ABSTRACT
Investigation of differences in psychic functioning of women with history of hysterectomy with adenectomy due to uterus myoma, women who were treated with metotrexate due to the same illness and the group of women who are in physiological perimenopause.

The population of 120 women was divided in three equal groups of 40. The first group consisted of women with history of hysterectomy with adenectomy due to uterus myoma, the second group consisted of women who were treated with metotrexate due to the same illness and the third group consisted of women in physiological perimenopause.

The Hamilton Scales were used for evaluation of depression and anxiety (HAMD and HAMA, 1960).

The t-test, the Kruskal-Wallis test and the Mann-Whitney test were used in statistical processing.

The usage of ANOVA on HAMD scale scores is shown in listed groups of patients. Achieved result p=0.001, shows that there is statistically significant difference in levels of depression between groups. The result is confirmed by Mann-Whitney test and the Kruskal-Wallis test (p=0.0001). The usage of ANOVA in HAMA scale scores in investigated groups. Achieved result p=0.002, shows that there is statistically significant difference in levels of anxiety. The result is confirmed by Mann-Whitney test and the Kruskal-Wallis test (p=0.000). Significantly higher levels of depression and anxiety were registered in hysterectomized women compared to women from other groups. There is no significant difference in levels of anxiety and depression between the group of women treated with methotrexate and the group of those in physiological perimenopause.

Hysterectomy with adenectomy influences negatively on woman's later quality of life. This surgical procedure increases the risk of developing psychiatric difficulties that accompany this life phase are partly the consequence of psychological reaction to an end of reproductive period. In most of the hysterectomized women the process of inner-psychic suffering reaches the level of full-blown depression. Significantly lower levels of depression and anxiety were registered in population of women who were in physiological perimenopause, and also in population of those who were treated conservatively with methotrexate due to uterus myoma. From the aspect of mental health, the advantage of conservative treatment of uterus myoma compared to surgery is obvious.

Keywords: myoma, perimenopause, methotrexate, depression, estrogen.
Experiences from our practice are contributing the observation that especially risky population for developing psychic sphere dysfunction is made of women who have undergone hysterectomy with adnexectomy. In such cases menopause starts abruptly and leaves no time for organism to adapt to hormonal and psychological stress. One of the most common indications for this surgical procedure are complications of benign tumor of woman’s genitals – uterus myoma. These tumors are most commonly developed during the reproductive period, they grow throughout the pregnancy, and their regression occurs after the menopause. It is most definitely certain that local hyperestrogenemy is the key factor in their progression. More than one half of women who have been diagnosed with uterus myoma do not have symptoms of illness. In other half difficulties in terms of inappropriate bleeding from uterus, anemia, pressure on nearby organs, the pain in pelvic area and abdomen, rarely polycystemia and ascites have been reported. In one third of women plentiful (hipermenorrhea), lengthened (menorrhagia) or both plentiful and lengthened (menometrorrhagia) menstrual bleedings, which lead to hypochromic anemia, have been reported. Due to the pressure on nearby organs frequent urination, stress incontinence, opstipation, tenesms, can occur, and with intraligament myoma, thrombosis and pulmonary embol can occur. Surgical operative procedures are radical and palliative. Observation on adverse effects of hysterectomy with adnexectomy on woman’s later quality of life based on practical experience, has brought our attention on new possibilities for conservative treating of uterus myoma. It has been proven that methotrexate, the anti-metabolite class drug, used in 5 to 10 mg doses/month during three consecutive months, significantly favorably acts on decrease in plentiful menstrual bleedings in patients with uterus myoma in per menopausal period (p<0.001), and evidently decreases tumor volume (10).

Analyzing the differences in psychic functioning between following 3 groups of perimenopausal women: those who had hysterectomy with adnexectomy due to uterus myoma, women who were treated with metotrexate due to the same illness and the group of women who are in physiological perimenopause.

