Clinical treatment test of Melsmon on menopausal disorder

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I Abstract

The sexual life cycle of a female is divided into 5 stages, which are childhood, adolescence, maturity, menopause and aging.

Among above mentioned stages, menopause is considered as part of aging phenomenon. During this stage, the body faces various phase change symptoms such as whole body tiring, easy to feel tired, fatigue legs, palpitation, losing breath, numb hand and legs etc.

This is call menopausal disorder.

There are still space for debating the definition and cause of menopausal disorder and it is difficult to get consistent opinion. However, during the menopause, the irregular incretion due to rapid decline of ovarian functional has affected autonomic nerve system through diencephalons and it is believed that the malfunction of the autonomic nerve system has caused the menopausal disorder.

Even there is irregular incretion, menopausal disorder is not happened to all the females. Each female also shows various degree of symptom and there are difference in happening timing and the continuity period. This is believed due to it involves various happening factors and becomes more complicated.

Therefore, there are various type of medicines and so called effective therapy methods been applied on menopausal disorder and the effects of them are varied.

This is the character of this sickness. As it is sickness happened due to various complicated causes and therefore it is said that it requires various medicine to cure it, or in another way, it will not be effective if it is not treated with various methods.

The main substance of Melsmon is extracted from placenta and it has 25 years of medical history as a medication used for menopausal disorder (The number of years can be known from the publishing year of p25 of Hieda Kentaro's paper regarding “Medication by Placenta Liquid and Methodology of Neuropathology”). Melsmon is an injection medicine of 1 ampule (2ml) which consists 100mg of placenta extract from frozen fresh placenta by a unique method. It consists of various amino acid, nucleic acid substance, mineral and other recognized substances as well as some unrecognized effective and beneficial substances.

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Although the mechanism of effect is still not fully understood, it has been recognized as effective substance in promoting breathing of cells, activation of reticulum endothelium system, enhancing curing of wound, anti-fatigue etc via animal experiments and etc. All of these biological effects are positive effects onto the biological process. Melsmon has demonstrated "Placenta liquid can drastically improve various symptoms from menopause until aging stage" (p.74 of previous chapters) and it is recognized by Minister of Welfare and been used to treat this symptom. The clinical needs is been continuing as it does not have any side effects.

If menopausal disorder is one of the phenomenon of aging, Melsmon which has activation effect on wide range of biological process can be easily believed to effectively treat various symptoms of menopause.

Therefore it is very interesting to discuss about the effect of Melsmon on menopausal disorder. We had conducted a group comparison between Melsmon and Placebo on the effectiveness, safety and result at various institutes.

The experiment was conducted from March-80 until December-80 with a total period of 10 months.

II Method

1. Patients

The patients are gathered from 7 institutes as shown in Table 1. They are patients diagnosed as menopausal disorder patient (include 12 cases of lacking of ovarian functional) by the medical doctors at those institutes.

However, the following patients are excluded for the experiment.

1) Patient who is still hoping for pregnancy
2) Patient who is suspected having organ diseases
3) Patient who has other complication of heart, lever and kidney
4) Other who is considered not suitable as per doctor recommendation

1 week before the test is conducted, the patients had undergone a observation period and all heart disease patients are excluded.

2. Test medicine

1) Type of medicine

M-1001: 2ml of Melsmon (One ampoule which consists of 100mg of placenta extract)

Table 1 Associate institute
(According to Japanese pronunciation)

Gynecology of Omiya Red Cross Hospital
Gynecology of Government School Union
Social Insurance Central General Hospital gynecology
Gynecology of Sanraku Hospital of Tokyo Academic Profession Association
Tokyo Welfare Annuity Hospital Gynecology
Capital Otsuka Hospital Gynecology
Yamanashi Central Hospital Gynecology

M-1002: Menstrual salt solution 2ml (comparison medicine)

The above 2 medicines are inserted into ampule of same colour, same shape, same amount, and apply the same label. Every box consists of 6 ampules.

