J Huazhong Univ Sci Technol [Med Sci]
DOI 10.1007/s11596-015-1401-x
35(1):129-134,2015

Effectiveness and Safety of Double-balloon Catheter *versus* Intra-amniotic Injection of Ethacridine Lactate for Termination of Second Trimester Pregnancy in Patients with Liver Dysfunction*

Na LI (李 娜), Peng WU (吴 鹏), Jie ZHAO (赵 捷), Ling FENG (冯 玲), Fu-yuan QIAO (乔福元), Wan-jiang ZENG (曾万江)#
Department of Obstetrics and Gynecology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

Summary: Severe liver dysfunction in pregnancy **(**SLDP**)** is rare but serious complications with high mortality rate. This study compared the effectiveness and safety of double-balloon catheter *versus* intra-amniotic injection of ethacridine lactate for the termination of second trimester pregnancy in patients with SLD. A total of 55 patients with indications of labor induction were enrolled and analyzed by retrospective control analysis method. Twenty-three cases adopted Cook double balloon dilation as Cook group, and 32 cases received intra-amniotic injection of ethacridine lactate as EL group. The primary outcome was evaluated by successful abortion rate and the difference in the induction-to-abortion interval. Secondary outcomes included liver function recovery and the frequency of adverse events. Both Cook and EL regimens were effective, with successful abortion rate of 87.0% and 93.8%, respectively (P=0.639). The induction-to-delivery interval was similar between Cook group and EL group (38.1±21.5 *vs.* 41.3±17.4, P=0.543). The liver disease status was more severe in Cook group than in EL group, but it did not show any significant difference after pregnancy termination between the two groups and the improvement rate also did not show any significant difference. Both treatments were safe and there was no significant difference in bleeding and cervical laceration adverse events between the two groups. Our study firstly compared double-balloon catheter and ethacridine lactate for the induction of labor in women with SLD during second trimester pregnancy.
Key words: severe liver dysfunction; labor induction; double-balloon catheter; mechanical method; ethacridine lactate

Severe liver dysfunction in pregnancy (SLDP) is an unusual but dramatic event because it can progress rapidly to fulminant disease and also because two lives are involved; up to 3% of all pregnancies are complicated by liver disorders[1], underlying chronic liver disease, pregnancy related etiologies including hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, the hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, and acute fatty liver of pregnancy[2]. In China, these conditions are among the leading causes of maternal and perinatal mortality[3, 4]. Liver disorders were once thought to be trimester-specific, but this is not always the case. Onset of only 28% of pregnancy appeared in second-trimester. Owing to its low incidence, only a few clinical studies concentrating on SLDP are available. As far as some fulminant cases, labor induction is a feasible method to alleviate the condition of liver disease. Obstetrical policies must be assessed with respect to detection of maternal infection and liver disease, especially in second trimester of pregnancy.

Intra-amniotic injection of ethacridine lactate (EL; Rivanol) which is a dye with antiseptic properties, is the most common method for second-trimester abortion in China since 1970[5]. Prostaglandin E1 analogue misoprostol induces normal physiological cervical ripening and increases the sensitivity of the uterine myometrium to oxytocin. Because of potential risk of elevating blood pressure in preeclampsia and eclampsia cases and impact on liver function, it is seldom applied in SLDP cases in our hospital. Mechanical devices such as single-balloon or double-balloon catheters cause pressure within the cervix, which results in the release of endogenous prostaglandins[6]. Various investigators have evaluated the effectiveness of these devices in comparison with prostaglandins and have reported that they are equally effective, with a lower incidence of tachysystole[7, 8].

Few studies focused on the optimum technique for cervical ripening and labor induction during second trimester of pregnancy with severe liver dysfunction. In this study, the Cook double balloon dilation (Cook Cervical Ripener Balloon, Cook OB/GYN, USA) was used to achieve ripening of the cervix in women with severe liver dysfunction within second trimester of pregnancy. As the case of severe liver dysfunction in second trimester of pregnancy is rare, we undertook a small pilot study to assess the practicality and efficacy of the device in this clinical setting.

1 MATERIALS AND METHODS

We conducted a retrospective analysis of patients at

Na LI, E-mail: w461357598@163.com
#Corresponding author, E-mail: wjzeng@tjh.tjmu.edu.cn
*This project was supported by a grant from the National Natural Science Foundation of China (No. 81372806).

