Alterations in Lipid Metabolism by Longacting Bromocriptine for Lactation inhibition

LAKTASYON INHİBİS YON UN DA KULLANILAN UZUN ETKİLİ BROMOKRİPTİNİN LİPİD METABOLİZMASINA ETKİLERİ

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SUMMARY

We examined the effects of longacting bromocriptine injection on lipid metabolism in the puerperium in 5 women who had lost their babies during the antenatal or early neonatal period. Fasting plasma concentrations of total cholesterol and triglycerides were studied prior to single longacting bromocriptine injection and in levels of triglycerides and very low density lipoprotein cholesterol were decreased singificantly in the 28th day (p<0.05). Mean fasting plasma total cholesterol, high density lipoprotein cholesterol, High density lipoprotein cholesterol/low density lipoprotein cholesterol ratio did not differ significantly (p>0.05). These results indicate that bromocriptine reduces some types of plasma lipid levels and does not increase the risk of cardiovascular disease.

Key Words: Bromocriptine, Lipid metabolism, Cardiovascular disease

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ÖZET

Antenatal veya erken neonatal dönemde bebeklerini kaybetmiş 15 hastada uzun etkili bromokriptin enjeksiyonunun lipid metabolizmasındaki etkileri çalışıldı. Uzun etkili bromokriptin enjeksiyonundan önce ve enjeksiyonun birinci, ondördüncü ve yirmisekizinci günlerinde açlık fora*l kolesterol, HDL-kolesterol, LDL-kolesterol, VLDL-kolesterol ve trigliserid seviyeleri ölçüldü. Ortalama trigliserid ve VLDL-kolesterol seviyeleri 28.günde anlamlı olarak azaldı (p<0.05). Ortalama total kolesterol, HDL-kolesterol konsantrasyonları ve HDL-kolesterol/LDL-kolesterol oranları değişmedi (p>0.05). Bu sonuçlara göre bromokriptinin ba - zı tip plazma lipidlerini azalttığı ve kardiovasküler hastalık riskini arttırmadığını düşünüldü.*

Anahtar Kelimeler: Bromokriptin, Lipid metabolizması, Kardiovasküler hastalık

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Ergot derivatives like ergonovine have a powerful vasoconstrictor effect and may cause myocardial infarction. Hydrogénation of ergot alkaloids as In bromocriptine changes this effect to vasodilation. Iffy et al have reported two cases of acute myocardial infarction in women receiving bromocriptine for lactation inhibition (1). Alterations in some types of serum lipoproteins may potentiate cardiovascular disease (CVD). We, therefore prospectively studied the effects of longacting bromocriptine on serum lipoproteins.

MATERIALS AND METHODS

The study was conducted on 15 women who delivered stillborn, immature or anomalous infants incompatible with life İn the Department of Obstetrics and Gynecology, Uludağ University Medicine Faculty, between May'91 and April'92. All of them were normotensive (blood pressure below 140/90 mmHg) and within 10% of their ideal body weight. None of them had known predisposition to diabetes mellitus and cardiovascular disease.

After fasting blood was obtained from the antecubltal vein, a single dose 50 mg longacting bromocriptine (Parlodel LA, Sandoz) was injected deep intramuscularly on the first postpartum day. Fasting blood samples were repeated on the first, fourteenth and twentyeight days after the iniection. All women had sufficient suppression of lactation.

Serum total cholesterol (Cholesterol enzymatique color A-01370, Biotrol-Paris, France) and triglycerides (Triglycerid enzymatique trinder A-01549, Biotrol-Paris, France) were studied enzymatically In analisator (Teenni con RA-1000 Analisator, USA). High density lipoprotein cholesterol (HDL-cholesterol) was determined

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Table 1. Alterations in fasting serum lipids and lipoproteins in the patients whose lactation is suppressed by longacting bromocriptine

	Pretreatment	1 st day	14th day	28th day
N	15	15	15	15
TC (mg/dl)	264+13	256+17	273±24	263±18
TG (mg/dl)	287±39	285±35	302±43	203+35*
LDL (mg/dl)	159±10,3	152±12.9	166±18.8	179+14.3
HDL (mg/dl)	48.0±2.6	49.0±2.9	47.0±2.8	43.7±2.9
VLDL (mg/dl)	57.1 ±7.8	56.9±7.9	60.5±8.6	40.7±7.0[a]
HDL/LDL	0.31+0.02	0.34±0.04	0.34±0.05	0.24±0.02
HDL/TC	0.18±0.01	0.19±0.02	0.19±0.02	0.16±0.02

Data were presented as mean+SEM in mg/dl
All the comparisons were in significant
a: Statistically significant when compared with the pretreatment levels
TC:Total cholesterol, TG: Triglyceride, HDL: HDL-cholesterol, LDL: LDL-cholesterol, VLDL: VLDL-cholesterol

after precipitation of low density lipoprotein cholesterol (LDL-cholesterol) with phosphotungstric acid+magnesium chloride. VLDL-cholesterol level was calculated by the formula of Friedewald et al (2). LDL-cholesterol level was obtained by substraction of HDL-cholesterol and VLDL-cholesterol from total cholesterol values.

Serum glucose, creatinine, uric acid, calcium, magnesium, lactic dehydrogenase, SGOT, SGPT, alkalen phosphatase, creatinine phosphokinase, total protein and albumin levels were studied in the routine biochemistry laboratory.

RESULTS

Mean age of the patients was 27 (range 18-39) mean gravidity 2.4 (range 1-5) and mean parity 0.9 (0-4).

