

The impact of laser therapy on fetal growth discordance in twin-to-twin transfusion syndrome

O impacto da terapia a laser no crescimento fetal na síndrome de transfusão feto-fetal

Renato A. Moreira de Sa ¹
Salomon J. Laurent ²
Yuichiro Takahashi ³
Masami Yamamoto ⁴
Yves Ville ⁵

¹ Disciplina de Obstetrícia. Centro de Ciências da Saúde. Universidade Federal Fluminense. Rua das Laranjeiras, 445. Laranjeiras. Rio de Janeiro, RJ, Brasil. CEP: 22.240-002

²⁻⁵ Department of Obstetrics and Gynaecology. Centre Hospitalier Intercommunal de Poissy-Saint-Germain en Laye. 10 Rue du Champ Gaillard, 78300 Poissy, France

Abstract

Objectives: to evaluate the impact of laser therapy on inter-twin discordance in twin-to-twin transfusion syndrome (TTTS).

Methods: biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL) and estimated fetal weight were prospectively collected during a five-year period (1999 to 2004). The inter-twin discordance was expressed as a percentage of the largest twin's measurements. The measurements were made the day before laser, twice following laser and after delivery. The mean values of discordance in measurements and in fetal weight were calculated. ANOVA was used to compare mean values.

Results: the mean (SD) discordance for BPD, HC, AC, FL and estimated fetal weight the day before laser were 8.53% (5.28), 8.75% (2.76), 16.19% (4.85), 12.92% (5.13) and 28.50% (6.46) respectively. At the 2nd ultrasound assessment after surgery were 4.37% (3.55), 3.73% (2.71), 8.90% (4.42), 6.61% (4.99) and 19.11% (8.01) respectively; and at birth the weight discordance was 18.55% (8.74). There was a significant decrease in discordance for HC and AC for each ultrasound assessment.

Conclusions: there was a decrease in fetal growth discordance following laser therapy in TTTS. These changes might be related to re-adaptation of blood flow following laser therapy.

Key words Fetal transfusion, Laser coagulation, Fetoscopy

Resumo

Objetivos: avaliar impacto da terapia a laser no crescimento fetal na Síndrome de transfusão feto-fetal (STFF).

Métodos: diâmetro biparietal (DBP), circunferência cefálica (CC) e abdominal (CA), comprimento do fêmur (CF) e peso fetal foram colhidos prospectivamente no período de cinco anos (1999 a 2004). A discordância entre os gêmeos foi expressa como porcentagem da medida do maior. As medidas foram feitas um dia antes do laser, duas vezes após e depois do nascimento. A cada exame e pós-parto foram calculadas médias das discordâncias entre medidas e peso fetal. ANOVA foi usada para comparar as médias.

Resultados: a discordância média (SD) para DBP, CC, CA, CF e peso fetal um dia antes do laser foi 8,53% (5,28), 8,75% (2,76), 16,19% (4,85), 12,92% (5,13) e 28,50% (6,46). No segundo exame pós-laser os resultados foram 4,37% (3,55), 3,73% (2,71), 8,90% (4,42), 6,61% (4,99) e 19,11% (8,01); e a discordância do peso fetal ao nascimento foi 18,55% (8,74). Houve diminuição significativa na discordância para CC e CA em cada exame.

Conclusões: houve redução significativa na discordância do crescimento fetal após o laser na STFF. Estas alterações podem estar relacionadas à readaptação dos fluxos sanguíneos após tratamento.

Palavras-chave Transfusão Feto-fetal, Coagulação por laser, Fetoscopia

Introduction

Birthweight discordance can affect up to a quarter of twin gestations and is a critical factor in the management of those pregnancies.^{1,2} The discordance is calculated as the intrapair weight difference, expressed as a percentage of the larger twin's weight.³ The incidence of discordance is directly related to the definition used. Most published studies have used a birth weight difference of 15% to 25%.³ Twin-to-Twin Transfusion Syndrome (TTTS) is often associated with growth discordance between Donors and Recipients.² Around 20% of monochorionic twins develop TTTS.^{4,5} The twins are often forced into specific discordant growth patterns, likely to be driven by unequal sharing of nutrients through unequal sharing of the placenta through chorionic plate inter-twin anastomoses.⁴⁻⁸ Laser therapy is the most effective first line treatment of TTTS; however, its effect on fetal growth has not been evaluated to date.