2) Distribution of medicine

The distribution of medicine is carried out by controller and Melsmon and Placebo are distributed in the same quantity randomly, which means in each group of medicine distributed to each institute consists of same quantity of Melsmon and Placebo.

3) Supply of medicine

The medicine is supplied as per sequence of distributed medicine No.

The medicine is supplied 1 ample each time and 3 times per week, and it is continued to be injected under the skin in 2 weeks time for 6 ampoules

4) Combined medicine

Unless it is necessary, combined medicine shall not be applied. In case it is necessary, the responsible doctor should record it accordingly.

3. Overall judgment

1) Investigation item before starting the test

Before starting the test, record the height, weight, age, marriage, occupation, diagnosis, severity, date of happening, symptom, history, main complain, initial medicine, period and delivery condition, previous records, combined sickness, general clinical inspection etc.

2) Check sheet

Before the test, the patients are asked to fill-in the check sheet as shown in Diagram 1 in order to know whether there is any complains and what is the degree of it. They will be asked to fill in the same questionnaire during 4th supply and 2 weeks after the supply.

The content of the check sheet before the test, during the 4th supply and after 2 weeks shall then be confirmed by the respective doctor and then summarized into Symptom Evaluation Sheet as shown in Diagram 2.

Diagram 1 Self-aware Symptom Survey

During 1st Check-up

Date (Day Month Year)
Name ( )

The purpose of the survey is to understand your symptoms better and it is important information for future treatment. Therefore, please mark a circle "O" at each appropriate condition which describe your recent condition. (Please answer all the questions)

		Very	Fairly	Slightly	No
1	Is the head heavy?				
2	Do you feel headache?				
3	Do you hard to fall asleep at night?				
4	Do you awake during sleep and cannot sleep well?				
5	Do you wake up early in the morning?				
6	Do you feel tired easily?				
7	Do you feel lazy to put out your hand to reach things?				
8	Do you feel uncomfortable and helpless?				
9	Do you feel nervous easily even for small incident?				
10	Do you become impatient easily?				
11	Do you feel depressed?				
12	Do you head or face feel hot?				
13	Do you feel dizzy?				
14	Do you always sweating?				
15	Do you feel fast heart beat and also loss breath?				
16	Do you feel that your hands and feet are cold?				
17	Do you worry because of no appetite?				
18	Do you feel like vomiting?				
19	Does your stomach always feel full?				
20	Do you have diarrhea problem?				
21	Do you have constipation problem?				
22	Do you have stiff neck?				
23	Do you have stiff shoulder?				
24	Do you feel any pain at your knuckles and joints?				
25	Does your waist feel painful?				
26	Do you always urinate?				
27	Do you eyes become tired easily and feel painful?				

Diagram 2 Symptoms Evaluation Sheet

3: Symptom is severe (++) , 2: Middle (+) , 1: Mild (±) , 0: Nil (-)

		Before M/D	2nd M/D	3rd M/D	4th M/D	5th M/D	6th M/D	2 week later	Improvement rate	
Medicine used									0Wk →4th	0Wk →2Wk
Mental symptoms	Head heavy	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Headache	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Difficult to sleep	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Shallow sleep	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Early wake	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Easy tired	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Laziness	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Uncomforted	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Nervous	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Impatient	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Depressed	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
Subtotal		Pt			Pt			Pt	%	%
	Feel heat	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Dizzy	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Sweating	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Fast beat / Loss breath	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Cold	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	No appetite	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Vomiting	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Stomach full	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Diarrhea	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Constipation	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Stiff neck	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Stiff shoulder	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Joint pain	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Waist pain	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Urinating	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
	Fatigue eyes	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0	3 2 1 0		
Subtotal		Pt			Pt			Pt	%	%
Total		Pt			Pt			Pt	%	%

3) Evaluation of symptom

Regarding the physical symptom and mental symptom, fill in the score (number) of each symptom of before test, before injection of 2nd, 3rd, 4th, 5th and 6th time and 2 weeks after supplied based on the following standard.

