

⋮

⋮

2002 12

가

.

가

가

.

,

. 5

,

가

,

,

가

.

.

	.....	i
<b>I.</b>	.....	<b>1</b>
1.	.....	1
2.	.....	3
<b>II.</b>	.....	<b>5</b>
1.	.....	5
2.	.....	6
3.	.....	8
<b>III.</b>	.....	<b>13</b>
1.	.....	13
2.	.....	14
3. 가	.....	14
4.	.....	14
5. Subgroup	.....	18
6. 가	.....	20
7.	.....	21
<b>IV.</b>	.....	<b>22</b>
1.	.....	22
2.	.....	24
3. Subgroup	.....	29
4. 가	.....	35
<b>V.</b>	.....	<b>36</b>
<b>VI.</b>	.....	<b>46</b>
	.....	48
	.....	58
<b>ABSTRACT</b>	.....	<b>60</b>

1.	WHO	-	.....	5
2.			.....	23
3.			.....	25
4. Subgroup		(	).....	32
5. Subgroup		(	).....	33
6.		(	).....	34
7.		(	).....	34

1.		.....	26
2.		.....	27
3.		.....	27
4.		.....	28
5.		.....	28
6.	funnel plot.....		35

가

가

가

가

1966

2002 9

MEDLINE, EMBASE

22

, 32

subgroup

가

-1.01 (95% CI : -

1.17~ -0.85)

-0.64) -0.88 (-1.12~

+0.17 (+0.10~+0.25), +0.26 (+0.19~+0.33), +0.48 (+0.38~+0.58)

Subgroup 15mg 가  
120 가 (p<0.05). 92kg 가  
44 가가 (p<0.05),  
92kg 가가 (p<0.05).

- 가 , 가

가 가 가

가 가

가 .

: , , , ,

# I.

## 1.

가 .

12 25kg/m<sup>2</sup> , 2000

64.3%가 (Flegal , 2002).

가

가 . 1998

26.3%가 25kg/m<sup>2</sup> 가

5 40% .

(Kennel , 1996), (Spector ,1994), (Stampfer ,1992) , (Pi-Sunyer,1993).

가

( ) 1200 ,

( ) 1400

1.2% ( ,2000).

(Young ,1993; Grunstein ,1994), , , , ,



(Zaadsstra, 1993; Lake, 1997) (Pi-Sunyer, 1993), (Lew, 1979; Lee, 1993), 5-15% (Goldstein, 1992) 가 . , , . 가 가 Phentermine-Fenfluramine (phen-fen) 1997 FDA (Gardin, 2000) 가 가 가 (Glazer, 2001; Haddock, 2002). (Sibutramine) 가 2000 FDA 2001 (McNeely, 1998; Nisoli, 2000) (Fujioka, 2000; Dujovne, 2001; Gokcel, 2001).

(McNeely, 1998) 가

가

가

가

(Hazenberg, 2000; Faria, 2002; Zannad

, 2002), McMahon (2002)

가

## 2.

가

(systematic review)

, , , , , , , ,  
, .

## II.

### 1.

가 가 (body mass index : BMI - / <sup>2</sup>)

가 25kg/m<sup>2</sup>, 30kg/m<sup>2</sup>

가 (Hodges, 1994; Ko, 1999) - 23-24.9kg/m<sup>2</sup>, 25-29.9

1, 30 2 (, 2000)( 1).

#### 1. WHO -

		(kg/m <sup>2</sup> )	
		WHO -	
	<18.5	<18.5	
	18.5-24.9	18.5-22.9	
	25.0	23.0	
	25.0-29.9	23.0-24.9	가
1	30.0-34.9	25.0-29.9	
2	35.0-39.9	30.0	
3	40		

## 2.

가.

가, , 가  
10-25%, 가 20-25%  
(Seidell , 1997), 30  
10.5%, 10.9% ( ,2001).  
2000 64.3%가 25kg/ m<sup>2</sup> 30.5%가  
30kg/m<sup>2</sup> (Flegal , 2002).

가  
가 가  
가 . 25kg/m<sup>2</sup> 1995  
1998 14.9%, 26.3% , 2000  
32.6% ( , 2000).

.

20-60 가 가 60  
(Seidell , 1997; Pi-Sunyer, 1998). 40-60  
가 ( , 2000).  
( , 2001).

가 ( , 2000).

가 .

가 . 가  
(Pi-Sunyer, 1998; , 2001).

(Seidell ,1997).

가 1 1kg 가  
(Seidell ,1997).

가 , 가

가 . 가 가

가 . 가

3.

가

3-6

가.

1)

가

1200-1800kcal,

1000-

1500kcal

500kcal

가

. 1 800kcal

( 가 , 2002; , 1999).