PATIENTS AND METHODS
The research has been done in Gynecology-Obstetric Clinic, Clinical Center Kragujevac, and in Psychiatric Clinic, Clinical Center Kragujevac, in period from April, 2000 to September, 2002. The research population consist of 120 per menopausal women, divided in three groups (40 each). The first group consisted of women with history of hysterectomy with adnexectomy due to uterus myoma, the second group consisted of women who were treated with methotrexate due to the same illness and the third group consisted of women in physiological perimenopause. The Hamilton Scales were used for evaluation of depression and anxiety (HAMD and HAMA). The t-test, the Kruskal-Wallis test and the Mann-Whitney test were used in statistical processing.

RESULTS
In Table 1, the usage of ANOVA on HAMD scale scores is shown in listed groups of patients. Achieved result p=0.001, shows that there is significant difference in levels of depression between groups. If the Kruskal-Wallis test is applied on the same groups, the result p=0.0001 is gained, which confirms existence of significant difference among groups. Table 1 shows existence of significant difference in mean value of HAMD scale scores between women who had hysterectomy with adnexectomy due to uterus myoma, those who were conservatively treated with methotrexate due to the same illness and women in physiological perimenopause. Particularly, significantly higher levels of depressiveness were present in hysterectomized women, compared to women in the other two groups. Between groups of women who were on therapy with methotrexate and those who were in physiological perimenopause there were no significant differences in HAMD scores values. The result was confirmed by Mann-Whitney test.

Table 1. T-test for HAMD scale scores in investigated groups (hysterectomy-methotrexate; hysterectomy-physiological perimenopause; methotrexate-physiological per menopause).

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>Xar ± SD</th>
<th>Xar ± SD</th>
<th>p</th>
<th>Mann-Whitney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hysterectomy-methotrexate</td>
<td>16.10 ± 4.74</td>
<td>12.10 ± 4.67</td>
<td>0.000</td>
<td>0.00001</td>
</tr>
<tr>
<td>(n=40)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hysterectomy-physiological perimenopause</td>
<td>16.10 ± 4.74</td>
<td>10.75 ± 3.71</td>
<td>0.000</td>
<td>0.0000</td>
</tr>
<tr>
<td>(n=40)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Methotrexate-physiological perimenopause</td>
<td>12.10 ± 4.67</td>
<td>10.75 ± 3.71</td>
<td>0.000</td>
<td>0.1176</td>
</tr>
<tr>
<td>(n=40)</td>
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</table>

Figure 1. Arithmetic mean of scores in HAMD in investigated groups.

In Table 2 the usage of ANOVA in HAMA scale scores in investigated groups is shown. Achieved result p=0.002 shows that there is statistically significant difference in levels of anxiety. If the Kruskal-Wallis test is applied on the same groups, the result p=0.001 is gained, which confirms existence of significant difference among groups.

Table 2 shows existence of significant difference in mean value of HAMA scale scores between women who had hysterectomy with adnexectomy due to uterus myoma,
those who were conservatively treated with methotrexate due to the same illness and women in physiological perimenopause.

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>Xsr ±SD</th>
<th>Xsr ±SD</th>
<th>p</th>
<th>Mann-Whytny</th>
</tr>
</thead>
<tbody>
<tr>
<td>hysterectomy-methotrexate</td>
<td>38.00±11.78 (n=40)</td>
<td>30.40±10.93 (n=40)</td>
<td>0.004</td>
<td>0.0006</td>
</tr>
<tr>
<td>hysterectomy-physiological perimenopause</td>
<td>38.00±11.78 (n=40)</td>
<td>29.00±13.00 (n=40)</td>
<td>0.002</td>
<td>0.0002</td>
</tr>
<tr>
<td>methotrexate-physiological perimenopause</td>
<td>30.40±10.93 (n=40)</td>
<td>29.00±13.00 (n=40)</td>
<td>0.604</td>
<td>0.2027</td>
</tr>
</tbody>
</table>

Figure 2. Arithmetic mean of scores on HAMA scale in investigated groups.

