

PREGNANCY IN A WOMAN WITH WILSON'S DISEASE TREATED WITH ZINC: A CASE REPORT

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Wilson's disease is a rare hereditary disorder of copper metabolism affecting 30 per million populations. Copper get deposited in liver, brain and kidney due to decreased hepato-cellular excretion and leading to diverse clinical manifestations. Patient may remain apparently asymptomatic or may present with fulminant liver disease or neuropsychiatric illness. Reproductive outcome in untreated Wilson's disease is poor. Women remaining untreated either suffer from infertility or experience recurrent pregnancy losses. Invention of copper chelating agents and their usage in these women resulted in successful pregnancy outcome. Penicillamine or zinc salts can be used as copper chelator in pregnancy with Wilson's disease with equal effectiveness in respect to pregnancy outcome. We report a case of previously undiagnosed Wilson's disease with three consecutive pregnancy losses who achieved a live birth after successfully treated with zinc salts. The several points regarding antenatal care, drug therapy and optimum time and mode of delivery for the woman with Wilson's disease are discussed here.

Keywords: Penicillamine; Wilson's disease; Zinc

Untreated Wilson's disease (WD) is associated with poor pregnancy outcome [1,2]. Excess copper from maternal circulation transported through placenta either led to spontaneous abortion or intrauterine fetal death (IUFD) [2,3]. Treatment with copper chelating agents started prenatally may improve the scenario [1-3]. This case report describes a successful pregnancy outcome of a woman with WD treated with zinc; who had a past obstetrical history of three fetal demises.

liver function tests, she was screened for other causes of recurrent pregnancy loss. Along with folic acid she was advised to continue zinc salts. Her second trimester was uneventful. She was advised beta blocker from 20 weeks of gestation with consultation with physician to combat the severity of portal hypertension. From early third trimester she developed intrauterine growth restriction. She was treated expectantly. Ultrasonography of fetoplacental profile done at 34 weeks of gestational age revealed asymmetric growth restriction with reduced liquor volume and reduced diastolic flow

Case Report

A fourth gravida Indian woman with past history of three IUFDs and repeated attacks of jaundice attended antenatal clinic at 12 weeks of gestation. She was 29 years of age, a known case of WD, diagnosed recently one month before conception. Her pretreatment 24 hours urinary copper excretion was high with low normal serum ceruloplasmin. She had also oesophageal varices evidenced by endoscopy. Since then she was being treated with zinc salts 50 mg twice daily.

On examination she was found to be mildly icteric with moderate hepatosplenomegaly. Apart from routine investigations and

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in umbilical artery. She was admitted. Antenatal cardiotocography (CTG) performed twice weekly up to 36 weeks revealed reassuring pattern. She complained of less fetal movement at 36 weeks 4 days. CTG monitoring showed a nonreassuring pattern. A decision of emergency caesarean section was taken. She delivered a living female by caesarean-section, weighing 1.9 kg; with Apgar score 5/8. Her postoperative period was uneventful. The baby was healthy. She continued having zinc salts along with other drugs. She has been discharged on sixth postoperative day with an advice of follow-up.

Discussion

Pregnancy poses a peculiar problematic state in women with WD. Pregnancy temporarily improves the disease process in mother. There is amelioration of disease symptoms and signs in antenatal period due to pregnancy induced elevation of serum-ceruloplasmin level. Another possible explanation of this quiescence may be sharing of the maternal copper burden by growing foetus. Whereas, the fate of pregnancy in untreated woman is usually fatal due to placental transfer of high copper load [2,3].

This woman had poor obstetric carrier as she was previously remained undiagnosed. Treatment with zinc salt during this pregnancy resulted in successful pregnancy outcome. Different studies in this context concluded, treatment with copper chelating agents in women with WD improved their pregnancy outcome [1-3]. Penicillamine, zinc salts or trientine, all had equal efficacy and safety pattern in respect to this [1]. However, poor renal parameter is a contraindication of zinc therapy, which was ruled out here initially [1].

Possibility of foetal affection by chelating agents, particularly by penicillamine, was previously another point of concern. Later Sheinberg and Sternleib concluded the safety of penicillamine in pregnancy [4]. However; it needs 25 to 50% dose reduction near term as the same delays wound healing. Zinc has some added advantages that it does not require dose reduction and unlike penicillamine, breast feeding can be offered [1]. Gastric irritation as well as poor absorption when taken with foods are the two main problems of zinc administration [3]. We advised her to take the medication with small protein meals to reduce the side effects as well as to maintain the bioavailability. Few studies recommended 50 mg zinc salts three times a day as an optimum [1,3]. But considering the low body weight of Indian woman and to lessen the severity of gastric irritation, we kept the dosing schedule twice a day.

Apart from clinical evaluation and serial liver function tests, we have followed Brewer et al. [3] regarding monitoring of the disease process by measuring urinary copper excretion. Copper excretion less than 125 µg through 24 hours urine was considered as an index of optimum control [3]. During antenatal period we have measured 24 hours urinary copper excretion in two occasions. Average 53% (128 µg) reduction of the 24 hours urinary copper excretion level from the pre-pregnant diagnostic value (241.29 µg/24 hours) not only here confirmed the quiescence of the disease, but also ensured the adequacy of the present dosing schedule of zinc. The abnormal gene in WD, ATP7B, which is present in hepatocytes, can be identified by genetic diagnosis. However, this expensive test is neither universally available nor very much conclusive [1]. So a combination of clinical findings and bio-chemical parameters could play as basic tools for diagnosis and subsequent follow-up in the low resource settings like us.

Despite strict surveillance the woman developed IUGR in third trimester. The preexisting disease process along with usage of beta blocker since midtrimester might be accountable for this. Apart from hepato-splenomegaly with varices and moderately deranged liver functions, this woman had no other system involvement. However, co-existing neuro-psychiatric illness and preexisting poor renal and hepatic profiles in some antenatal women with WD may turn their pregnancy-events more challenging. Proper monitoring of their growth restricted foetuses and timely delivery by selecting appropriate routes is mandatory in these cases like other high risk pregnancies.

Sudden omission of chelating agents in antenatal period is another point of concern. Mothers often get provoked for omission either for apprehension of fetal affection or due to severe gastric irritation. This could result in severe regression of disease process and even leading to death [1]. Intense counselling in this regard and stringent monitoring can avoid this situation.

As like other AR disorders the baby remains as carrier. If father is bi chance heterozygous, chance of fetal affection is 50% [1]. This new-born needed screening as the paternal status was unknown. Measurement of ceruloplasmin level in Guthrie dried blood spots of new-born had been advised, which they could not afford at that time [5]. However a negative blood or urine screening of a new born do not entirely rule out the disease process and a repeat screening should be advised at two to five years of age [1].

Zinc, penicillamine or trientine; any form of copper chelating agents can be offered to the pregnant women with WD. However, zinc has some added advantages over the others. A point to be remembered here that merely adequate copper chelation does

not necessarily assure a favourable pregnancy outcome in women with WD. Preexisting poor hepatic and renal profile or neuro-psychiatric illness should be taken into consideration simultaneously, which could turn even a well-chelated pregnancy complicated. Prepregnancy counselling in this regard and subsequent stringent antenatal monitoring of these women might avert fetomaternal complications to a certain considerable extent.

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