2)

가

가

National Heart, and Blood Institute (NHLBI)

30-45 3-5 가

3)

가

가 , , , , , , , ,

3-6

가

가  $25\text{kg/m}^2$

$23\text{kg/m}^2$

( 가 , 2002; NHLBI,



1998).

1)

가)

i. Phentermine

12.2kg

24

(Munro, 1968).

4.8kg

fenfluramine

ii. Phenylpropanolamine

가

가

(Horwitz, 2001).

)

i. Fenfluramine, Dexfenfluramine

가

(Arterburn

,2001; Conolly, 1997).

ii. Fluoxetine

FDA

(Arterburn, 2001; ,1999).

) -

i.

$\beta$ -phenylethylamine 1980

가

가

(Kelly, 1995).

(McNeely, 1998;

Luque, 2002),

$\beta_3$ -

가

(Stock

,1997; McNeely, 1998).

-

가

(Bray, 1996),

가 (James, 2000),

,

가

(Schuh, 2000),

2)

가)

(orlistat)

30%

. - 가 2

4.5% 7.6% 가 ,

가 (Sjostom ,1998).

### III.

#### 1.

가.

1

MEDLINE EMBASE(1966 ~2002 9 ) ,

KMBASE Sibutramine( )

2

· /

, cross-

over

5 mg

가

2.

가 1 (kg), 2  
(kg/m<sup>2</sup>), (mmHg),  
( / )

3. 가

가 가  
(Jadad ,1996)  
가

4.

가. (Effect size)

1)

( - )

(Glass 1976; Hedges & Olkins, 1985).

$$d_i = \frac{X_{ti} - X_{ci}}{S_{pi}} \quad \text{-----} \quad (1)$$

$$\text{Var}(d_i) = \frac{n_{ti} + n_{ci}}{n_{ti} \cdot n_{ci}} + \frac{d_i^2}{2(n_{ti} + n_{ci})} \quad \text{-----} \quad (2)$$

$$S_{pi}^2 = \frac{(n_{ti} - 1)S_{ti}^2 + (n_{ci} - 1)S_{ci}^2}{n_{ti} + n_{ci} - 2} \quad \text{-----} \quad (3)$$

$d_i : i$  ( )

$\text{Var}(d_i) : d_i$

$n_{ti} : i$  ,  $n_{ci} : i$

$X_{ti} : i$  ,  $X_{ci} : i$

$S_{ti} : i$

$S_{ci} : i$

$S_{pi} : i$

2)  $p$

$$t_i = \frac{X_{ti} - X_{ci}}{S_{pi} \sqrt{\frac{1}{n_{ti}} + \frac{1}{n_{ci}}}} \quad (1)$$

$$d_i = t_i \sqrt{\frac{1}{n_{ti}} + \frac{1}{n_{ci}}} \quad \text{-----} \quad (4)$$

,  $p < 0.05, 0.01, 0.001$

$p=0.05, 0.01, 0.001$

3)

$p$

가

$$\Delta = \frac{\sum d_i \omega_i}{\sum \omega_i} \quad \text{-----} \quad (5)$$

$$\text{Var}(\Delta) = \frac{1}{\sum \omega_i} \quad \text{-----} \quad (6)$$

$\Delta$  :

$\text{Var}(\Delta)$  :  $\Delta$

$d_i$  :  $i$

$\omega_i = 1 / \text{Var}(d_i)$  :  $i$

가

가

(homogeneity) ,  
 가 (fixed model  
 effect) , 가 DerSimonian (1986) (random  
 effect model) .  
 .  
 Cohen (1977) “0.8= ”, “0.5=  
 ”, “0.2=



## 5. Subgroup

가.