Tongji Hospital from April 2006 to February 2014. The study protocol was approved by the Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, China. Women eligible for inclusion had maternal indication for induction of labor, and a viable singleton pregnancy and different levels of hepatic function impairment. Exclusion criteria were any contraindication for vaginal delivery, women with uterine scar or placenta previa and those women with SLD but liver function returning to normal after active treatment. Liver dysfunction diagnostic criteria were alanine aminotransferase (ALT)>40 U/L and / or aspartate aminotransferase (AST)>40 U/L, total bilirubin (TBIL)>17.1 μmol / L, total bile acid (TBA)>10 μmol/L. Serum biochemical indicators of SLD were defined as follows: ALT or AST≥200 U/L, or TBIL≥100 μmol/L. A total of 55 patients were enrolled and analyzed by retrospective analysis method. Twenty-three cases adopted Cook double balloon dilation as Cook group, and 32 cases received intra-amniotic injection of ethacridine lactate as EL group. Patients were informed about the potential advantages and disadvantages of both treatment options and their side effects. All patients in the study groups signed a written informed consent prior to labor induction.

In Cook group, a double-balloon catheter was inserted through the cervix, and balloons on either side of the cervix were inflated with 80 mL of normal saline in accordance with the recommendations from the manufacturer. Placement of the catheters was performed with the aid of the speculum depending on clinician preference after cleaning the cervix with antiseptic solution, and proper placement of the catheter was confirmed with digital examination. Participants in the EL group underwent an ultrasound-guided amniocentesis with intra-amniotic injection of 100 mg ethacridine lactate. Other than the way of labor induction, the cervical ripening process and labor induction management were identical for the two treatment groups.

If the double-balloon catheter was not spontaneously expelled within 12 h of placement, it was manually removed. Following spontaneous expulsion or manual removal of the double-balloon, all subjects received routine obstetrical care at the discretion of their individual providers. Labor progress abnormalities were diagnosed and managed according to the recommendations of the American College of Obstetricians and Gynecologists[9]. A successful termination was defined as an abortion that occurred within 72 h of the first intervention (the placement of the double-balloon catheter or the intra-amniotic injection of EL). Oxytocin was administered to those women who were not in labor. After fetal expulsion, spontaneous placental delivery was allowed, unless more than 100 mL bleeding occurred or 30 min had elapsed without spontaneous expulsion of the placenta. In these cases, the placenta was manually removed. Curettage of the uterus was performed if there was clinical evidence of retained placental tissue or a suspicion of incomplete abortion.

Maternal demographic characteristics, the indication for induction and the outcome data of induction were recorded. Antenatal and postnatal laboratory findings were recorded as well. Outcome in terms of time from induction to delivery and successful inductions within 24, 48, and 72 h were all considered as the primary parameters used to evaluate the efficacy. The secondary parameters used to evaluate the efficacy or adverse events included the volume of bleeding, oxytocin administration, vaginal midwifery, postpartum curettage and cervical laceration. Herein, the bleeding volume was measured with the weighing method. The initial dry weight of surgical dressings used was subtracted from the combined weight of all surgical dressings used during the abortion. The volume of blood loss was then calculated according to the specific gravity of blood (1.05). Other outcome variables included improvement in the Bishop score after ripening.

All analyses were conducted by using SAS 8.2 software (SAS Institute, Cary, NC, USA). Descriptive statistics for continuous variables included mean, standard deviation, median, interquartile range and percentage. Homogeneity and normality were examined. Differences in the continuous variables were compared by using Student's *t*-test and the Mann-Whitney U test. Differences in the categorical variables were analyzed using the Chi-square test and the Fisher exact test. *P* values less than 0.05 were considered statistically significant.

2 RESULTS

The maternal demographics including age, parity, gestational age, history of liver diseases, regular prenatal examination of both groups, and Bishop Score at study entry were similar between the two groups. Most of the women were nulliparous and from rural area, and few of them received regular prenatal examinations. Eight (34.8%) women in the Cook group and 14 (43.7%) women in the EL group had history of liver diseases. The liver disease status was more severe in Cook group than in EL group. Twelve (52.2%) women in the Cook group and seven (21.9%) women in the EL group were SLD (P=0.020) (table 1).

