

Measurement of Gallbladder Contraction by Ultrasonography in Post-Menopausal Women

POST-MENAPOZAL KADINLARDA ULTRASONOGRAFİK OLARAK SAFRA KESESİ KONTRAKSİYONUNUN ÖLÇÜMÜ

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Summary

We investigated the fasting and post-prandial gallbladder volume in two groups of healthy non-obese women: a) Control non-pregnant women (n:10), b) Post-menopausal women (n:10). Scans were taken after a 12 h fast. After the baseline measurement the gallbladder volumes were rescanned in 15 min intervals for 60 min. At the end of this period all volunteers received a standard liquid test-meal and scans were performed again for one h. The mean baseline gallbladder volume was 22.22 ± 4.26 ml in the non-pregnant (control) group. In the post-menopausal group the basal volume was 20.83 ± 3.92 ml, and it was 6.25% lower than that of the non-pregnant group. However, this difference between the two groups was statistically non-significant. After administration of the test meal the post-prandial gallbladder volumes were reduced during the first few minutes compared to the baseline. The volumes decreased from 20.90 ± 3.80 to $14.40 \pm 7.80 - 7.80 \pm 1.6$ ml in post-menopausal women ($p < 0.01-0.001$) and from 22.72 ± 3.83 to $19.74 \pm 3.68 - 10.75 \pm 3.26$ in the control group ($p < 0.01-0.001$), respectively. Post-prandial mean gallbladder volumes were significantly different from the control group ($p < 0.02-0.001$).

In conclusion the post-prandial gallbladder volume is significantly reduced in post-menopausal women compared to non-pregnant women.

Key Words: Gallbladder volume, Ultrasonography, Menopause

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Özet

Sağlıklı, obez olmayan kadınların açlık ve postprandial safra kesesi hacimleri, olgular iki gruba ayrılarak değerlendirildi: a) Gebe olmayan kontrol grubu (n:10), b) Post-menopozal grup (n:10). 12 saatlik açlık sonrası ultrasonografik ölçümler yapıldı. Bazal ölçüm yapıldıktan sonra 15 dk. aralıklarla 60 dk. süre ile olguların kese hacimleri saptandı. Bu sürenin sonunda tüm olgulara standart sıvı test yemeği verilerek ölçümler aynı şekilde bir saat süre içinde yenilendi. Post-menopozal grupta bazal kese hacmi 20.83 ± 3.92 ml. olup gebe olmayan kontrol grubundan %6.25 daha düşük idi. Bununla birlikte arada istatistik fark saptanmadı. Test yemeğinden sonraki dakikalarda bazal değerlere göre azalma saptandı. Postmenopozal grupta hacim 20.90 ± 3.80 'den $14.4 \pm 7.80 - 7.80 \pm 1.6$ ml'e ($p < 0.01-0.001$), kontrol grubunda ise 22.72 ± 3.83 'den $19.74 \pm 3.68 - 10.75 \pm 3.26$ ml'e azaldı ($p < 0.02-0.001$).

Sonuç olarak, postprandial safra kesesi hacmi post-menopozal kadında, gebe-olmayan kadınlara oranla belirgin olarak azalmaktadır.

Anahtar Kelimeler: Safra kesesi hacmi, Ultrasonografi, Menapoz

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The use of estrogen has been reported to cause gallstone formation in post-menopausal women(1). Estrogen treatment was associated with a 40% increase in biliary cholesterol secretion, an increase in the lithogenic index of gallbladder bile, and a

Table 1. The mean volume in healthy subjects and post-menopausal women

Groups	The Mean Volume in Different Time (X±SEM) (ml)									
	Baseline	15	30	45	60	Ens	75	90	105	120
Post-Menopausal	20.8±3.9	20.9±3.8	20.9±3.8	20.9±3.7	20.9±3.8		14.4±4.8*	9.8±3.4**	8.4±2.8**	8.0±2.6**
Control	22.2±4.2	22.8±3.5	21.8±3.4	22.4±4.2	22.7±3.8		19.7±3.6* [†]	17.2±3.8* [«]	14.7±4.4** ^{††}	11.9±3.5** ^{««}

*p<0.01, **p<0.001 Difference from baseline

[†]p<0.02, ^{††}p<0.001, [«]p<0.01 Difference from control

moderate reduction in the percentage of chenodeoxycholic acid of bile. In a study, anovulatory women were treated with conjugated estrogen and studied by a real-time ultrasonography after a regular meal ingestion or intravenous infusion of cholecystokinin (CCK-8)(2). Neither the gallbladder volume nor its emptying was altered by Premarin.