We aimed to evaluate the impact of laser therapy on inter-twin discordance in TTTS by serial assessment of fetal biometry measures and estimated fetal weight between fetuses following surgery when both fetuses were born alive.

Methods

This study included all live-born neonates born after 24 weeks of gestation from pregnancies complicated by TTTS and treated by laser therapy before 26 weeks' during a five-year period (1999 to 2004).

TTTS was diagnosed with the association of severe polyhydramnios defined by a deepest pool above 80mm (recipient twin) showing a distended bladder, and oligohydramnios defined by a deepest pool below than 20mm (donor twin) showing small or no bladder on ultrasound.

Only pregnancies in which we performed laser therapy and when both infants were born alive were included in the study. Cases that needed repeat-laser or another treatment were not included. Gestational age was established on the basis of best obstetric estimate including last menstrual period and first-trimester ultrasound. All pregnancies were diagnosed to be monochorionic and diamniotic by ultrasound examination at 6-14 weeks of gestation.

Ultrasound examination was performed on the day before laser and twice following surgery. Biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL) were collected prospectively.⁹ The

interval between the ultrasound measurements was of at least two weeks.¹⁰ Estimated fetal weight was calculated using Hadlock et al.⁹ formula: $\log_{10}(\text{EFW}) = 1.326 + 0.0107(\text{HC}) + 0.0438(\text{AC}) + 0.158(\text{FL}) - 0.00326(\text{AC} \times \text{FL})$. At the time of laser therapy, Quintero's stages and umbilical Doppler were collected in each case. Laser surgery was performed as previously described.¹¹

The inter-twin discordance in BPD, HC, AC, FL and estimated fetal weight (mean \pm -SD) were calculated for each pair and expressed as a percentage of the larger twin's measurements [$100 \times (\text{larger twin's measurement} - \text{smaller twin's measurement}) / \text{Larger twin's measurement}$].

Normality of the distribution of measurements was tested using a Shapiro-Wilks test ($p > 0.05$). The ANOVA Post Hoc Test was used to compare the mean values of intertwin discordances at the day before laser with the mean values at the 1st and 2nd ultrasound assessment and after birth, respectively.

All calculations were performed using the SPSS software package (release 10.0, SPSS Inc., Chicago, IL, USA). For all tests used, a value of $p < 0.05$ was considered statistically significant.

Results

183 cases of TTTS presenting before 26 weeks' were treated by laser surgery since 1999. 55 of these gave birth to two liveborn twins, eight of whom underwent other therapeutic procedures including repeat-laser, amniodrainage or fetal blood transfusion. 47 twin pregnancies therefore met our inclusion criteria. The mean gestational age was 21.4 weeks' (+ 2.5SD), 24.5 weeks' (+ 2.9SD) and 27.9 weeks' (+ 2.7SD) at laser therapy, 1st and 2nd ultrasound assessment post-laser respectively. The mean gestational age at delivery was 31.2 weeks' (+ 3.7SD). Critically abnormal umbilical artery Doppler flow velocity waveform patterns with either absent or reverse end-diastolic flow were present at the time of diagnosis in 8 (17.0%) and 3 (6.4%) donor and recipient fetuses respectively. There were 9 (19.1%), 21 (44.7%), 16 (34.0%) and 1 (2.1%) cases classified as Quintero's Stages 1, 2, 3 and 4 respectively.

The mean discordance in HC, AC, FL and estimated fetal weight one day before laser, at 1st and 2nd ultrasound assessment and at birth are shown in Table 1.

There was a significant difference ($p < 0.05$) in HC and AC between ultrasound assessment the day before laser and at 1st and 2nd assessment following laser, respectively. The decrease in discordance for

BPD, FL and estimated fetal weight became significant only after the second assessment following laser (Table 2, Figures 1 and 2).

Tabela 1

Rate of liter-twin discordance.

