

Evidence Based Management of Oligohydramnios

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Abstract

Background: Oligohydramnios, or abnormally decreased amount of amniotic fluid, complicates approximately 1 to 2 percent of pregnancies. It poses a risk to the fetus by contributing to perinatal morbidity and mortality, and due to iatrogenic preterm delivery. An increase in operative delivery increases the risk to the mother. Oligohydramnios may result from known etiological factors or it may accompany other pregnancy complications. When no etiological factor or association is identified, it is termed "Isolated Oligohydramnios".

Treatment strategies: This review presents the various treatment options for oligohydramnios in the light of current available evidence. Maternal hydration whether orally or by intravenous route is perhaps the most well studied intervention. Many therapeutic agents have also been tried. Of these, L-arginine and sildenafil have been supported by several studies but conclusive evidence for the same could not be identified

Conclusions: In cases of isolated oligohydramnios, therapeutic intervention is desirable to prolong the pregnancy so as to avoid preterm delivery and to prevent adverse perinatal outcome. Based on present scientific evidence we recommend that oral hydration therapy should be offered to the eligible women. Use of sildenafil citrate for this purpose cannot be recommended till its safety is well established in view of the recent reports of adverse fetal outcome.

Introduction

Oligohydramnios is an abnormally decreased amount of amniotic fluid in pregnancy. It complicates approximately 1 to 2 percent of pregnancies [1]. Sonographically, it is defined as amniotic fluid volume <5 percentile expected for gestational age; Amniotic Fluid Index (AFI) <5 cm or Single Deepest Pocket of liquor (SDP) <2 cm [2,3].

Evaluation of amniotic fluid provides important information about fetal structural and functional integrity and is predictive of pregnancy outcome. Oligohydramnios

can be present as isolated abnormality in an uncomplicated pregnancy, or can be associated with complicated pregnancy. The various possible etiological factors responsible for oligohydramnios are as under [4,5]:

- Preterm rupture of membranes
- Congenital abnormalities
 - Bilateral renal agenesis or cystic dysplasia
 - Obstruction of the urinary tract
 - Meckel-Gruber syndrome
 - VACTERL (vertebral, anal, cardiac, tracheo-esophageal, renal, limb) association
 - Sirenomelia

- Sacral agenesis
- Intra Uterine Growth Restriction (placental insufficiency)
- Post-term pregnancy
- Drugs like Angiotensin-converting enzyme inhibitors & Prostaglandin synthase inhibitors
- Twin- to -twin transfusion
- TRAP (twin reverse arterial perfusion sequence)
- Fetal demise
- Idiopathic

The risks associated with oligohydramnios depend on the gestation of the pregnancy at which it is diagnosed. Early onset Oligohydramnios is often associated with more serious complications such as compression of fetal organs resulting in birth defects, pulmonary hypoplasia and increased risk of miscarriage or stillbirth. If detected in the latter part of pregnancy, the associated complications could be IUGR, preterm birth, intra uterine fetal demise, intra-partum fetal distress and birth asphyxia. During labor, oligohydramnios can cause cord compression, meconium stained fluid, abnormal fetal heart rate, operative interventions, increased risk of cesarean delivery, lower Apgar scores, intensive care unit admission and neonatal death [6,7].

Occasionally Oligohydramnios in mid-pregnancy may not have an identifiable etiology and is termed "isolated oligohydramnios" (IO) [8]. The pathophysiology of IO itself is not clearly understood, but it reflects chronic or late-onset placental insufficiency [9]. In term pregnancies with IO, the baby should be delivered; and in preterm IO conservative management is advisable to minimize perinatal morbidity due to prematurity [10].