Recently, we have demonstrated that the fasting and post-prandial gallbladder volumes were larger in third trimester pregnant women than in non-pregnant women (3). The post-prandial volumes were reduced to the non-pregnant value, but they were still greater than in the control group in the post-partum period. The gallbladder motility has not been investigated yet in the post-menopausal period.

Therefore, we investigated the fasting and post-prandial gallbladder volumes in two groups of healthy, non-obese women: a) non-pregnant women as control, b) post-menopausal women.

Materials and Methods

Twenty healthy volunteer women, participated in this study after agreeing to accept the test procedure. All subjects completed the protocol as expected. Written consent of each patients was obtained, and the study was approved by the Ethics Committee of Karadeniz Technical University School of Medicine. The age range of non-pregnant, fertile subjects (n:10) was 32±5, and the post-menopausal group (n:10) was 53±4 years old.

None of the subjects had any known illness and none was on medication. All volunteers had normal fasting serum aspartate aminotransferase, alkaline phosphatase and bilirubin levels.

Scans were performed at 9 am after 12 h of fasting. After the baseline measurement, the gall-

bladder volumes were rescanned in 15 min. intervals for 60 min. All volunteers received a standard liquid test meal (250 cal/250 ml) at the end of the scanning (16.7% Protein, 30% fat, 53.3% carbohydrate, Ensure, Abbott) and then scans were performed again in 15 min intervals for 60 min.

The gallbladder volume and its emptying time were measured using ultrasonography (4). Using a 3.5 or 5-MHz transducer real time ultrasound, scans were obtained with Siemens Sonoline SC 2 3.5 MHz. Subjects were scanned supine in the right anterior oblique position by a radiologist trained in ultrasonography. The gallbladder was visualized in the longitudinal and transverse planes, and measurements of maximum length, width, and height were taken in duplicate. The volume of the gallbladder was subsequently calculated using the ellipsoid method (volume = 0.52 x length x width x height) (4).

The results were expressed as mean ± SEM unless otherwise stated. For statistical analysis, the Wilcoxon matched pairs signed-rank test or the Wilcoxon U test was used. The level of significance was set at p<0.05.

Results

The mean basal gallbladder volume was 22.22±4.26 ml in the non-pregnant (control) group. In the post-menopausal group the baseline volume was 20.83±3.92 ml, and it was 6.25% lower than that of the non-pregnant group. However the difference between the two groups was statistically non-significant. After administration of the test meal, the post-prandial gallbladder volumes were reduced during the first few minutes compared to the baseline in post-menopausal women. The volumes decreased from 20.90±3.80 to 14.40±4.80 -