Discordance rate	Mean (%)	SD
BPD		
Pre-laser	8.53	5.28
1st US after laser	6.04	2.28
2nd US after laser	4.37	3.55
HC		
Pre-laser	8.75	2.76
1st US after laser	4.96	2.40
2nd US after laser	3.73	2.71
AC		
Pre-laser	16.19	4.85
1st US after laser	10.59	3.94
2nd US after laser	8.90	4.42
FL		
Pre-laser	12.92	5.13
1st US after laser	8.98	5.78
2nd US after laser	6.61	4.99
Weight		
Pre-laser	28.50	6.46
1st US after laser	21.42	7.53
2nd US after laser	19.11	8.01
Birth	18.55	8.74

BPD = biparietal diameter; HC = head circumference; AC = abdominal circumference; FL = femur length; SD = standard deviation

Tabela 2

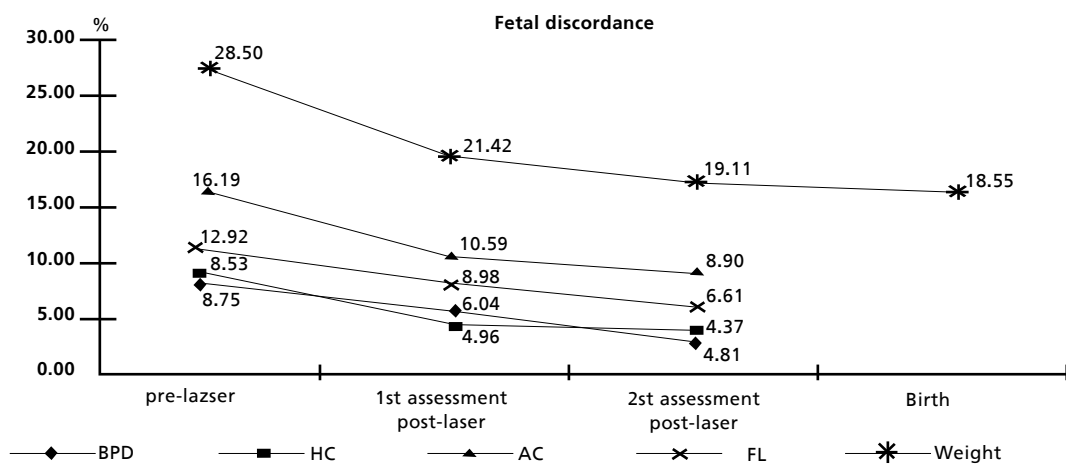
Changes in fetal discordance over time.

Ultrasound measurement	Multiple Comparisons	<i>p</i>	
BPD	Pre-laser	1st assessment	0.11
		2nd assessment	0.03*
HC	Pre-laser	1st assessment	0.00*
		2nd assessment	0.00*
AC	Pre-laser	1st assessment	0.03*
		2nd assessment	<0.001*
FL	Pre-laser	1st assessment	0.18
		2nd assessment	0.02*
Weight	Pre-laser	1st assessment	0.07
		2nd assessment	0.02*
		Birth	<0.001*

BPD = biparietal diameter; HC = head circumference; AC = abdominal circumference; FL = femur length; SD = standard deviation

Figura 1

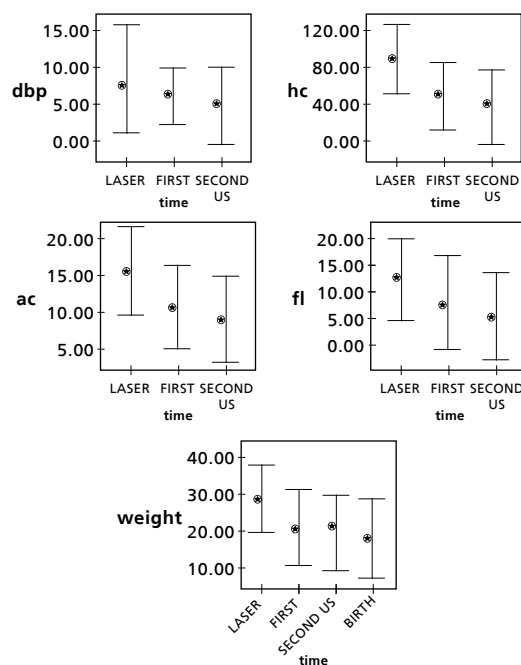
Fetal discordance across time



BPD = biparietal diameter; HC = head circumference; AC = abdominal circumference; FL = femur length.

