Menopause is defined as the period of one full year without a period. The cause of the onset of menopause is increasing due to the decline in ovarian function follicular degeneration (atresia). In women aged about 50 years, only a few primordial ovarian follicles that survive are still the response to gonadotropin secretion and capable to mature into the follicle. In the process of menopause, a decline in estrogen production will completely disappear in the mid 50s years (1, 2). Based on a study by Siregar M.F.G. (2016), alternatively, menopause can be diagnosed by vaginal pH $\geq 5.5$ (3).

The symptoms such as hot flushes and night sweats, insomnia, and vaginal dryness, osteoporosis, arteriosclerosis, dyslipidemia, decreased mood, irritability, and headaches. Study by Siregar M.F.G. et al. (2016) showed that 50-56 year age women who complained about menopause were based on Menopause Rating Scale (MRS) (4). Other symptoms include neurological symptoms such as memory problems (5). Cognitive function related to individual perception, memory, thinking, logic and alertness. Along with physical decline, decli-
ne in cognitive function is a marker of primary aging (6).

Memory problems during menopause is currently associated to hormonal changes. This is supported by Siregar M.F.G. (2016) study which states that the increased cortisol levels > 10 ng / ml are associated with psychological disorders during perimenopause (7). The brain is an important target for estrogen, which affects brain function through its effect on blood vessels and the immune system (8).

Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is a questionnaire used to assess cognitive impairment in the elderly. This test is valid: it reflects the cognitive decline of the past, it gives valid results similar to dementia, and it is correlated with most of the cognitive tests (9, 10).

Paramedics, partners of doctors, have an essential position in the management of a patient. The performance of paramedics is therefore of great importance, the maintenance of which greatly depends on the person’s cognitive function. In paramedics who are menopausal, cognitive impairment can be fatal if experienced by those who work in the area of work that require a high degree of concentration, such as an emergency room.

Therefore, the objective of this study is to determine the association of serum estradiol levels and cognitive function assessed based on IQCODE in aged menopausal paramedics.

Methods

This study is a cross-sectional study to assess the association between serum estradiol levels and cognitive function of postmenopausal women using IQCODE questionnaire conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine USU Dr. H. Adam Malik and began in January-February 2017.

The whole population in this study is the menopausal paramedic female or had not menstruate for 12 months working in RSUP H. Adam Malik who meets inclusion criteria: 1) Passed Minnesota Multiphasic Personality Inventory- Lie Scale (L-MMPI Scale, questionnaire test), 2) do not consume alcohol, 3) do not smoke, 4) do not suffer from diabetes mellitus, degenerative diseases, or other chronic diseases, 5) do not have a history of treatment of organic mental disorder, 6) willing to participate in this study. The research subjects will be excluded if the blood sample is damaged, and subjects withdraw from the study. The sample size is 43 people.

This research has received approval from the Ethics Committee of the Faculty of Medicine, University of North Sumatra.

Paramedics who participated as a sample in the study with the inclusion and exclusion criteria were given informed consent, then filled out the form L-MMPI questionnaire then tabulated. If L-MMPI questionnaire passed, patients then filled out questionnaires IQCODE. Then blood was drawn from the median cubital vein about 3ml to measure the estradiol serum levels. The blood sample was sent to a clinical laboratory Prodia (accredited) in the city of Medan. Then the data were tabulated and analyzed statistically.

Data were analyzed using descriptive and analytical analysis. Kruskal Wallis is used to determine differences in serum estradiol levels based on the variables studied (> 2 variables) in the data that are not normally distributed. Correlation test Spearman is used to determine the relationship between serum estradiol levels with changes in cognitive function research subjects. Confidence intervals of 95% and p <0.05 were considered statistically significant.

Results

In Table 1 it was found that all the study subjects were aged under 60 years with the distribution of research subjects aged 40-49 years by 32.6% and aged 50-59 years by 67.4%. Most of the research subjects number of children’s (parity) are children ≥2 (multiparous) is 90.7% then grandemultipara as much as 9.3%.

The majority Body Mass Index of research subjects is overweight 55.8% then normoweight is 27.9% and obesity is 16.3%. The duration of the study subjects experienced menopause was 2 years is 39.5%, then 3 years is 30.25% and ≥ 4 years is 30.25%.