Women who had hysterectomy with adnexectomy are significantly more anxious compared to women who underwent conservative treatment with methotrexate and those in physiological perimenopause. On the other hand, there is no significant difference in mean values on HAMA scale between groups of women treated with methotrexate and those in physiological perimenopause. The result is confirmed by Mann-Whitney test.

**DISCUSSION**

Hysterectomy with adnexectomy is invasive surgical procedure, which according to our experiences in large number of women agitates the process of inner psychic suffering, often achieving levels of manifest depression. The need of modern woman for prolongation of hormonal cyclic occurrences in organism, requires more precise selection of women patients planned for surgical treatment of this tumors. The prolongation of woman’s lifetime, realization of maternal role in later life years and need to maintain sexual functions, makes preserving of uterus clinician’s primary objective. With regard that hyperestrogenemcy is one of the key factors in progression of these tumors, present conservative treatment is mostly based on usage of medications that have anti-estrogen action. Changes in psychic functioning that follow menopause are for quite same time familiar to every clinician with experience. States of emotional lability, irritability, loss of self-esteem, decreased libido, low self-estimate, insomnia, states of fear and depression that often follow menopause, are associated with deficit of estrogen hormones (12). On the other hand, the connection between estrogen and mood is not completely cleared yet although there are reports that their mechanisms of action are most likely on level of central neurotransmission of increased activity of norepinephrine and tryptophan as serotonin precursor and initiating activity of system of endogenous opiates (12).

By realizing the complex process of psychological occurrences in perimenopause, famous psychoanalyst Helen Dutch claimed that „overcoming of psychic complaints that follow the loss of bleeding is one of the most hardest tasks of woman’s being”. The consequence of hysterectomy with adnexectomy is abrupt onset of menopause, when the time required for organism to adapt on hormonal stress lacks. In psychological sense the loss of organs which in archetype sense represent the symbols of womanhood and womanly qualities can start or elicit existent conflicts associated to SELF concept and sexuality. The source of conflict can be the fact that in most women sense of womanhood is associated with the idea „to be a mother“, and that the loss of menstruation for the great number of women is equal to absence of sexual attraction (14). Our observations, that anticipating loss of reproductive organs evokes destabilization in psychic functioning in significant number of women, and with the circumstance that uterus myoma are most often benign tumors of woman’s genitals, pointed our interests to conservative treatment of these tumors. In order to establish the influence of hysterectomy with adnexectomy on psychic functioning, we followed the psychic functioning of two more groups of women. One of the investigated groups consisted of women that were treated with methotrexate due to the uterus myoma, and the other group consisted of women in physiological perimenopause. Methotrexate is the anti-metabolite class drug proven to have an advantage over surgical treatment, used in therapy of uterus myoma whose size doesn’t exceed the size of uterus that corresponds the 12 week gestation pregnancy. Administration of this drug is possible in ambulatory conditions, it doesn’t evoke artificial menopause, and the adverse effects after three consecutive treatments when used in 5–10 mg doses/month have not been reported. The effects of its usage are decrease in tumor size and decrease in plentifulness of menstrual bleedings in woman with the condition. By investigating the differences in psychic functioning between the groups listed above, we came to conclusion that hysterectomized women are the population with high risk of developing dysfunction in psychic sphere, compared to women treated with methotrexate or those in physiological menopause. From aspect of mental health preserving, which is primary, conservative treatment with methotrexate stands out as a new, significant possibility in treating per menopausal women, with condition of uterus myoma.

Results of our research show that hysterectomy with adnexectomy negatively influences woman’s later quality of life. This invasive surgical procedure increases the risk of developing dysfunction in psychic sphere. Significantly higher levels of depressiveness and anxiety are registered in women who had hysterectomy with adnexectomy, compared to those treated with methotrexate due to the
same illness, and those in physiological perimenopause. On the other hand, statistically significant difference in levels of depressiveness and anxiety between the groups of women conservatively treated with methotrexate and the group of those in physiological perimenopause has not been registered. From the aspect of mental health preserving, the advantage of conservative treatment with methotrexate is obvious.

REFERENCES