The antenatal laboratory indices included ALT, AST, alkaline phosphatase (ALP), total bilirubin (TBIL), direct bilirubin, bile acid, creatine, serum albumin (ALB), cholesterol (CHOL), cholinesterase (CHE), blood glucose, and white blood cell count, blood platelet count, and fibrinogen, prothrombin time, prothrombin time activity (table 2). Markers of hepatocyte damage were analyzed in liver function tests. Fibrinogen, prothrombin time, and prothrombin time activity reflect coagulation function. In our study, the levels of ALT, AST, ALP and PT in the Cook group were significantly higher (P=0.012, P=0.001, P=0.007, and P=0.017 respectively) and the prothrombin time activity was significantly lower in the Cook group than those in the EL group (P=0.006). There were no significant differences in the other biochemical indices between the two groups.

Table 1 Baseline characteristics of women with hepatic function impairment

Characteristics	Cook group (n=23)	EL group (n=32)	P value
Age (year)	27.2±4.8	27.0±5.4	0.861
Gestational age (day)			
At diagnosis	185.3±39.6	165.3±39.6	0.072
At labor induction	191.6±39.1	172.3±37.0	0.068
At delivery	193.5±38.6	174.2±36.5	0.064
Living area			
Rural	17 (73.9%)	20 (63%)	0.374
Urban	6 (26.1%)	12 (37%)	
Parity			
Nulliparous	16 (69.6%)	24 (75.0%)	0.655
Parous	7 (30.4%)	8 (25.0%)	
Having history of liver diseases	8 (34.8%)	14 (43.7%)	0.503
Regular prenatal examinations	4 (17.3%)	5 (15.6%)	1.000
Severe liver dysfunction	12 (52.2%)	7 (21.9%)	0.020
Bishop scores			
Nulliparous	1.0 (0–4)	0.9 (0–4)	0.819
Multiparous	2.3 (0–4)	1.4 (0–4)	0.229

Cook: COOK Medical's Cervical Ripening Balloon; EL: ethacridine lactate
Values are given as x±s or number of women (percentage).

Table 2 Laboratory findings of Cook group and EL group

Items	Cook group (n=23)	EL group (n=32)	P value
ALT (U/L)	134.0 (77.0–821.0)	88.5 (45.5–127.8)	0.012
AST (U/L)	143.0 (78.0–786.0)	74.5 (46.0–98.0)	0.001
TBIL (mg/dL)	30.1 (7.7–192.4)	12.7 (6.3–54.3)	0.103
Direct bilirubin (mg/dL)	16.3 (1.9–147.8)	3.7 (1.4–22.6)	0.100
Bile acid (mg/dL)	13.7 (7.1–83.5)	11.0 (5.6–27.3)	0.210
ALP (U/L)	172.0 (110.0–215.0)	117.0 (80.5–158.0)	0.007
ALB (g/L)	30.4±5.2	31.7±5.5	0.383
CHOL(mmol/L)	5.0±2.2	5.7±2.7	0.329
CHE (U/L)	4748.2±1796.4	4286.3±1003.4	0.229
GLU (mmol/L)	5.2±1.4	4.9±1.2	0.493
Creatinine (mmol/L)	76.0 (39.0–104.0)	46.3 (38.0–94.0)	0.335
White blood cell count ($\times10^9$/L)	9.7±4.3	9.2±3.9	0.714
Blood platelet count ($\times10^{12}$/L)	169.0±95.1	187.7±96.7	0.480
Fibrinogen (g/L)	4.2 (3.4–5.0)	4.5 (4.0–5.0)	0.314
PT (s)	14.7±9.2	11.3±1.7	0.017
Prothrombin time activity (%)	101.9±35.3	128.2±30.3	0.006

Values are given as x±s or median (interquartile range).

The most common maternal indication for labor induction in women enrolled was pregnancy with severe hepatitis, which accounted for 52.2% and 53.1% in the Cook group and EL group, respectively. Another important indication was severe preeclampsia, accounting for 34.8% and 34.4%, respectively. There was one woman with acute fatty liver of pregnancy in the Cook group, and there were two women diagnosed with intrahepatic cholestasis of pregnancy and one woman diagnosed with hyperemesis gravidarum in the EL group. The other two reasons of labor induction in the Cook group included pregnancy after liver transplantation and pregnancy with idiopathic liver damage. The other one reason of labor induction for the EL group was pregnancy with acute cholecystitis (table 3).