In Table 2, it was found a decline in cognitive function in most of the research subjects. Most are with the moderate decline (24 people, 55.8%) followed by a slight decline (13 people, 30.2%) and severe decline (1 people, 2.3%). But it was also found an increase in cognitive function (improvement) is 3 people (7%) or no changes at all (no change) is 2 people (4.7%).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number (n / %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>14 (32.6)</td>
</tr>
<tr>
<td>50-59</td>
<td>29 (67.4)</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
</tr>
<tr>
<td>Multipara</td>
<td>39 (90.7)</td>
</tr>
<tr>
<td>Grandemultipara</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td></td>
</tr>
<tr>
<td>Normoweight</td>
<td>12 (27.9)</td>
</tr>
<tr>
<td>Overweight</td>
<td>24 (55.8)</td>
</tr>
<tr>
<td>Obese</td>
<td>7 (16.3)</td>
</tr>
<tr>
<td>Long Menopause</td>
<td></td>
</tr>
<tr>
<td>2 years</td>
<td>17 (39.5)</td>
</tr>
<tr>
<td>3 years</td>
<td>13 (30.25)</td>
</tr>
<tr>
<td>≥4 years</td>
<td>13 (30.25)</td>
</tr>
</tbody>
</table>

Table 1 - FREQUENCY DISTRIBUTION RESEARCH SUBJECT.
Table 3 shows that serum estradiol levels increase with weight gain. The research subject with a body mass index (BMI) normoweight had a mean serum estradiol level at 10.15 pg/ml (median) with a minimum-maximum values of 8.99-49.12 pg/ml. Overweight BMI had a mean serum estradiol levels of 37.11 pg/ml (median) with a minimum-maximum values of 9.75-97.21 pg/ml, while the obese BMI had a mean serum estradiol level of 133.06 pg/ml (median) with a minimum-maximum values of 15.13-341.69 pg/ml. "Kruskal Wallis" statistical test is to determine differences between the mean serum estradiol levels based on body mass index gained significant difference (p < 0.05).

Table 4 shows that the serum estradiol level decreases with the duration of menopause experience. The research subject with 2 years of menopause experience had a mean serum estradiol levels of 53.22 pg/ml (median) with a minimum-maximum values of 8.99-341.69 pg/ml. While 3 years of menopause experience had a mean serum estradiol level at 18.16 pg/ml (median) with a minimum-maximum values of 8.99-97.21 pg/ml, whereas with ≥4 years of menopause experience had a mean serum estradiol level at 15:13 pg/ml (median) with a minimum-maximum values of 8.99-160.29 pg/ml. "Kruskal Wallis" statistical test is to determine differences between the mean serum estradiol levels obtained by the duration of menopause was no significant difference (p> 0.05).

Table 5 shows that the serum estradiol level decreases with decline in cognitive function (increased score IQCODE). The decline in cognitive function with severe decline is not included in the Table because there is only one person who experienced it. "Kruskal Wallis" statistical test is to determine differences between the mean serum estradiol levels based on decline in cognitive function as measured by a score IQCODE found significant differences (p <0.05).

Table 6 shows that with the Spearman correlation test there is an association of (negative correlation) decrease in serum estradiol levels in line with increasing score IQCODE (cognitive decline) with a correlation coefficient r = -0.764 and p value <0.001. The Table also shows that the strength of the relationship is strong (r = 0.764).

Discussion

The research shows that all of the subject aged below 60 years with most menopausal for two years, generally have children ≥2 (multiparous), and overweight status (overweight) (Table 1). Fallahzadeh et al. in 2010 reported that menopausal symptoms are associated with
socio-demographic, lifestyle, low socio-economic status, education, employment, higher body mass index, and age (11).

Table 2 showed that with the questionnaire IQCODE, most of the paramedics who menopausal experience cognitive decline (38/88.1% of the study sample 43). Most of the cognitive function impairment is moderate decline (55.8%). Cognitive function is put into the most basic context, is the ability to learn, retain, and memorize information. The slower processing of the information is the earliest sign of cognitive decline. This will trigger a cascade of changes that eventually lead to a decline in memory function, concentration, IQ, and changes in temperament. The hormone has the potential to increase the speed of the brain. Some hormones are associated with neurogenesis, so it is not a coincidence that the speed of the brain increased significantly around age of 13, where the steroid hormone levels increased dramatically (12, 13).