Figura 2

Fetal discordance across time



BPD = biparietal diameter; HC = head circumference; AC = abdominal circumference; FL = femur length

Discussion

Both the presence of inter-twin anastomoses and unequal placental sharing are likely to be the main causes for fetal growth discordance and amniotic fluid imbalance to develop in TTTS.⁵

Established treatments of TTTS include serial amnioreduction and laser therapy. Recent results have shown better survival for laser therapy, and obliteration of chorionic plate anastomoses could halt the pathophysiological process.¹¹⁻¹³ Endoscopic laser ablation is feasible in pregnancies that are complicated by severe fetofetal transfusion syndrome and appears to be associated with improved perinatal outcome.¹⁴ Laser coagulation of the umbilical cord vessels is an effective method of treating monozygotic twin pregnancies with reversed

arterial perfusion (TRAP) sequence.¹⁵ This study suggests that the inter-twin discordance decreases after laser therapy in successful cases leading to the birth of two liveborn twins.

The incidence of intrauterine fetal death increases with increasing fetal weight discordance in twins at of the same sex.^{2,16} TTTS carries a high mortality mainly related to intra-uterine death and severe preterm delivery. Early fetal death following laser can be related to perioperative factors, such as placental abruption, hemorrhage or infection. Late fetal death may be related to either recurrence of TTTS or severe growth restriction.

Severe discordance in birthweight has been associated with adverse perinatal outcomes specially when >25%.¹⁷⁻²¹

The design of our study does not allow to draw these definitive conclusions on the effect of laser therapy on fetal growth. These changes in fetal growth could also have occurred in a control group without laser therapy. However, an untreated control group with severe TTTS before 26 weeks' is unlikely to allow double survival. González-Quintero *et al.*⁸ have shown that early fetal growth discordance diagnosed as early as 20 weeks, increases with advancing gestation until birth and Rodis *et al.*¹⁷ reported similar findings in their study by concluding that twins who ultimately become discordant exhibit demonstrable differences as early as 23 to 24 weeks. Fetal weight discordance at birth was 18% and compares favorably with the results from Duncombe *et al.*²² who reported 34% discordance in birth weight in a series of 69 TTTS, treated with amnioreduction and septostomy. Our results suggest that fetoscopic laser surgery of the chorionic plate may influence the natural history of fetal discordance caused by TTTS. Indeed the mean estimated fetal weight discordance went down from 28% at 21 weeks' before laser to 18% at the time of delivery. This decrease was already significant at 28 weeks' at second assessment after laser. The overall reduction in estimated fetal weight discordance throughout gestation was over 30%.

Following laser therapy in TTTS, there is a decrease in fetal growth discordance. These changes might be related to the readjustment in blood flows following laser therapy.

References

1. Talbot GT, Goldstein RF, Nesbitt T, Johnson JL, Kay HH. Is size discordance an indication for delivery of preterm twins? *Am J Obstet Gynecol* 1997; 177: 1050-4.
2. Branum AM, Schoendorf KC. The effect of Birth Weight Discordance on Twin Neonatal Mortality. *Obstet Gynecol* 2003; 101: 570-4.

