Table 1 - An analysis of muscle disease types during the months of July 2000 to September 2004.

Muscle disease type	Cases diagnosed n	(%)
Dystrophies	46	(37.4)
a. Duchenne/Beckers	29	
b. Limb girdle dystrophy	11	
c. Fasciscapular humeral dystrophy	2	
d. Myotonic dystrophy	1	
e. SCARMD	3	
Myositis	25	(20.3)
a. Autoimmune	21	
b. Viral	1	
c. Inclusion body	3	
Neurogenic atrophy	24	(19.5)
a. Nerve origin	12	
b. ALS	6	
c. Spinal muscular atrophy	5	
d. Myelitis	1	
Mitochondrial myopathy	11	(8.9)
Type II atrophy	8	(6.5)
a. Disuse	4	
b. II b atrophy	3	
c. Paraneoplastic syndrome	1	
Metabolic myopathy	5	(4.1)
a. Glycogen storage disease	3	
b. Lipid storage disease	2	
Congenital muscular dystrophy	2	(1.6)
End stage muscle disease	1	(0.8)
Stiffman syndrome	1	(0.8)

SCARMD - Severe childhood autosomal recessive muscle dystrophy, ALS - amytrophic lateral sclerosis

stage muscle disease (1 case, 0.8%) and Stiffman syndrome (1 case, 0.8%). The muscle biopsy of congenital muscular dystrophy showed severe dystrophic findings by light microscopy. However, the ultrastructural findings confirmed the diagnosis in metabolic and mitochondrial myopathies. Collectively, these findings showed that the classification of muscle diseases in subtypes with a different clinical presentation is useful in clinical practice.

Muscle samples were obtained from the thigh, at a site in the lateral portion of quadriceps femoris by the needle method for the histochemical and electron microscopical investigations.[1-3] The procedure is carried out under sterile conditions. The skin and subcutaneous tissue at the biopsy site were anesthetized by the local infiltration of 2% lidocaine. After anesthesia, a small scalpel incision, approximately 1 cm long using a size 15 blade, is made in the skin and deep fascia to facilitate the pathway of the needle. Upon removal of the needle from the muscle, the wound is closed over with pressure and skin Elastoplast. Frozen specimens were stored at -70ºC until sectioning. For light microscopy, all sections were taken in series and stained with the following histological and immunocytochemical staining list: hematoxylin and eosin mATPase at alkaline and acidic pH; Nicotinamide adenine dinucleotide; gomori trichrome; phosphorylase; succinate dehydrogenase. However, double fixation with 2.5% glutaraldehyde followed by 2% osmium tetroxide of fresh samples, provides the optimal preservation for ultrastructural investigations of muscle samples from patients with mitochondrial and metabolic myopathies.

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Pregnancy outcome following exposure to orlistat, ramipril, glimepiride in a woman with metabolic syndrome

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Most babies are exposed to drugs in utero. Drugs given to mothers during pregnancy can affect the fetus by acting directly on the embryo and produce lethal, toxic or teratogenic effects such as altering placental function, changing the myometrial activity, altering the biochemical dynamics of the mother and by acting indirectly. The use of drugs during pregnancy is a complicated problem, especially for new drugs.

Orlistat, a new drug, has pancreatic lipase inhibitory property that decreases the absorption of ingested dietary fat.[1] Data for the use of orlistat in treating obesity in pregnant women are not available currently. In case of hypertension and angiotensin converting enzyme (ACE) inhibitors in pregnancy,

the available data demonstrate that they are human teratogens if used in the second and third trimesters, and no harm is caused when their use is limited to the first trimester.[2] However, no special report has been presented for ramipril use in pregnancy.