Table 3 Indication for labor induction

Indication for labor induction	Cook group		EL group	
	n	%	*n*	%
Severe viral hepatitis	12	52.2	17	53.1
Severe preeclampsia	8	34.8	11	34.4
Acute fatty liver of pregnancy	1	4.3	0	0
Hyperemesis gravidarum	0	0	1	3.1
Intrahepatic cholestasis of pregnancy	0	0	2	6.3
Others	2	8.7	1	3.1

Values are given as number of women (percentage).

It made no significant difference between the two groups regarding the Bishop score before the labor induction intervention. The second Bishop score (after spontaneous expulsion or removal of the devices, or injection of ethacridine lactate) also did not differ significantly (table 4).

Table 4 Bishop scores before and after treatment

Bishop scores	Parity	Cook group (*n*=23)	EL group (*n*=32)	*P* value
Before treatment	Nulliparous	1.0 (0–4)	0.9 (0–4)	0.819
	Multiparous	2.3 (0–4)	1.4 (0–4)	0.229
After treatment	Nulliparous	6.1 (4–9)	6.2 (4–9)	0.932
	Multiparous	7.4 (6–9)	6.8 (3–9)	0.398

Data are presented as median (range).

The proportion of women who delivered within 24 h was 30.4% and 15.6% in the Cook group and EL group, respectively; 56.5% and 78.1% of women in the Cook group and EL group, respectively, delivered within 72 h but after 24 h. Overall, 20 (87.0%) women in the Cook group and 30 (93.75%) women in the EL group delivered within 72 h. In other words, the success rate in the Cook group and EL group was 87.0% and 93.8%, respectively. However, 3 women in the Cook group and 2 in EL group delivered after 72 h (table 5).

Table 5 Time to abortion after balloon insertion or intra-amniotic injection of ethacridine lactate

Time to abortion	Cook group *n* (%)	EL group *n* (%)	*P* value
≤24 h	7 (30.4%)	5 (15.6%)	0.190
>24 h, ≤72h	13 (56.5%)	25 (78.1%)	0.087
>72 h	3 (13.1%)	2 (6.3%)	0.697

Data are expressed as number of women (percentage).

The interval from induction to delivery (induction-to-abortion time) in the Cook group (38.1±21.5 h) was shorter than that in the EL group (41.3±17.4 h) (*P*=0.543). Besides the induction-to-abortion time, the secondary parameters used to evaluate the efficacy or adverse events included the volume of bleeding, oxytocin administration, postpartum curettage and cervical laceration. The bleeding volume measured with the weighing method was 130.0 (100.0–165.0) mL and 125.0 (100.0–145.0) mL in the Cook group and EL group, respectively (*P*=0.247). In addition, three patients in the Cook group experienced heavy bleeding (>500 mL); it happened during the course of the labor induction in two of them, and another one experienced a sudden increase in vaginal bleeding 8 h after labor induction. It is worth mentioning that the three patients were all turned out to be critical patients with poor coagulation function. In the process of labor induction, seven patients, accounting for 30.4% of the women in the Cook group, received oxytocin to promote uterine contraction; whereas in the EL group, three (9.4%) women used oxytocin for that. One of the women in the Cook group underwent vaginal midwifery and one woman in the Cook group and two women in the EL group experienced cervical laceration. The rate of cervical laceration was low in our study, and no instance of this was serious. Except that, no other serious complications, such as uterine rupture, occurred. Six (26.1%) women in the Cook group and 13 (40.6%)

women in the EL group, respectively, experienced postpartum curettage *(P*=0.263) (table 6).

Table 6 Induction outcome data

Items	Cook group (*n*=23)	EL group (*n*=32)	*P* value
Induction-to-abortion time (h)	38.1±21.5	41.3±17.4	0.543
Bleeding (mL)	130.0 (100.0–165.0)	125.0 (100.0–145.0)	0.247
Use of oxytocin	7 (30.4%)	3 (9.4%)	0.100
Vaginal midwifery	1	0	
Successful cases	20 (87.0%)	30 (93.8%)	0.639
Postpartum curettage	6 (26.1%)	13 (40.6%)	0.263
Cervical laceration	1 (4.3%)	2 (6.3%)	

Values are given as $\bar{x}\pm s$, median (interquartile range) or number of women (percentage).