92kg

34kg/m<sup>2</sup>

44

80%

24

15mg

가 120

가

subgroup

가

t-test

가

가

가

Metawin 2.0

SAS 8.1

## 6. 가

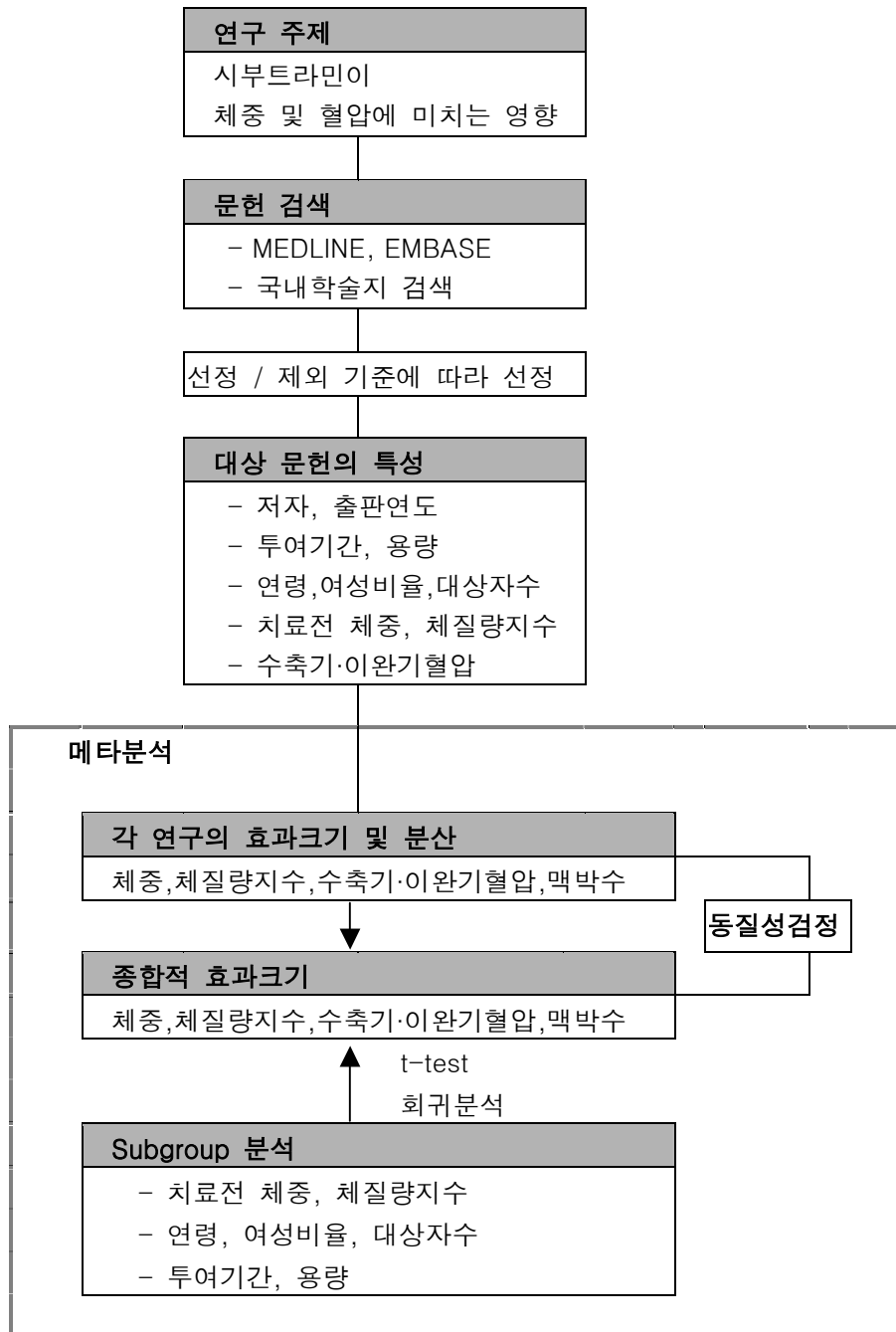
가. Funnel plot

, funnel plot  
(Egger, 2001).

. Fail-safe N

가  
Rosenthal(1979)  
Fail-safe N . 0.05 .

7.



## IV.

### 1.

EMBASE 361 , MEDLINE 175 ,  
34 2 가 가 .  
1 (Hansen ,1998), 가 5  
(Hanotin ,1998; Wadden TA ,2000; 2001; Gokcel ,2002; Rodrigues ,2002), cross-  
over 3 (Rolls ,1998; Fanghanel ,2001; Starling ,2001),  
5 (Bray ,1996; Bach ,1999; Walsh  
,1999; James ,2000; Hansen ,2001) 22  
, 6  
32 .  
22 1 , ,  
, . 1991 1 , 1998-  
1999 5 , 2000-2001 11 , 2002 5 .  
8 52 , 24 8 , 14 .  
5 30mg 가 32  
13 10mg , 19 15mg ( 2).

2.