Treatment Strategies for Isolated Oligohydramnios

Oral Hydration Therapy

Rapid oral hydration in women with no other high risk factor has been found to be effective in increasing amniotic fluid volume. Intake of 250 mL of water (or hypotonic solution) in 15 min, total of 2 litres in 2hours can lead to an increase in fluid volume in both oligohydramnios and normohydramnios, with minimal risks to the mother and the baby. Hydration with water reduces maternal plasma osmolality and increased utero-placental perfusion. Maternal hydration has advantage over other interventions as it was cheap, easily available, non-invasive and does not require hospitalization or extensive monitoring. However it requires consistent and long term therapy as shown below (Table 1):

Authors (Year)	Study design (Sample size)	Methodology	Results	Mean Gestational age at diagnosis	Neonatal distress/ adverse events	Conclusion
Kilpatrick, et al. [11]	Randomized controlled blinded trial, (36)	Hydration group (n = 19) (AFI<6 cm) oral hydration 2000 ml/2-4 h was given. Control Group (n = 19) normal amount of fluid	The mean post-treatment AFI was higher in the Hydration group (6.3 versus 5.1; p < .01)	At term 37±4.8 (Hydration gp); 39±2.4 (Control Gp)s	None reported	Maternal oral hydration increases amniotic fluid volume in women with decreased fluid levels
Flack, et al. [12]	Non-randomized intervention study (20)	Study group(n=10) (AFI< or = 5 cm) and Control group(n=10) (AFI > 7 cm) were recruited and AFI determined before and after oral hydration by having the patient drink 2 L of water over 2 hours.	The mean AFI increased from 4.3 to 7.5 cm. No change in AFI was observed in women with normal AFI	36 weeks (Study group); 35 weeks (Control gp)	None	Short-term maternal oral hydration increases the amniotic fluid index in women with decreased amniotic fluid volume in third trimester
Fait, et al. [13]	Prospective, nonrandomized interventional study [60]	IO (AFI<6 cm). Study Group: (n = 30) instructed to drink 2litresof water daily for 1week. Control Group: women with normal AFI (routine hydration)	The mean AFI increased significantly in the Study Group after 1 week (p<0.01).	(Preterm) 29 weeks (Study gp) 28 weeks (Control gp)	Not reported	Long term oral hydration significantly increases the AFI in selected women with reduced fluid.
Ghfarnejad,	Randomized	Study group AFI < 6 cm) and	The mean AFI	-	Not	Acute oral hydration

et al. [14]	controlled trial (44)	Control group (AFI > 7 cm)	increased significantly after intervention in the study group		reported	is a noninvasive, easily accessible and cheap intervention, and an effective way of increasing AFI.
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Table 1: Oral Hydration Long Term Therapy.

Intravenous Hydration Therapy

Several studies on maternal hydration by intravenous fluids over a short duration found an increase in the AFI. Better results were achieved by intravenous hypotonic solution of 2L administered within a single day.

Significant improvements were not reported by isotonic hydration. The mechanism of action was similar to oral hydration i.e improvement in utero-placental perfusion. However, the increase in fluid volume was transitory (Table 2).