3: The symptom is severe (almost cannot work) (++)

2: The symptom is medium level (slightly affecting the work) (+)

1: The symptom is mild (Almost can work like normal) (±)

0: There is no symptom (-)

4) Overall evaluation

The respective doctor shall evaluate based on patient Subjective Symptoms Survey Sheet and check-up. Then he will carry out overall evaluation by the completed Symptom Evaluation Sheet. The effectiveness, safety and usefulness of after 4th supply and after 2 week shall be compared with the condition of before test and it shall be evaluated based on the following evaluation method.

a) Calculate the improvement rate of symptom at after 4th supply and 2 weeks after test based on the following equation.

$$\text{Improvement Rate} = \frac{(\text{Total score before supplying}) - (\text{Total score after supplying})}{\text{Total score before supplying}} \times 100$$

b) The effectiveness shall be judged by responsible doctor according to improvement rate after 2 week from the calculation a) based on the following standard

Very effective: The improvement rate is above 70%

Effective: The improvement rate is above 50% and below 70%

Slightly effective: The improvement rate is above 30% and below 50%

Not effective: The improvement rate is above 0% and below 30%

Getting worse: The improvement rate is below 0%

c) Safety is judged by responsible doctor based on the following 4 levels, “Totally no side effect”, “Mild side effect and continue treatment”, “Require appropriate treatment for the side effect” and “Severe side effect and require to stop supply”

d) Usefulness is judged by responsible doctor based on the following 5 levels, “Very useful”, “Useful”, “Quite useful”, “Hardly to say” and “Not advisable” with the consideration of both effectiveness and usefulness

5) Side effect

The side effect will be observed at every check-up

If there is side effect, the happening incident shall be recorded (happening date and time, severity, treatment etc). In case of details recording is necessary, record it in the Remark column.

The doctor shall then judge whether it is appropriate to continue the test treatment

6) General clinical inspection

Before and after (2 week after supply) injection of medicine, red blood count, white blood count , hemoglobin, hematocrit value, GOT, GPT, bilirubin, urine sugar level, urine protein, blood pressure and pulse are measured.

If there is abnormality found during the inspection after completion of supply, investigation shall be conducted and documented.

7) Stop supply of medicine

During the test, if the responsible doctor judges that it is impossible to continue the test due to worsen of symptom or side effect, the supply of medicine will be stopped.

If the test is stopped, the reason of stop and incident must be recorded in the case card.

In case of the supply is stopped due to severe side effect, the responsible doctor must report to controller immediately.

8) Drop-out standard

In any of the following cases, it shall be considered drop-out

a) The supply does not reach 2/3 of the prescription

b) The data recording is obviously insufficient

c) Test is terminated due to side effect and worsen of symptom

However, cases of drop-out due to side effect should be considered to be added into safety check item and cased of drop-out due to symptom worsening should be considered to be added into usefulness check item if deemed necessary.

d) Other, it is decided to be dropped-out based on meeting and discussion

4. Regulation of exclusion from analysis

The following cases have been excluded from the statistical analysis.

Table 2 No. of sickness case and no. of analysis exclusion

		Melsmon	Placebo	Total	
Total of sickness case		34 (53.1)	30 (46.9)	64 (100)	
No. of analysis exclusion		3 (4.7)	6 (9.4)	9 (14.1)	$\chi 2=0.852$ N.S.
Actual analysis cases		31 (48.4)	24 (37.5)	55 (85.9)	
Reason of exclusion	Do not come to hospital check-up	3	5	8	
	Below supply prescription	0	1	1	

Table 3 Age distribution of patient

Age (year old)	Melsmon	Placebo	Total	
30 ~ 39	4 (12.9)	4 (16.7)	8 (14.5)	
40 ~ 49	22 (71.0)	16 (66.6)	38 (69.1)	$\chi 2=0.170$ N.S.
50 ~	5 (16.1)	4 (16.7)	9 (16.4)	
Total	31 (100)	24 (100)	55 (100)	
Average	45.3 ± 0.83 *	44.7 ± 1.02 *		

Unit: No. of person ( ): % *S.E.

