Role of indomethacin in polyhydramnios

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Abstract

Objective: To observe the role of indomethacin in polyhydramnios.

Method: This was a prospective, longitudinal and analytical study conducted in Kathmandu University Hospital, Dhulikhel from 1st July 2011 to 1st of December 2012. There were 32 patients included in the study. Indomethacin was administered orally at the dose of 25 mg three times a day for 1 week. The patients were admitted for observation of clinical symptoms, fundal height, fetal status and amniotic fluid index measurement. After the delivery, baby was investigated for any abnormality of fetal circulation.

Results: There were total of 2700 deliveries in 1 year. Among them 46 cases were of polyhydramnios. The frequency was 1.7%. Among the 46 cases, 32 (69.6%) were idiopathic who were included whereas 8 (17.4%) were of diabetes mellitus, 4 (8.7%) were Rh isoimmunisation, and 2 (4.3%) were fetal anomalies. The mean age group was 24.5+/-4.2 years. There were total 10 (31.3%) patients presented at 29 weeks of gestation whereas only 5 (15.7%) patients at 32 weeks of gestation. Regarding the gravid index, 17 (53.1%) patients were primigravida. There was statistically significant reduction in amniotic fluid volume following 1 week administration of indomethacin.

Conclusion: Though there are many modes of treatment for polyhydramnios, the 1 week therapy with indomethacin is equally beneficial.

Key words: idiopathic, indomethacin, polyhydramnios.

Introduction

Polyhydramnios is defined as the amniotic fluid volume of >2000ml or amniotic fluid index of >/-24cm or >95% centile for gestational age[1]. Polyhydramnios is one of the dreaded complication in obstetric practice, as it affects not only mother but also the fetus. The overall incidence is 1-2%[2-6]. It causes maternal complications like antepartum hemorrhage, respiratory embarrassment, abnormal presentation, uterine dysfunction and also postpartum hemorrhage. The fetal complications are mainly of congenital malformation[7]. Diabetes mellitus, twins pregnancy, Rh isoimmunisation are associated with polyhydramnios. Idiopathic cause is also one of the important factors. There are several therapeutic methods to treat the polyhydramnios. But, treatment is only indicated if symptomatic like respiratory embarrassment, excessive uterine activity or premature opening of os[1]. The medical management of polyhydramnios is use of indomethacin which was first described by Cabrol[8]. The main aim of our study is to observe the role of indomethacin in polyhydramnios.

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Competing interests: None

Methods

This was a prospective, longitudinal and analytical study conducted in the Department of Obstetrics and Gynecology of Kathmandu University Hospital, Dhulikhel, Kavre from 1st July 2011 to 1st of December 2012. There were total 46 patients enrolled for the study after taking informed consent. Patients with amniotic fluid index of 24 cm or more and idiopathic cases were included. All the patients enrolled for the study were investigated for diabetes mellitus, Rh-isoimmunisation, TORCH infection and also for any placental abnormality or fetal abnormality, if found positive then they were excluded. So there were 32 patients included in the study. The indomethacin was administered orally 25 mg three times a day for 1 week. The drug was stopped if complications like oligohydramnios, fetal distress or serious maternal side effects (severe gastric irritation or vomiting). The patients were admitted in hospital for close observation of clinical symptoms, fundal height and fetal status. Similarly, the AFI was measured. The renal function test, complete blood count was investigated at the time of admission and once a week. For the monitoring of fetal status, fetal echocardiography was performed within 24 hours after the end of the treatment. After the delivery, baby was investigated for any abnormality in the form of echocardiography, renal function test and ultrasonography of abdomen within 24 hours of delivery. The baby was followed up after 4 weeks and every month till 6 months of age. All the data were entered in the SPSS 16 software and final analysis was done.

Results

There were total of 2700 deliveries in 1 year duration. Among them, 46 cases were of polyhydramnios. So, the frequency was 1.7%. Among the 46 cases, 32 (69.6%) cases were idiopathic who were included in the study, whereas 8 (17.4%) cases were of diabetes mellitus, 4 (8.7%) cases were Rh isoimmunisation and 2 (4.3%) cases were fetal anomalies.

As shown in Table 1, there were total 20 patients within the age group of 18-25 years. The mean age group was 24.5+/-4.2 years. There were total 10 patients presented at 29 weeks gestation whereas only 5 patients at 32 weeks of gestation. There were 17 primigravida in the study. There were total 10 patients delivered at 38 weeks of gestation. There was statistically significant reduction in amniotic fluid volume with prior indomethacin therapy 30.0938+/-3.34 (mean+/-S.D.) to post indo-methacin therapy 20.593+/-4.10 (mean+/-S.D.) The p value was 0.00. Regarding the delivery of fetus, all the babies were delivered normally and had no complications till 6 months of follow up.

