	5 (10%)	NS

Itisquiteevidentfromtheabovetablethattherewerenostatisticallysignificantdifferencesinboththegroupswith respecttobirth weight, APGARscoreand neonatalcomplications.

In our study, we evaluated maternal and neonatal complications in GDM patients with metformin andinsulintherapy.Inmeta-analysis3studiesmeasuredFBS,PPBSandHbA1Clevelstochecktheefficacyof metformin, the results were similar to our study, metformin was equally effective as insulin

inachieving glycaemic control in GDM patients. Metformin reduces hyperglycemia by suppressinghepaticgluconeogenesis,increasesinsulin sensitivityandperipheraluptakeof glucose.These effects are potentially useful in especially in GDM, when glucose control deteriorates withchanges to insulin resistance. Moreover, our findings, in accordance with the results of previousreviews, suggest that neonatal outcomes don't deteriorate with the use of metformin as compared withinsulininshortterm.Atthesametime,theresultsofstudiesforthelong-termimpactofmetforminuseareencouraging.Astudyfollowedtheneonateswhosemothersreceivedmetforminandfoundthattheydisplayednormalweightandsocialandmotorskillsat6monthsandtherewerenodifferencesinheight,weight, motor, or social skills between the neonatal groups at 18 months. Moreover, the results ofRowan et al. on this issue are both encouraging and reassuring which intrigue the possibility of benefitin children and adolescents with intrauterine exposure to metformin.[16-18.] The study conducted byHellmuth et al on GDM and T2DM conclude that in his study, GDM patients had increased incidenceofpreeclampsiaandperinatallossinmotherstreatedwithmetformin.Inourstudy,weidnotfindthisdifference. The reason of difference might be because of inadequately matched control groups in thestudy. The metformin group had other increased risk factors for preeclampsia unrelated to metforminuse.Inaddition,theirstudytheantidiabeticmedicationwasstartedsevenweekslaterthaninthewomentreated with insulin. In our study, control patients for metformin patients were matched for pre-pregnancy BMI and age. Therefore, there were no significant differences in BMI or age of the patientsbetween the groups. The disturbance in glucose metabolism was slightly more severe in insulin group.Thatis whyneonates ofinsulingroup havemoreincidences of hypoglycemia.

CONCLUSION: In our study, we found that the oral anti diabetic medication metformin is equallyeffective as insulin in the treatment of GDM patients and without higher risks for maternal or neonatalcomplications. Metformin could be used in women with GDM in view of the comparative glycemiccontrol and neonatal outcomes, especially for those mild GDM patients. However, the risk of pretermbirthcouldnotbeignored.Cliniciansshouldweighinpracticeaccordingtothecondition ofthepatients.Further studies with larger sample sizes must be completely designed to assess maternal and neonatalcomplicationsandtoevaluatelong-termfollow-upofchildrenforthesafetyofmetforminasauniversaltreatmentin GDM patients.

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