Authors (Year)	Study design (Sample size)	Methodology	Results	Gestational age at diagnosis	Neonatal distress/adverse events	Conclusion
Yan Rosemberg, et al. [15]	Randomized, double blind placebo controlled (44)	Treatment group (AFI<6cm) intravenous infusion of (1/2) NS at 1000 mL/h for 2 hrs. Placebo group received an iv infusion of (1/2) NS at 10 mL/h for 2 hrs	The AFI increased significantly in both groups (p <.05)	Third trimester	None	There are short-term increases in the AFI in patients with oligohydramnios whether treated with intravenous fluids or not. The short-term increase may be due to diurnal variations
Lorzadeh, et al. [16]	Randomized clinical trial (80)	Control group: normal hydration, Group A: oral 2L/2h. Group B: iv infusion of 2L/2h. NS Group C: iv infusion of 2L/2h hypotonic fluid	Mean AFI changes was statistically greater in oral water group, in comparison with IV isotonic and IV hypotonic groups (p<0.0001).	>35weeks	None	Significant increase in the AFI was seen by both IV hypotonic and isotonic fluid infusion as well as oral hydration. However, with regard to IV hydration, oral hydration was more effective for increasing the AFI.
Umber A [17]	Quasi experimental study (50)	Intravenous hydration group (n=25) (AFI <=5cm), 2L/2hrs of 5%D/W. Oral hydration group (n=25) (AFI<=5 cm), 2L/2hrs of water	Intravenous group (mean change in AFI 4.5 cm ± 1.25; P value < 0.05); In oral hydration group (mean change AFI 4.3 ± 1.23, 4.79; P value < 0.05).	28-40 weeks	None reported	Maternal intravenous as well as oral hydration increases AF volume in women with oligohydramnios but neither appears to be advantageous over the other
Patrelli, et al. [18]	Prospective randomized controlled study (137)	IO (AFI<5 cm). Group A: 66 patients with IO Subgroup A1 (n = 33): 1500 ml iv (Ringer solution) + 1500 ml oral daily for 6 days. Subgroup A2 (n = 33): 1500 ml iv (Ringer solution) + 2500 ml oral daily for 6 days. Group B: 71 women with normal AFI (routine hydration)	The mean AFI increased in group A after therapy. The mean AFI at birth was greater in subgroup A2 in comparison to A1 (P<0.001).	Early preterm 31.5 ±1.2 VS 31.4 ±1.3	None reported	In pregnancies complicated by IO and treated with intravenous hydration therapy for 6 days the quantity of AF is significantly improved. But oral hydration was better than intravenous route

Table 2: Intravenous Hydration Therapy.

Drugs

Among the pharmaceutical agents, L- arginine is a promising drug for the treatment of oligohydramnios. Nitric oxide synthesized from L-arginine is a potent vasodilator, improves utero-placental perfusion by reducing the viscosity of blood. Several studies have reported an improvement in amniotic fluid volume after

L-arginine intake of 3gm as sachet daily for 2-4 weeks. It is noninvasive and does not require monitoring and has an added advantage that its administration does not require hospitalization. However most of these studies have small number of women and no meta-analysis for the same could be identified in literature (Table 3).

Authors (Year)	Study design (Sample size)	Methodology	Results	Gestational age at diagnosis	Neonatal distress/ adverse effects	Conclusion
Sreedharan, et al. [19]	Prospective observational study (100)	Patients with AFI < 5th percentile for the particular gestational age were prescribed sachets of L-arginine 3g for 1 to 4weeks.	The average change in AFI was 2.03±0.39 cm	The mean gestational age at diagnosis was 31.1±2 weeks	None reported	L-arginine is effective in increasing amniotic fluid index in cases of oligohydramnios far from term.
Hebbar, et al. [20]	Prospective interventional study (50)	11 patients (AFI 4-8cm) with gestational hypertension. Were administered L-arginine (one sachet 3 g, twice daily. Others received both l-arginine and intravenous hydration (500 ml of fructodex 10%	Those who received only l-arginine showed an increase of 1.8 cm in AFI and those who received combined intervention improved their AFI score by 2.5 cm.	29-35 weeks	No adverse neonatal or maternal events were noted	Intravenous infusion of fructodex and oral l-arginine can be used a cheap and feasible method in resource-poor countries
Soni, et al. [21]	Retrospective study (100)	All patients with AFI < 8 cm were started on L- arginine 3gm/ 3 times a day, continued till adequate improvement in liquor was noted	The mean AFI at the end of therapeutic intervention was 8.753 an increase of 3.332 cm could be obtained	The mean gestational age at the time of recruitment was 32.3 weeks	None reported	L-arginine supplementation is promising in improving volume of amniotic fluid in oligohydramnios and prolonging pregnancy by a mean of 2.4 weeks

Table 3: Small number of women and no meta-analysis for the same could be identified in literature.