Our Toxicology Information and Follow-up Service, Karadeniz Technical University, Trabzon, Turkey is a counseling service for pregnant and lactating women and their health professionals. We provide information on the teratogenic risks of drugs depending on available data. We follow up women throughout pregnancy and lactation period. In addition, we perform periodic checks of all babies.[3] Among the 659 cases followed by our center for drug exposure in pregnancy, we have one pregnant woman with metabolic syndrome that used orlistat and ramipril in addition to glimepiride, thiocolchicoside, simvastatin, metformin, ciprofloxacin and aspirin, which were prescribed by her physicians who were unaware of her pregnancy. By presenting this case, our objective is to call attention on the use of multiple and new drugs in pregnancy in controlling the metabolic syndrome of the mother.

Our patient, a 33-year-old, gravida 7, para 3 Caucasian woman, has suffered hypertension, type II diabetes mellitus, hypercholesterolemia, and morbid obesity (body mass index (BMI) = 42 kg/m^2) for 5 years and urolithiasis for 6 months. She has a history of 3 induced abortions with her own decision after exposure of multiple drugs (ramipril, glimepiride and metformin) in her previous pregnancies. She is currently married to a second cousin (third lane consanguineous marriage). Due to her irregular menses, the patient was not aware of her pregnancy until the 8th week. During the first 7 gestational weeks of her seventh (present) and unplanned pregnancy, she used orlistat (360 mg/day), ramipril (5 mg/day), glimepiride (2 mg/day), thiocolchicoside (4 mg/day), simvastatin (20 mg/day), metformin (1700 mg/day), ciprofloxacin (1000 mg/day) and aspirin (100 mg/day). Except for ciprofloxacin and thiocolchicoside, she used these drugs continuously. After the diagnosis of pregnancy at the 8th week, all the drugs were stopped. Methyldopa (750 mg/day) and insulin therapy were started. In the last trimester, the dosage of methyldopa was increased to 1000 mg/day. In the outpatient follow-up visits, blood glucose levels and arterial blood pressure were not optimal. She was hospitalized 3 times during pregnancy period to regulate blood glucose level and arterial blood pressure. In the hospitalization periods, her serum glucose level varied between 70-210 mg/dl, and her arterial blood pressure was between 120/85-160/100 mm Hg. The insulin dose was increased to 12 IU 4 times daily (regular insulin 12 IU 3 times and neutral protamine Hagedom (NPH) insulin 12 IU once a day) in the last trimester. Her glycosylated hemoglobin (HbA1C) was found to be 8 and 8.5% in the follow-up in the second and third trimesters. The patient could not exercise. At the beginning of her pregnancy, she weighed 110 kg, and at the end of her pregnancy, she weighed 131 kg. The results of triple marker screening and amniocentesis were normal in the 17th week. Ultrasonographical examinations were made monthly between the 8th-28th weeks and weekly during the 29th-37th weeks; and all were found normal. Umbilical Doppler ultrasonography was normal when checked in the 18th, 32nd, 33rd, 34th, and 37th weeks. The patient delivered a female infant (3470 gr, 51 cm with APGAR scores of 5-7 at 1 and 5 minutes) at the 38th week with an uncomplicated normal spontaneous vaginal delivery. The baby had no minor or major congenital malformations.

Maternal high BMI is associated with adverse reproductive outcomes, including some birth defects. Data for the use of new drugs for treating obesity in pregnant women are very few. While there was no available report regarding orlistat use in literature, there was only one report of 2 cases with good fetal outcomes about sibutramine use in pregnancy.[4] Our case was exposed to 8 drugs during pregnancy due to obesity, metabolic syndrome, urolithiasis and urinary tract infection. Of these drugs, only aspirin at the dose used by this case seems safe in pregnancy.