All patients received a reexamination of liver function (5–7 days after delivery) and some of the biochemical indices were recorded. The average value of ALT in the Cook group and EL groups was 46.4 U/L and 56.3 U/L, respectively (*P*=0.493), and the mean value of AST was 42.3 U/L and 45.8 U/L, respectively (*P*=0.693). Other laboratory findings are shown in table 7, and they also did not achieve statistical significance (table 7).

Table 7 Improvement in liver function after pregnancy termination in two groups

Laboratory findings	Cook group (*n*=23)			EL group (*n*=32)			*P* value
	Before	Improved	%	Before	Improved	%	
ALT(U/L)	22	19	83.4	26	18	69.2	0.189
AST (U/L)	23	18	78.3	25	19	76.0	0.852
ALP (U/L)	19	14	73.7	17	11	64.7	0.721
TBIL (mg/dL)	11	9	81.8	12	6	50.0	0.193

Data are presented as number of women and percentage.

3 DISCUSSION

With the physiological changes that occur during pregnancy, liver histology and function also undergo a series of adaptive changes. Three possible etiologic relationships between liver disease and pregnancy include pregnancy in patients with preexisting liver disease, newly acquired liver disease during pregnancy (ie, acute viral hepatitis), and liver disease that is specific to pregnancy, such as AFLP and preeclampsia, which may be complicated by HELLP syndrome. In our study, the most common maternal indication for labor induction is pregnancy with severe viral hepatitis. In women enrolled to this study, 52.2% in Cook group and 53.1% of cases in EL group had severe viral hepatitis, and 34.8.3% in Cook group and 34.4% of cases in EL group were pregnancy with primarily severe preeclampsia, which were consistent with the Merle's report[10].

A majority of pregnant women with liver disease could be treated to maintain pregnancy to the third trimester of gestation, but pregnancy should be terminated in some severe cases, because the maternal laboratory parameters and maternal survival could be significantly improved after delivery[11, 12]. However, specific to second trimester of gestation, the timing and mode of terminating pregnancy are great challenge for obstetrician because of immature fetus. Owing to its low incidence, few clinical studies concentrating on these cases, in our study, labor induction is an effective approach to terminate the pregnancy and recover the liver dysfunction.

The ideal methods for cervical ripening are safe for the mother's liver function, incur a low cost, have minimal maternal discomfort, and do not require extensive monitoring. The double-balloon Ripener Device was successfully used in all indications for induction (pregnancy-induced hypertension, pregnancy with heart and liver complication, fetal growth retardation, previous caesarean sections, diabetes mellitus and elective inductions). In our clinical analysis, the Cook cases all presented more severe hepatocyte damage, the ALT (479.9.9±642.1 U/L) and AST (530.8±766.3 U/L) are significantly higher than those in the EL group (123.7±123.0 U/L and 174.2±36.5 U/L), which perhaps partly explained why three cases of the Cook group experienced heavy bleeding during and after delivery. On the other hand, all these three cases have obvious coagulation defect.

For second trimester pregnancy termination, ethacridine was first used by Miranov in Russia in 1950[13]. Some authors have used it for second trimester pregnancy termination by the transcervical route, for it is an inexpensive, effective and safe method[14]. It has been reported to be the most common method in Sweden and China in combination with oxytocin infusion[15, 16]. In our current study, we could get the same success rate with the previously published data to 93.8% within 72 h and the mean induction-delivery interval of 41.3 h[17], with comparatively higher success rate and shorter induction-delivery interval than Cook group (87% of success rate and 83.1 h of induction-delivery interval), although this difference is not significant between study groups. Furthermore, the EL group seems to have little impact on the liver dysfunction recovery, the two groups were

comparable with regard to postnatal laboratory findings.