Recently, Sildenafil citrate has emerged as a new drug for the treatment of fetal growth restriction and oligohydramnios. Sildenafil citrate relaxes muscles in the walls of blood vessels and increases blood flow to particular areas of the body notably the pelvic vasculature. Although sildenafil has been used with success in erectile dysfunction in men and also for pulmonary arterial hypertension, only a few studies have reported its success in managing oligohydramnios. This

has been observed at a low dose of 25mg thrice daily. It has been tried more extensively in pregnancies with IUGR. However, recent reports of higher rates of intrauterine fetal demise in pregnancies treated with sildenafil has halted most studies till these losses can be investigated. While the studies and dosages used are enlisted in Table 4, it cannot be recommended for use until cleared (Table 4).

Authors (Year)	Study design (Sample size)	Methodology	Results	Gestational age at diagnosis	Neonatal distress/ adverse effects	Conclusion
Choudhary, et al. [22]	Case report	AFI =4.5cm and fetal weight 550gm.Sildenafil citrate 25 mg vaginally twice a day was started at 27 weeks. All medications were continued	Ultrasound at 30 weeks showed an AFI of 7.5 and a fetal weight of 1,000 g.	27 weeks	None	In this case of early-onset FGR, sildenafil citrate therapy was successful in managing FGR and

		with weekly monitoring of fetal weight and AFI.				accompanied severe oligohydramnios
Premlatha, et al. [23]	Prospective interventional Study(100)	women with severe early onset fetal growth restriction and oligohydramnios were treated with with Sildenafil citrate 25 mg three times a day	AFI was improved, disappearance of uterine artery notches, and changes in the umbilical artery Doppler like disappearance of reduced end diastolic flow.	22- 34 weeks	Headache and palpitation were reported in few cases	Sildenafil therapy improves perinatal outcomes in pregnancies complicated with intrauterine growth restriction and Oligohydramnios.
Maher, et al. [24]	open-label randomized trial (184)	IO with AFI<5cm were recruited. Sildenafil group(n=82) 25 mg every 8 hours) plus intravenous infusion of 2 L isotonic sol. Hydration group (n=84) received only fluid therapy	The amniotic fluid volume was higher in the sildenafil group at the final assessment (11.5 compared with 5.4 cm, P=.02). The sildenafil group delivered later (38.3 compared with 36.0 weeks of gestation, P=.001)	>30 weeks	None reported	Sildenafil citrate increases amniotic fluid volume in pregnancies complicated by oligohydramnios
Dunn, et al. [25]	Systematic review	Pregnant women who were exposed to Sildenafil citrate(SC) compared to no SC or placebo.	-	-	No severe adverse neonatal outcome	SC is safe in pregnancy and this underpins its potential as a therapy for selected maternal and fetal disorders.
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Table 4: Studies and Dosages.

Timing of Delivery

Timing of delivery in patients with isolated oligohydramnios is controversial. Observational studies have reported that prolonging the pregnancy till 37 completed weeks in patients with isolated mild oligohydramnios and no other comorbid condition, resulted in a good perinatal outcome. However pregnancies which were remote from term should be managed conservatively and should be kept under regular follow up with frequent assessment of AFI. Pregnancies with moderate to severe oligohydramnios may be delivered at 35 completed weeks after administration of antenatal steroids. Emergency delivery may have to be done anytime that fetal compromise is suggested on fetal surveillance by cardiotocograph or on Doppler [1].

Conclusion

In cases of isolated oligohydramnios, therapeutic intervention is desirable to prolong the pregnancy so as to avoid preterm delivery and to prevent preinital consequences of operative delivery. We recommend that oral hydration therapy should be offered to the eligible women as it is safe, inexpensive, does not require admission and no side effects have been reported so far. Sildenafil citrate holds promise but should be used with caution in pregnancy as no large controlled trials have been done to prove its efficacy. Further studies that show more definitive results, along with an establishment of safety, have to be assessed before the drug can be prescribed for this condition.

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