Good control of diabetes mellitus throughout gestation is important for an optimal maternal and infant outcome. Oral antidiabetics are not the treatment of choice during pregnancy.[2,3] Carefully designed insulin therapy provides better control of mother's blood glucose, thereby preventing fetal and neonatal complications that occur with this disease.[2,3] In our case, optimal glucose levels could not be achieved in spite of using glimepiride and metformin in the first 7 gestational weeks before the diagnosis of pregnancy, and insulin therapy after the pregnancy diagnosis. Recent reports have shown that even in western countries, perinatal mortality was 5 times, and neonatal mortality was 15 times greater in the offspring of diabetic women. These high results may be the consequence of poor medical and social care prior to conception as well as during the perineonatal period. There are limited data on the use of glimepiride and metformin in pregnancy. In a clinical study, the prevalence of congenital malformations was found to be 52% for a patient group exposed to metformin and 15% for the control group.[2] There was no available data for the use of glimepiride in pregnant animals, and there was only one human case report[5] documenting persistent hypoglycemia in a newborn of a mother who used the drug until delivery. Our case had used glimepiride during the first 6 gestational weeks. Since insulin is still the treatment of choice for

diabetes in pregnancy, insulin was started in our case when the pregnancy was diagnosed. But, she had been exposed to both glimepiride and metformin up to the time of that diagnosis. In addition to oral antidiabetic drugs, the patient was also exposed to orlistat for obesity during first 7 gestational weeks. There was no report on the use of orlistat in pregnancy in humans.[2] Teratogenic studies have been conducted in rats and rabbits at doses up to 800 mg/kg/day. Neither study showed embryotoxicity or teratogenicity. This dose is 23 and 47 times the daily human dose calculated on a body surface area basis for rats and rabbits. However, the manufacturer does not recommend the use of orlistat during pregnancy. The patient was also exposed to simvastatin. There are limited data on the use of this drug during human pregnancy.[2] Based on animal data and limited human experience, simvastatin exposure does not appear to present a significant risk for the baby. A case report of a diabetic, hypertensive and obese woman exposed to another new statin indicated a normal fetal outcome.[3]

The management of chronic hypertension in pregnancy is one of the most controversial areas, despite the relative frequency of the condition (1.5-2%). Association between chronic hypertension and increased risk for morbidity and mortality to both mother and fetus is undisputed; stillbirth, placental abruption, intrauterine growth retardation and hypoxic effects of superimposed pregnancy-induced hypertension are common in fetus. There are many reports showing that ACE inhibitors are safe if taken during the first trimester, and among these drugs, fetal exposure to captopril and enalapril in the second and third trimesters has been found to be associated with teratogenicity and severe toxicity in the fetus and newborn.[2] Angiotensin converting enzyme inhibitors may cross the human placenta in pharmacologically significant amount. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists should be discontinued due to fetotoxicity. The use of ACE inhibitors during pregnancy was reported to be associated with poor fetal outcomes, including oligohydramnios, renal tubular dysplasia, cranial malformations, and fetal death. Our case was exposed to ramipril, an ACE inhibitor, which was prescribed for treatment of chronic hypertension. No report about ramipril use in human pregnancy has been located, and no teratogenic effect was found in animals. Since the ACE inhibitors share the same mechanism of action, ramipril might cause the same malformations as the other ACE inhibitors. When the patient's pregnancy was diagnosed, this drug was also stopped and methyldopa, which is considered to be safe for pregnant women[2] was started.

Our case was exposed to ciprofloxacin and thiocolchicoside for treatment of urinary tract infection and urolithiasis. No case of thiocolchicoside exposure in pregnancy was reported in either humans or animals. While there are some studies that concludes that the use of ciprofloxacin in pregnancy does not appear to be associated with an increased risk of major congenital malformations, some other studies have concluded that fluoroquinolones should be considered as contraindication or at least not the first choice during pregnancy, and physicians should be encouraged to select safer alternatives.

To our knowledge, this is the first case in the literature that has evaluated the effects on the fetus of using orlistat, ramipril and thiocolchicoside during pregnancy, in addition to 5 other drugs in the same case in the first trimester. The baby had no congenital anomaly and that case may contribute to the very limited knowledge regarding human exposure to at least 3 prescribed drugs (orlistat, ramipril and thiocolchicoside) for which no previous literature is available.

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