The current study has limitations that are worth mentioning. First, this study is certainly biased by its retrospective non-randomized design. In our clinical experience, for safety concern, some pregnancy patients with more severe liver dysfunction such as acute fatty liver cases were chosen to induce labor by using Cook Cervical Ripener Balloon device, that is why the values of liver profile in Cook group were obviously higher than those of EL group. Second, we did not address patient satisfaction with the cervical ripening process. Comparison of patient satisfaction towards two labor induction methods (intra-amniotic injection of ethacridine lactate and trans-cervical double balloon catheter for cervical ripening) would be interesting since both methods do not imply repeated vaginal examinations. In a further study, the patients' satisfaction during the labor induction will be considered to modify the clinical trial design.

Despite these limitations, our study has shown that the Cook and EL regimens are both effective and safe for the termination of second trimester pregnancy with severe liver dysfunction. Their effectiveness and low cost are especially welcome in developing settings where technical and financial resources are limited. However, Because liver function can be recovered promptly in Cook group, to some fulminant cases, we recommend that the Cook device could be considered to be employed in priority in particular conditions such as acute fatty liver of pregnancy.

Acknowledgement

We gratefully acknowledge Yashvina Shamloll for language polishing.

Conflict of Interest Statement

The authors declare that there is no conflict of interest with any financial organization or corporation or individual that can inappropriately influence this work.

REFERENCES

1 Ch'ng CL, Morgan M, Hainsworth I, *et al*. Prospective study of liver dysfunction in pregnancy in Southwest Wales. Gut, 2002,51(6):876-880
2 Hay JE. Liver disease in pregnancy. Hepatology, 2008,47(3):1067-1076
3 Liang J, Li WM, Wang YP, *et al*. Analysis of maternal mortality in China from 1996 to 2000. Zhonghua Fu Chan Ke Za Zhi (Chinese), 2003,38(5):257-260
4 Li XM, Ma L, Yang YB, *et al*. Clinical characteristics of fulminant hepatitis in pregnancy. World J Gastroenterol, 2005,11(29):4600-4603
5 Lu ZL. Family planning theory and practice (Chinese). Guangzhou, China: Guangdong Science & Technology Press, 1988
6 Jozwiak M, Bloemenkamp KW, Kelly AJ, *et al*. Mechanical methods for induction of labour. Cochrane Database Syst Rev, 2012,3:CD001233
7 Fox NS, Saltzman DH, Roman AS, *et al*. Intravaginal misoprostol *versus* Foley catheter for labour induction: a meta-analysis. BJOG, 2011,118(6):647-654
8 Vaknin Z, Kurzweil Y and Sherman D. Foley catheter balloon *vs* locally applied prostaglandins for cervical ripening and labor induction: a systematic review and metaanalysis. Am J Obstet Gynecol, 2010,203(5):418-429
9 ACOG Practice Bulletin Number 49, December 2003: Dystocia and augmentation of labor. Obstet Gynecol, 2003,102(6):1445-1454
10 Merle P, Trepo C, Zoulim F. Current management strategies for hepatitis B in the elderly. Drugs Aging, 2001,18(10):725-735
11 Suzuki S, Watanabe S, Araki T. Acute fatty liver of pregnancy at 23 weeks of gestation. BJOG, 2001,108(2):223-224
12 Paternoster DM, Gerace PF, Manganelli F, *et al*. Acute hepatic failure in pregnancy. Eur J Obstet Gynecol Reprod Biol, 2004,112(2):230-232
13 Nabriski SA, Kalmanovitch K, Lebel R, *et al*. Extraovular transcervical injection of rivanol for interruption of pregnancy. Am J Obstet Gynecol, 1971,110(1):54-56
14 Beller FK, Kolker M, Douglas GW. Lack of coagulation defect after terminating second-trimester pregnancy by the catheter technique. Am J Obstet Gynecol, 1973,115(6):822-826
15 Ingemanson CA. Legal abortion by extra-amniotic instillation of Rivanol in combination with rubber catheter insertion into the uterus after the twelfth week of pregnancy. Am J Obstet Gynecol, 1973,115(2):211-215
16 Hou S, Chen Q, Zhang L, *et al*. Mifepristone combined with misoprostol versus intra-amniotic injection of ethacridine lactate for the termination of second trimester pregnancy: a prospective, open-label, randomized clinical trial. Eur J Obstet Gynecol Reprod Biol,151(2):149-153
17 Tien KH. Intraamniotic injection of ethacridine for second-trimester induction of labor. Obstet Gynecol, 1983,61(6):733-736

(Received Sep. 15, 2014; revised Nov. 20, 2014)