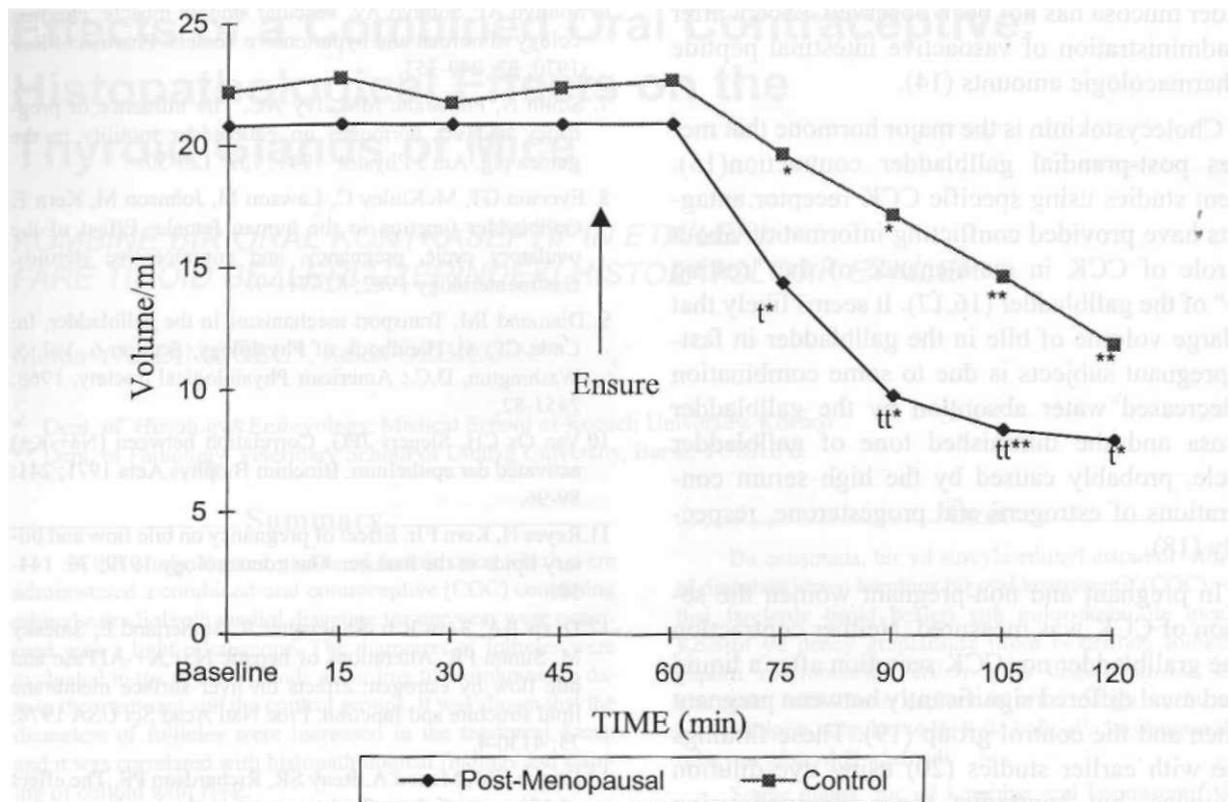


Figure 1. The mean volume in healthy subjects and post-menopausal women.

7.80±1.6 ml in post-menopausal women (PO.01-0.001) and from 22.72±3.83 to 19.74±3.68 - 10.75±3.26 in the control group (p<0.01-0.001), respectively. Post-prandial mean gallbladder volumes in the post-menopausal group were significantly different from the control group (p<0.02- 0.001).

Discussion

This study demonstrated that the post-prandial gallbladder volume is significantly reduced in post-menopausal women compared to non-pregnant women. Because the hormonal changes of the post-menopausal period are complex, it is not possible to identify with certainty the mediators of the alterations in the gallbladder function. Nevertheless, progesterone, a known inhibitor of smooth muscle contraction (5-7), may be one of the possible candidates. A previous study showed a direct correlation of fasting and residual volume with serum progesterone concentrations up to 80 ng/ml. This is

consistent with, but not proof of, progesterone mediation (8),

Increased gallbladder volume during fasting could be due to decreased water absorption by the gallbladder mucosa. The large amount of water that is normally absorbed from the gallbladder produces an eight to ten fold increase in the concentration of the organic components of bile (8,9). Water absorption is dependent on active absorption of sodium, which is mediated by the sodium pump in the gallbladder epithelium (10). The activity of the sodium pump which is believed to be sodium-potassium ATPase (ATP-phosphohydralase), may be decreased by estrogens which are present in large concentrations in the serum in the late pregnancy. Sodium-potassium-ATPase activity is reduced in livers of pregnant hamsters (11) and of rats treated with ethinyl estradiol (12). Fluid transport by the guinea-pig gallbladder in vitro is inhibited by 17 α -estradiol (13). Active water secretion by the gall-

bladder mucosa has not been observed, except after the administration of vasoactive intestinal peptide in pharmacologic amounts (14).

Cholecystokinin is the major hormone that mediates post-prandial gallbladder contraction (15). Recent studies using specific CCK receptor antagonists have provided conflicting information about the role of CCK in maintenance of the "resting tone" of the gallbladder (16,17). It seems likely that the large volume of bile in the gallbladder in fasting pregnant subjects is due to some combination of decreased water absorption by the gallbladder mucosa and the diminished tone of gallbladder muscle, probably caused by the high serum concentrations of estrogens and progesterone, respectively (18).

In pregnant and non-pregnant women the secretion of CCK was measured. Neither contraction of the gallbladder nor CCK secretion after a liquid mixed meal differed significantly between pregnant women and the control group (19). These findings agree with earlier studies (20) using dye dilution techniques, but contradict those obtained using pregnant animals (7,21).