3. Cheung VY, Bocking AD, Dasilva OP. Preterm discordant twins: what birth weight difference is significant? *Am J Obstet Gynecol* 1995; 172: 955-9.
4. van Gemert MJC, Major AL, Scherjon SA. Placental anatomy, fetal demise and therapeutic intervention in monochorionic twins and the transfusion syndrome: new hypotheses. *Eur J Obstet Gynecol Reprod Biol* 1998; 180: 717-24.
5. van Gemert MJC, Vandenbussche FPHA, Schaap AHP, Zondervan HA, Nikkels PGJ, van Wijngaarden WJ, van Zalen-Sprock RM, Sollie-Szarynska KM, Stoutenbeek PH. Classification of discordant fetal growth may contribute to risk stratification in monochorionic twin pregnancies. *Ultrasound Obstet Gynecol* 2000; 16: 237-44.
6. Blickstein I. Normal and abnormal growth of multiples. *Semin Neonatol* 2002; 7: 177-85.
7. Senoo M, Okamura K, Murotsuki J, Yaegashi N, Uehara S, Yajima A. Growth pattern of twins of different chorionicity evaluated by sonographic biometry. *Obstet Gynecol* 2000; 95: 656-61.
8. González-Quintero VH, Luke B, O'Sullivan MJ, Misiunas R, Anderson E, Nugent C, Witter F, Mauldin J, Newman R, D'Alton M, Grainger D, Saade G, Hankins G, Macones G. Antenatal factors associated with significant birth weight discordancy in twin gestations. *Am J Obstet Gynecol* 2003; 189: 813-7.
9. Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements—a prospective study. *Am J Obstet Gynecol* 1985; 151: 333-7.
10. de Jong CL, Gardosi J, Baldwin C, Francis A, Dekker GA, van Geijn HP. Fetal weight gain in a serially scanned high-risk population. *Ultrasound Obstet Gynecol* 1998; 11: 39-43.
11. Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. *N Engl J Med* 2004; 351: 136-44.
12. De Lia JE, Kuhlmann RS, Lopez KP. Treating previable twin-twin transfusion syndrome with fetoscopic laser surgery: outcomes following the learning curve. *J Perinat Med* 1999; 27: 61-7.
13. Hecher K, Plath H, Bregenzler T, Hansmann M, Hackeloer BJ. Endoscopic laser surgery versus serial amniocenteses in the treatment of severe twin-twin transfusion syndrome. *Am J Obstet Gynecol* 1999; 180 (3 Pt 1): 717-24.
14. Sepulveda W, Surerus E, Vandecruys H, Nicolaidis KH. Fetofetal transfusion syndrome in triplet pregnancies: outcome after endoscopic laser surgery. *Am J Obstet Gynecol* 2005; 192: 161-4.
15. Ville Y, Hyett JA, Vandenbussche FP, Nicolaidis KH. Endoscopic laser coagulation of umbilical cord vessels in twin reversed arterial perfusion sequence. *Ultrasound Obstet Gynecol* 1994; 4: 396-8.
16. Demissie K, Ananth CV, Martin J, Hanley ML, MacDorman MF, Rhoads GG. Fetal and neonatal mortality among twin gestations in the United States: the role of intrapair birth weight discordance. *Obstet Gynecol* 2002; 100: 474-80.
17. Rodis JF, Vintzileos AM, Campbell WA, Nochimson DJ. Intrauterine fetal growth in discordant twin gestations. *J Ultrasound Med* 1990; 9: 443-8.
18. Victoria A, Mora G, Arias F. Perinatal outcome, placental pathology, and severity of discordance in monochorionic and dichorionic twins. *Obstet Gynecol* 2001; 97: 310-5.
19. Erkkola R, Ala-Mello S, Piironen O, Kero P, Sillanpaa M. Growth discordancy in twin pregnancies: a risk factor not detected by measurements of biparietal diameter. *Obstet Gynecol* 1985; 66: 203-6.
20. Hollier LM, McIntire DD, Leveno KJ. Outcome of twin pregnancies according to intrapair birth weight differences. *Obstet Gynecol* 1999; 94: 1006-10.
21. Yalcin HR, Zorlu CG, Lembet A, Ozden S, Gokmen O. The significance of birth weight difference in discordant twins: a level to standardize? *Acta Obstet Gynecol Scand* 1998; 77: 28-31.
22. Duncombe GJ, Dickinson JE, Evans SF. Perinatal characteristics and outcome of pregnancies complicated by Twin-Twin Transfusion Syndrome. *Obstet Gynecol* 2003; 101: 1190-6.

Recebido em 25 de agosto de 2003

Versão final em 20 de junho de 2005

Aprovado em 26 de julho de 2005