1) Non-target (refer to II-1)
2) If severe complication happens
3) Drop-out case (refer to II-3-8)

5 Statistical analysis

Melsmon group and Placebo group are been analyzed and compared by $\chi 2$-Test, 2 x C segregation experiment method, exact-test of Fisher and U-test of Mann Whitney.

III Result

1. No. of sickness case

There are total 64 cases accumulated from 7 institutes (**Table 1**) and there are 9 cases been excluded (**Table 2**) based on Regulation of exclusion from analysis (II-4), statistical analysis is carried out on the remaining 55 cases.

There is no significant difference to show that Placebo group has more exclusion cases than Melsmon group in statistical analysis example.

The total of exclusion from analysis of both groups is 14.1% from total cases. This is a common figure in such test treatment and therefore it is not considered as a problem.

2. Background factor

1) Age distribution

Age distribution is as shown in **Table 3**. There is no significant difference shown in between Melsmon group and Placebo group. Besides, there is no significant difference shown in the average age of both groups.

Among the 55 cases used for statistical analysis, 40~49 years old group consist of 69.1% and it is more than half of the cases.

2) Other factor

Other background factors for both Melsmon group and Placebo group which are considered include weight (P>0.05), in-house/external patient (P>0.10), marriage/single (P>0.10), new/existing patient (P>0.10), severity (P>0.10), initial prescription (P>0.10), with/without period (P>0.10), period cycle (P>0.10), any climacteric (P>0.10), no. of delivery (P>0.10) etc and there is no significant difference found between 2 groups.

3. Overall judgment

1) General improvement

Before the test begin, the main complain is as per shown in **Table 4**. The ratio between mental symptom and physical symptom is about 4:5.

Table 4 Main complain when beginning the test

	Symptoms	Very	Fairly	Slightly	Total
Mental symptoms	Head heavy	3	5	18	26
	Headache	3	11	17	31
	Difficult to sleep	1	7	17	25
	Shallow sleep	0	7	18	25
	Early wake	0	9	12	21
	Easy tired	1	22	15	38
	Laziness	0	12	16	28
	Uncomforted	4	5	15	24
	Nervous	3	5	18	26
	Impatient	3	11	18	32
	Depressed	2	7	16	25
Physical Symptoms	Feel heat	2	16	18	36
	Dizzy	2	12	18	32
	Sweating	0	9	12	21
	Fast beat / Loss breath	2	6	23	31
	Cold	3	18	8	29
	No appetite	0	4	11	15
	Vomiting	0	4	18	14
	Stomach full	0	9	18	27
	Diarrhea	0	0	4	4
	Constipation	1	9	14	24
	Stiff neck	6	20	12	38
	Stiff shoulder	6	23	10	39
	Joint pain	1	3	9	13
	Waist pain	2	15	16	33
	Urinating	0	1	11	12
	Fatigue eyes	3	5	15	23

Unit: No. of person

The improvement of symptoms after 4th supply and after 2 weeks is shown in **Table 5**.

At the 4th supply, there are 4 cases of "very effective" in Melsmon group. However, there is no statistical significant difference found between Melsmon group and Placebo group.

After 2 week supply, there is a significant difference found between Melsmon group and Placebo group. The total of "very effective" and "effective" of Melsmon group is 77.4% and for Placebo group is 25.0%. This analysis also shows that there is a great significant difference ($P<0.005$)

2) Improvement of each symptom

The symptoms of menopausal disorder is segregated into mental symptom and physical symptom and the improvement evaluation shall be as followed.

a) Mental symptom

The improvement of mental symptoms after 4th supply and after 2 weeks are shown in **Table 6**.

At the 4th supply, there is already a significant difference found between Melsmon group and Placebo group ($P<0.025$)

After 2 weeks, the significant difference is even more obvious ($P<0.01$). The total of "very effective" and "effective" of Melsmon group is 67.8% and for Placebo group is 25.0%. This analysis also shows that there is a significant statistical difference ($P<0.005$)

b) Physical symptom

The improvement of mental symptoms after 4th supply and after 2 weeks are shown in **Table 7**.