Table 1. Distribution of age group, gestational age at presentation and delivery and the gravid index

Age (years)	
• 18-25	20
• 26-34	11
• 35-40	1
Parity	
• Primi	17
• Multi	15
Gestational age in weeks at presentation	
• 28	7
• 29	10
• 30	6
• 31	4
• 32	5
Gestational age in weeks at delivery	
• 37	7
• 38	10
• 39	6
• 40	4
• 41	5

Discussion

There are various literatures available which describes the importance of indomethacin in polyhydramnios. Indomethacin is an anti-prostagladin which causes reversible inhibition of cyclo-oxygenase enzyme. It causes the decrease production of amniotic fluid by increase absorption of fluid by lungs, reducing the urine output and also impairs the prostaglandin mediated response of renal vasculature[7,10,11]. The frequency of polyhydramnios was 1.7% in our study which corresponds with the other study mentioned in literature which showed the incidence of 1-2% respectively[2-6]. The causes of polyhydramnios in our study was mainly idiopathic which was similar to study performed by Maymon et al[12], Tariq S et al[13] and Panting Kemp et al[14]. Regarding the age group our study showed that 20 (62.5%) patients were within 25 years of age group, which differ from the study performed by Tariq S et al[13] which showed only 30.4% within 30 years age group. This difference could be because of early marriage and early pregnancy within our community. The gestational week at diagnosis of polyhydramnios in our study was 28-32 weeks similar to study performed by Carmona F et al[15]. The multigravida was more as compared to primigravida in our study which is similar to study performed by Tariq S et al[13] and we cannot find obvious reason for this. There was significant reduction in AFI in our study which was similar to other study mentioned in the literature[7,8,10]. Our study was different from the other study as we had administered the indomethacin at the dose of 75 mg for 1 week only. Despite that there was significant reduction in the AFI score. Our study showed that the mean gestational age of delivery was 38+/-2.45 weeks, which was similar to other study[8].

Table 2. Summary of published literature on maternal and fetal outcome after indomethacin therapy in polyhydramnios

Authors	*Maternal and fetal outcome after indomethacin therapy in polyhydramnios*
Vermillion ST et al[19]	*Fetal outcome* – ductal constriction 50%, gestational age range 24.7-35 weeks, return to normal after discontinuation of treatment. (n=72)
Dudley DK et al[18]	*Fetal outcome* – Indomethacin used for tocolysis in gestations of less than 35 weeks. No cases of premature closure of the ductus arteriosus or persistent fetal circulation were observed. (n=167)
Kramer WB et al[17]	No maternal or fetal complications.
Moise KJ Jr et al[16]	*Fetal outcome* – The gestational ages ranged from 26.5 to 31.0 weeks. The detection of ductal constriction in 7 of the 14 fetuses by chocardiography. Return to normal after discontinuation of treatment. (n=14)
Mamopoulos M et al[10]	Normal fetal and maternal outcome. (n=15)
Carmona F et al[15]	*Maternal outcome* – Acute renal failure in one case, reversed after discontinuation of indomethacin.
	Fetal outcome – constriction of the fetal ductus arteriosus in one case which returned to normality after indomethacin suppression; one newborn developed a disseminated intravascular coagulation and died 15 h after birth. (n=7)
Cabrol D et al[8]	Normal *maternal* and *fetal* outcome.
Abhyankar S et al[7]	Normal *maternal* and *fetal* outcome. (n=12)

The use of indomethacin has raised the concern regarding fetal abnormalities like ductus contriction, intraventicular hemorrhage, renal failure and necrotizing enterocolitis but there are different study for and against this hypothesis (Table 2)[16-20]. The indomethacin also causes minimal side effects to the mother in the form of nausea, vomiting and dyspepsia as it is the prostaglandin synthetase inhibitor[21]. Not only that but it also causes hematological effect in form of prolongation of bleeding time and also rarely cause severe hypersensitivity reaction[22,23]. However, there was no maternal or fetal complications so far noted in our study group. This was similar to other study[10]. The main limitation of our study is that the sample size is small and study of one and half year duration. So it is required to do the study for long period and also to do the multi-institutional study within Nepal will tell us about the efficacy of indomethacin more broadly.

Conclusion

Though there are many modes of treatment for polyhydramnios, the 1 week therapy with indomethacin is equally beneficial.

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