Mean fasting serum glucose was 81 ±5 mg/dl and steadly rose to 88±5, 87+4 and 96±7 mg/dl on the first, fourteenth and twentyeight days respectively, but these differences were statistically insignificant. Serum creatinine, uric acid, calcium, magnesium, lactic dehydrogenase, SGOT, SGPT, alkalen phosphatase, creatinine phosphokinase, total protein and albumin levels did not differ significantly (p>0.05).

Mean serum lipids and lipoprotein levels were shown in Table 1. Mean serum VLDL-cholesterol and triglyceride levels were decreased significantly on the 28th day when compared with the pretreatment and the first and fourteenth day levels, other lipids and lipoproteins (total cholesterol) did not change throughout the effective therapeutic levels of bromocriptine (Figure 1 and 2).

DISCUSSION

Lactation is inhibited in almost all women receiving iongacting bromocriptine injection. This single dose preparation is well tolerated either systematically or locally (3,4). Effective therapeutic level is maintained about four weeks and serum prolactin level falls to normal nonlactating level with the standard 50 mg dose. Lactation suppression may be successful even with low dose bromocriptine (20-30 mg) but rebound phenomena with a gradually increasing levels of prolactin were reported (5).

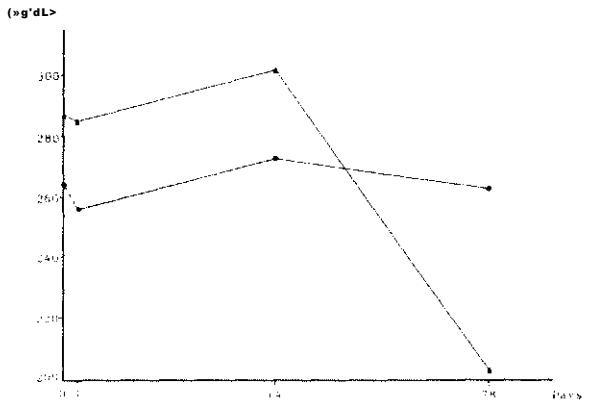

Figure **1 Serum total cholesterol and triglyceride levels. •: Total cholesterol •: Triglyceride**

One of the known risk factors for the cardiovascular disease is the alterations in plasma lipoproteins. Especially elevated levels of LDL-clohesterol and VLDL-cholesterol are important. HDL-cholesterol acts as a cardioprotective agent, but pharmacological augmentation of HDL-cholesterol has not been rewarding as lowering the LDL-cholesterol. So, the HDL-cholesterol/LDL-cholesterol ratio becomes more reasonable in determining the risk of CVD. Elevated triglyceride levels are another important risk factor for middle aged women, especially if combined with obesity and diabetes.

The effects of bromocriptine on lipid metabolism were studied in animals. Reduction in body fat stores and total plasma cholesterol and triglyceride levels were reported in several species (6). Bromocriptine im-

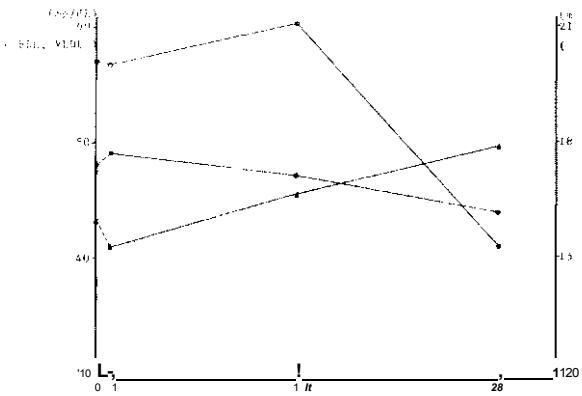

Figure **2Serum HDL, LDL, VLDL cholesterol levels •: HDL cholesterol, A: LDL cholesterol** o: **VLDL cholesterol**

plants in obese female pigs decreased the body fat stores and plasma triglycerides. Cincotta et al concluded that decreased plasma lipids are the result of reduced hepatic lipogenesis (7). Despite these intensive researches on animals, we could not encounter any study done on humans. Our results were completely compatible with the results obtained in animal studies.

It is obvious that alterations in lipid metabolism may change the risk of CVD in a long time period. The decrease in VLDL-cholesterol and triglycerides in a four week period in women receiving bromocriptine may not be an important factor for CVD. But, our findings together with the studies on animals indicate that bromocriptine does not increase the risk of CVD.

REFERENCES

1. **Iffy L, Tentlove W, Frisoli G. Acute myocardial infarction in the puerperium in patients receiving bromocriptine. Am** J **Obstet Gynecol 1986; 155:371-2.**
2. **Friedewald WT, Levy RI, Frederickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. Clin Chem 1972; 18:499-502.**
3. **Rolland R, Nijdam W, Weyer A, Lancranjan I. Prevention of puerperal lactation with Parlodel Long-Acting (Parlodel LA). Eur J Obstet Gynecol Reprod Biol 1986; 22:337-43.**
4. **Kremer JAM, Rolland J, Van Dertleijden RFM, Schellekens LA, Vosmar MBJG, Lancranjan I. Lactation inhibition by a single injection of a new depot-bromocriptine. Br J Obstet Gynecol 1990; 97:527-32.**
5. **Peters F, Del Pozo E, Conti A, Breckwoldt M. Inhibition of lactation by a Long-Acting Bromocriptine. Obstet Gynecol 1986; 67:82-5.**
6. **Cincotta AH, Meier AH. Reductions of body at stores and total plasma cholesterol and triglyceride concentrations in several species by bromocriptine treatment. Life Sci 1989; 45:2247-54.**
7. **Cincotta AH, Meier AH, Southern LL. Bromocriptine alters hormone rhythms and lipid metabolism in swine. Ann Nutr Metab1989; 33:305-14.**