At the 4th supply, there are 12 cases of "very effective" and "effective" in Melsmon group. However, there is no statistical significant difference found.

After 2 weeks, there is a high level of significant difference is ($P<0.01$). The total of "very effective" and "effective" of Melsmon group is 77.4% and for Placebo group is 29.2%. This analysis also shows that there is a statistical significant difference ($P<0.005$)

3) Improvement rate based on symptom severity

The judgment of symptom severity is conducted by the responsible doctor before the test and the effect after 2 week is shown in **Table 8**.

There is no significant difference shown in the mild severity between Melsmon group and Placebo group. However for the middle level group, Melsmon group is 89.4% and Placebo group is 8.3% and therefore is shows a high level of statistical significant difference ($\chi 2=20.553$; $P<0.005$). There is only 1 severe case and therefore there is no comment on it.

Table 5-1 Overall improvement rate after 4th supply

	Very effective	Effective	Slightly effective	Not effective	Getting worse	Total	Very effective + Effective
Melsmon	4 (12.9)	8 (25.8)	6 (19.4)	12 (38.7)	1 (3.2)	31 (100)	12 (38.7)
Placebo	0	4 (16.7)	3 (12.5)	13 (54.1)	4 (16.7)	24 (100)	4 (16.7
Total	4	12	9	25	5	55	16

Unit: No. of person ( ): % $\chi 2 = 7.398$ $\chi 2\ (4.0.05) = 9.49$

Table 5-2 Overall improvement rate after 2 weeks supply

	Very effective	Effective	Slightly effective	Not effective	Getting worse	Total	Very effective + Effective
Melsmon	15 (48.4)	9 (29.0)	3 (9.7)	4 (12.9)	0	31 (100)	24 (77.4)
Placebo	4 (16.7)	2 (8.3)	4 (16.7)	13 (54.1)	1 (4.2)	24 (100)	6 (25.0)
Total	19	11	7	17	1	55	30

Unit: No. of person ( ): % $\chi 2 = 16.100$ $\chi 2\ (4.0.05) = 14.86$

Table 6-1 Mental symptom improvement rate after 4th supply

	Very effective	Effective	Slightly effective	Not effective	Getting worse	Total	Very effective + Effective
Melsmon	5 (16.1)	4 (12.9)	8 (25.8)	13 (41.9)	1 (3.3)	31 (100)	9 (29.0)
Placebo	0	2 (8.3)	2 (8.3)	13 (54.2)	7 (29.2)	24 (100)	2 (8.3)
Total	5	6	10	26	8	55	11

Unit: No. of person ( ): % $\chi 2 = 13.084$ $\chi 2\ (4.0.05) = 11.14$

Table 6-2 Mental symptom improvement rate after 2 weeks supply

	Very effective	Effective	Slightly effective	Not effective	Getting worse	Total	Very effective + Effective
Melsmon	12 (38.8)	9 (29.0)	5 (16.1)	5 (16.1)	0	31 (100)	21 (67.8)
Placebo	2 (8.3)	4 (16.7)	4 (16.7)	12 (50.0)	2 (8.3)	24 (100)	6 (25.0)
Total	14	13	9	17	2	55	27

Unit: No. of person ( ): % $\chi 2 = 13.385$ $\chi 2\ (4.0.01) = 13.28$

Table 7-1 Physical symptom improvement rate after 4th supply

	Very effective	Effective	Slightly effective	Not effective	Getting worse	Total	Very effective + Effective
Melsmon	5 (16.1)	7 (22.6)	6 (19.4)	13 (41.9)	0	31 (100)	12 (29.0)
Placebo	1 (4.2)	2 (8.3)	5 (20.8)	15 (62.5)	1 (4.2)	24 (100)	3 (12.5)
Total	6	9	11	28	1	55	15