In conclusion, this study demonstrated that the post-prandial gallbladder volume is significantly reduced in post-menopausal women compared to non-pregnant women. Incomplete emptying of the gallbladder in non-pregnant women could contribute to cholesterol-gallstone formation and thus suggests that a pregnancy may increase the risk of gallstones.

REFERENCES

- Kern E Jr. Epidemiology and natural history of gallstones. *Semin Liver Dis* 1983; 3: 87-96.
- Everson GT, McKinley C, Kern F Jr. Mechanisms of gallstone formation in women: Effects of exogenous estrogen (Premarin) and dietary cholesterol on hepatic liquid metabolism. *J Clin Invest* 1991; 87: 237-46.
- Kapıcıoğlu S, Gürbüz G, Şentürk Ö, Uslu M. Measurement of gallbladder volume by ultrasonography in pregnant women. *T Gastroenterol* 1997; 8:429-33.
- Dodds VJ, Groh WJ, Darweesh RMA, Lawson TL, Kishk SMA, Kern MK. Sonographic measurement of gallbladder volume. *Am J Roentgenol* 1985; 145: 1009-10.
- Cohen S. The sluggish gallbladder of pregnancy. *N Engl J Med* 1980; 302: 397-8.
- Somlyo AP, Somlyo AV. Vascular smooth muscle: pharmacology of normal and hypertensive vessels. *Pharmacol Rev* 1970; 22: 249-353.
- Smith N, Pomaranc MM, Ivy AC. The influence of pregnancy and sex hormones on gallbladder motility in the guinea pig. *Am J Physiol* 1941; 132: 129-50.
- Everson GT, McKinley C, Lawson M, Johnson M, Kern F. Gallbladder function in the human female: Effect of the ovulatory cycle, pregnancy, and contraceptive* steroids. *Gastroenterology* 1982; 82: 711-9.
- Diamond JM. Transport mechanisms in the gallbladder. In: Code CF, ed. *Handbook of Physiology*. Section 6. Vol. 5. Washington, D.C.: American Physiological Society, 1968; 2451-82.
- Van Os CH, Siegers JFG. Correlation between (Na⁺-K⁺) activated der epithelium. *Biochim Biophys Acta* 1971; 241: 89-96.
- Reyes H, Kern F Jr. Effect of pregnancy on bile flow and biliary lipids in the hamster. *Gastroenterology* 1979; 76: 144-50.
- Davis RA, Kem F Jr, Sholwalter R, Sutherland E, Sinesky M, Simon FR. Alterations of hepatic Na⁺,K⁺-ATPase and bile flow by estrogen: effects on liver surface membrane lipid structure and function. *Proc Natl Acad Sci USA* 1978; 75: 4130-4.
- France VM, Menon A, RcaY SR, Richardson PS. The effect of 17a-oestradiol on fluid transport in the in vitro guinea-pig gallbladder. *J Physiol (Lond)* 1977; 266: 67P-8P. abstract.
- Jansson R, Steen G, Svanvik J. Effects of intravenous vasoactive intestinal peptide (VIP) on gallbladder function in the cat. *Gastroenterology* 1978; 75: 47-50.
- Ivy AC, Oldberg E. A hormone mechanism for gallbladder contraction and evaluation. *Am J Physiol* 1988; 86: 599-613.
- Konturenk JW, Konturek SJ, Kurek A, Bogdal J, Oleksy J, Rovati L. CCK receptor antagonism by loxiglumide and gallbladder contractions in response to cholecystokinin, sham feeding and ordinary feeding in man. *Gut* 1989; 39: 1136-42.
- Nicderan C, Beinges T, Rovar L, Srohmeyer G. Effects of toxiglumide on gallbladder emptying in healthy volunteers. *Gastroenterology* 1989; 97: 1331-6.
- Bravennan DZ, Johnson ML, Kern F Jr. Effects of pregnancy and contraceptive steroids on gallbladder function. *N Engl J Med* 1980; 302: 362-4.
- Radberg G, Asztely M, Cantor P, et al. Gastric and gallbladder emptying in relation to the secretion of cholecystokinin after a meal in late pregnancy. *Digestion* 1987; 42: 174-9.
- Davison J, Davison M, Hay D. Gastric emptying time in late pregnancy and labor. *J Obstet Gynaen Br Emp* 1970; 77: 37-41.
- Ryan J, Bhojwan A, Wang H. Effect of pregnancy on gastric motility in vivo and in vitro in the guinea pig. *Gastroenterology* 1987; 93: 29-34.