Table 3 showed that the higher the body mass index is the higher the levels of estradiol are which the statistical test found significant differences (p < 0.05). But Table 4 showed that there was no significant difference between estradiol levels and duration of menopause (p > 0.05). After the post-menopausal, ovaries are not functioning anymore, estradiol levels are between 20-30 pg/ml, but still can be found other types of sex steroids with normal levels in the blood. In fact, the ovaries of postmenopausal women still have the ability to synthesize the sex steroids. In addition, certain body tissues, such as fat, uterus, liver, muscle, skin, hair, and even part of the neural system of the bone marrow (bonemarrow) have the ability to aromatize androgen into estrogen (14).

Table 5 showed that estradiol serum levels decrease as the decline in cognitive function (increased score IQCODE), and with a statistical test to determine differences between the mean of estradiol serum levels based on the decline in cognitive function were significant differences (p < 0.05). The correlation test showed there is an association of (negative correlation) decrease in serum estradiol levels in line with increasing score IQCODE with a statistical test to determine differences (p < 0.05) and p value < 0.001 (Table 6).

Effects of estrogen on the neural function involve several mechanisms. Estrogen receptor (ER) is located in vital brain regions involved in cognition. These receptors are expressed in neurons and glial cells at all levels rostral-tails of the brain and spinal cord. The cerebral cortex and hippocampus both contain ERs. Estrogen is thought to improve cognitive function, in part by modulating the activity of acetylcholine in the basal forebrain neurons (this system for the project and the cerebral cortex and the hippocampus is involved in learning and memory) (15-17).

Estrogen works on estrogen receptor (ER) through the mechanism of genomic “traditional” and rapid effect “non-traditional” in the membrane. In the traditional model of the action of estrogen, estrogen binds to ERα or ERβ in the nucleus, so that estrogen dimerizes and binds to elements in response to estrogen (ERE) on DNA, or interacts with a factor of transcription in the target gene, thereby initiating transcription of genes and proteins sensitive to estrogen (18, 19).

Estrogen can also produce a rapid effect of the process that is not dependent on traditional genomic mechanisms. The mechanisms that are not classic, estrogen binds to a membrane-bound receptors, including estrogen receptor bound to the protein-G (GPER) that can activate second messengersystems resulting in rapid response varied from seconds to minutes. While activation of ERα or ERβ nucleus will result in genomic response traditionally, these receptors, or a modified form of the protein also contributes to the rapid effect of estradiol on synapse plasticity. Evidence suggests that there should be a combination of the genomic work as well as those initiated by a membrane that occur simultaneously or continuous estrogen receptor in order to affect transcription (19, 20).

Hogervorst et al. (2004) studied the serum levels estradiol and testosterone and its relationship to cognitive abilities in 145 healthy elderly women. The results showed that the recall verbal was significantly associated (p < 0.01) in the total serum estradiol levels were higher (21).

Bagger (2005) showed that the risk for cognitive impairment in women receiving hormonal therapy for 2 to 3 years at menopause early declines to 64% when examined 5-15 years after hormonal therapy is completed (22).

Estrogen deficiency at menopause increases free radicals and oxidative stress would trigger apoptosis DNA in all cells that are affected by the enzyme catalase. Estrogen deficiency can result in its impact on quality of life, including cognitive function. Siregar MFG et al. (2015) on changes in levels of the enzyme catalase between menopausal women and women of reproductive showed that levels of the enzyme catalase increased in postmenopausal women, which in turn will increase the levels of serum estradiol (23).

Conclusion

IQCODE questionnaires can be considered its use to assess cognitive function in the paramedical personnel who are aged menopausal women.

Suggestions. Results of IQCODE questionnaires showing a change in the form of slight decline, moderate decline, and the severe decline can be considered not to put the paramedical personnel in the working area of patients who require a high concentration, because it can be fatal to the patient.
Relationships of Cognitive Function Based on Informant Cognitive Decline in the elderly with serum estradiol levels on paramedic with menopause age in H. Adam Malik General Hospital

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