Unit: No. of person ( ): % $\chi 2 = 5.878$ $\chi 2$ (4.0.05) =9.49

Table 7-2 Physical symptom improvement rate after 2 weeks supply

	Very effective	Effective	Slightly effective	Not effective	Getting worse	Total	Very effective + Effective
Melsmon	13 (41.9)	11 (35.5)	2 (6.5)	5 (16.1)	0	31 (100)	24 (77.4)
Placebo	4 (16.7)	3 (12.5)	8 (33.3)	8 (33.3)	1 (4.2)	24 (100)	7 (29.2)
Total	17	14	10	13	1	55	31

Unit: No. of person ( ): % $\chi 2 = 13.964$ $\chi 2$ (4.0.01) =13.28

Table 8 Physical symptom improvement rate after 2 weeks supply

		Very effective	Effective	Slightly effective	Not effective	Getting worse	Total	Very effective + Effective
Mild Symptom	Melsmon	3 (27.3)	4 (36.3)	2 (18.2)	2 (18.2)	0	11 (100)	7 (63.6)
	Placebo	3 (25.0)	2 (16.7)	2 (16.7)	5 (41.7)	0	12 (100)	5 (41.7)
	Subtotal	6	6	4	7	0	23	
Middle level symptom	Melsmon	12 (63.1)	5 (26.3)	1 (5.3)	1 (5.3)	0	19 (100)	17 (89.4)
	Placebo	1 (8.3)	0	2 (16..7)	8 (66.7)	1 (8.3)	12 (100)	1 (8.3)
	Subtotal	13	5	3	9	1	31	
Severe symptom	Melsmon	0	0	0	1 (100)	0	1 (100)	0
	Placebo	0	0	0	0	0	0	0
	Subtotal	0	0	0	1	0	1	
Total		19	11	7	17	1	55	

Unit: No. of person ( ): %

Table 9 Comparison of side effect

		Melsmon	Placebo	Total
No side effect		28 (90.3)	23 (95.8)	51
Type of side effect	Breast Pain	1	0	1
	Injection part reddish and pain	1	1	2
	Upper abdomen rashes	1	0	1
	Subtotal	3 (9.7)	1 (4.2)	4
Total		31 (100)	24 (100)	55

Unit: No. of person ( ): % $\chi 2 = 0.124$ N.S.

4. Side effect and safety

If there is any complain during supplying the medicine and the responsible doctor judges it as a side effect, the data is as per shown in **Table 9**. There is no significant difference found between Melsmon group and Placebo group.

The judgment of side effect is judged by responsible doctor based on the pre-explained standard. The safety and side effect of the medicine are shown in **Table 10**. There is no significant difference found between Melsmon group and Placebo group. All side effects are also mild side effect and they have not obstruction to the supply of medicine and no special remark is required

5. Clinical inspection value

There is no difference found between Melsmon group and Placebo group for the changes which considered being clinically meaningful at various clinical values before and after supplying the medicine.

6. Usefulness

Usefulness which consists of the effectiveness and safety of medicine is judged by doctor (**Table 11**). Items which are judged "Very useful" and "useful" for Melsmon group is 77.4% and for Placebo group is 25.0%. Therefore it is judged useful for Melsmon group and there is a significant difference between 2 groups ($P<0.005$).

IV Observation

Menopausal disorder is mainly symptoms caused by abnormal incretion and malfunction of autonomic nerve system due to decline of ovary function. Besides, there are also many reports mentioned that ovary lacking disease after surgery due to artificial castration shows difference in incretion condition as well as biological response towards external hormone. However, both show the same symptoms and therefore there are treated in same method.

The Bio-stimulator by the founder of cornea transplant, W.P. Filatov said, Melsmon which developed 25 years ago based on "Organizational Therapy" has treated menopausal disorder as aging phenomenon by activation of cells breathing, activation of reticulum endothelium system, injury curing etc, which is different from traditional medicine that it is treating by activation effect to the wide range of biological process.

From this meaning, it was very interesting to evaluate the effect of Melsmon to menopausal disorder. This clinical experiment has again proved that it has a clinical meaning.

After excluding heart disease patients during the 1 week observation before the test for the clinical experiment, it is to evaluate and compare between Melsmon group and Placebo group on the menopausal disorder patient.

The total of "very effective" rate and "effective" rate of overall symptoms improvement for Melsmon group is 77.4% and for Placebo group is 25.0%. It obviously shows that Melsmon group has a great result and it has a statistical significant difference compared to Placebo group ($P<0.005$).

Then it is segregated into mental symptom and physical symptom for evaluation. Regarding the improvement rate for mental symptoms, the total of "very effective" rate and "effective" rate for Melsmon group is 67.8% and for Placebo group is 25.0%, which means Melsmon group is significantly high ($P<0.005$). The total of "very effective" rate and "effective" rate of physical symptoms improvement for Melsmon group is 77.4% and for Placebo group is 29.2%, which means Melsmon group is significantly high ($P<0.005$). When compared improvement rate between mental symptom and physical symptom for Melsmon group, it seems physical symptom has slightly better improvement but there is no significant difference between both results.

From these result, it is obviously showing that Melsmon is significantly effective to improve the symptoms of menopausal disorder. Besides it is an overall improvement.

When looking into the effectiveness according to severity as per doctor judgment, the total of "very effective" and "effective" for mild symptom is 63.6% for Melsmon group and 41.7% for Placebo group. There is no statistical significant difference between both groups. Regarding middle level severity, Melsmon group is 89.4% and Placebo group is 8.3%. Therefore it has a high degree of significant difference ($P<0.005$). There was only 1 example available for severe symptom and therefore cannot be compared.

Table 10 Side effect and safety

	Totally no side effect	Mild side effect and continue supply	Require treatment for side effect	Stop supply due to side effect	Total
Melsmon	28 (90.3)	3 (9.7)	0	0	31 (100)
Placebo	23 (95.8)	1 (4.2)	0	0	24 (100)
Total	51	4	0	0	55

Unit: No. of person ( ): % $\chi 2 = 0.607$ N.S.

Table 11 Usefulness judgment

	Very useful	Useful	Quite useful	No judgment	Not recommended	Total
Melsmon	12 (38.7)	12 (38.7)	3 (9.7)	4 (12.9)	0	31 (100)
Placebo	4 (16.7)	2 (8.3)	4 (16.7)	3 (54.2)	1 (4.1)	24 (100)
Total	16	14	7	17	1	55

Unit: No. of person ( ): % $\chi 2 = 16.419$ $\chi 2$ (4.0.005) = 14.86

From the above results, it can be observed that middle level symptom of menopausal disorder of Melsmon group demonstrated great improvement and high effectiveness. The fact that it has great effectiveness for middle level symptom which is more common compared to mild symptom patient, it can be said that Melsmon has proven effectiveness.

Regarding side effect, Melsmon group happening rate is 9.7% and there is no significant difference compared to Placebo group. Beside the symptoms of side effect are breast pain, reddish and pain at injection part, rashes at upper abdomen etc which were mild symptoms and therefore the injection was possible to continue the test.

Based on above, it shows that Melsmon has demonstrated great effectiveness on female menopausal disorder. If it is discovered in early stage, it is not necessary to be taken for long period and there is no side effect similar to hormone medication. Therefore it can be considered very useful.

V Conclusion

Effectiveness, safety and usefulness of Melsmon for menopausal disorder (include patient with ovary lacking diseases) under obstetrics and gynecology, is tested through group comparison by multi-facilities and taken as menses saline as Placebo. There are total 55 cases and it is analyzed statistically and the following conclusions are obtained:

1) Symptom improvement after 2 weeks of supply, Melsmon group shows obvious effectiveness for mental symptom, physical symptom and overall effect.
2) Regarding improvement level based on severity of symptom, it is obviously effective for middle level severity.
   There was only one example of severe symptom and therefore cannot be compared.
3) Both groups have only mild side effect and therefore no special remark.

From above, as it is effective to middle level severity symptom and it is safe as it does not have any major side effects, Melsmon can be concluded as very safe and very effective medicine.

Reference Documents

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