저자, 연도	기간 (주)	용량 (mg)	대상자 수(명)	연령 (세)	여성 (%)	치료전 체중 (kg)	치료전 BMI (kg/m <sup>2</sup> )	SBP (mmHg)	DBP (mmHg)
1 Weintraub 등, 1991 a	8	5	37	47.09	71.75	.	.	.	.
2 Weintraub 등, 1991 a	8	20	39	45.98	68.31	.	.	.	.
3 Hanotin 등, 1998 a	12	5	115	39.65	90.44	83.66	32.25	.	.
4 Hanotin 등, 1998 b	12	10	118	37.20	86.40	84.50	32.00	.	.
5 Hanotin 등, 1998 c	12	15	121	37.45	85.95	86.20	32.67	.	.
6 Seagle 등, 1998 a	8	10	30	34.35	100	87.50	32.90	.	.
7 Seagle 등, 1998 b	8	30	29	34.55	100	88.05	33.10	.	.
8 Apfelbaum 등, 1999	52	10	159	37.67	74.64	96.68	35.49	.	.
9 Bray 등, 1999 a	24	5	194	43.53	80.86	96.33	34.84	.	.
10 Bray 등, 1999 b	24	10	186	43.49	80.15	95.45	34.53	.	.
11 Bray 등, 1999 c	24	15	185	43.96	82.75	95.30	34.58	.	.
12 Bray 등, 1999 d	24	20	183	43.28	78.76	96.58	34.74	.	.
13 Bray 등, 1999 e	24	30	188	43.54	81.64	96.41	34.90	.	.
14 Hansen 등, 1999	8	15	32	38.87	78.15	100.40	33.91	.	73.12
15 Cuellar 등, 2000	24	15	65	38.53	87.19	87.92	35.85	.	.
16 Fanghanel 등, 2000	24	10	84	38.81	91.65	86.94	35.81	117.28	77.45
17 Finer 등, 2000	12	15	90	53.89	52.43	83.60	30.79	.	.
18 Fujioka 등, 2000	24	20	121	54.26	47.03	98.75	33.95	128.00	79.00
19 Hazenberg 등, 2000	12	10	113	47.91	66.00	95.38	33.66	152.75	97.57
20 McMahan 등, 2000	52	20	211	52.50	60.67	86.70	34.34	133.73	83.97
21 박철영 등, 2001	12	10	90	32.84	78.20	86.40	32.50	123.22	80.46
22 Dujovne 등, 2001	24	20	303	45.45	53.09	100.90	35.30	119.90	77.80
23 Gokcel 등, 2001	24	20	54	48.01	100	95.53	38.42	129.51	86.87
24 Smith 등, 2001 a	52	10	311	41.45	84.47	87.00	32.65	.	.
25 Smith 등, 2001 b	52	15	310	42.29	81.87	87.00	32.54	.	.
26 Wirth 등, 2001	44	15	606	43.40	75.43	98.47	34.80	.	.
27 Faria 등, 2002	24	10	86	48.50	85.50	.	39.45	149.85	92.58
28 McMahan 등, 2002	52	20	120	51.26	57.78	97.39	33.92	129.37	82.55
29 SerranoRios 등, 2002	24	15	134	53.58	67.34	93.10	.	.	.
30 Sramek 등, 2002	12	20	61	52.69	72.11	95.09	33.92	131.80	82.33
31 Zannad 등, 2002 a	24	10	123	39.09	83.07	91.07	34.00	121.11	75.24
32 Zannad 등, 2002 b	24	20	120	37.60	84.00	91.45	33.65	121.40	75.45

2.

-1.01 (95% :-1.17~-0.85) ( 3, 1).	-0.26	-2.14
-0.88 (-1.12~-0.64) ( 3, 2).	-0.28	-1.97
+0.17 (+0.10~+0.25) 가 ( 3, 3).	-0.38	+0.60
+0.26 (+0.19~+0.33) 가 ( 3, 4).	-0.11	+0.73
+0.48 (+0.38~+0.58) 가 ( 3, 5).	+0.18	+1.29

3.

저자	용량 (mg)	체중 변화		BMI 변화		SBP변화		DBP 변화		맥박수 변화	
		ES <sup>†</sup>	Var <sup>‡</sup>	ES	Var	ES	Var	ES	Var	ES	Var
1 Weintraub 등 a	5	-0.68	0.12	.	.	.	.	.	.	.	.
2 Weintraub 등 b	20	-1.48	0.13	.	.	.	.	.	.	.	.
3 Hanotin 등 a	5	-0.26	0.04	.	.	.	.	.	.	+0.35	0.04
4 Hanotin 등 b	10	-0.96	0.04	.	.	.	.	.	.	+0.63	0.04
5 Hanotin 등 c	15	-0.90	0.04	.	.	.	.	.	.	+0.59	0.03
6 Seagle 등 a	10	-1.72	0.18	-1.45	0.17	.	.	.	.	.	.
7 Seagle 등 b	30	-2.14	0.22	-1.97	0.20	.	.	.	.	.	.
8 Apfelbaum 등	10	-0.85	0.03	.	.	.	.	+0.36	0.03	+0.69	0.03
9 Bray 등 a	5	-0.59	0.02	.	.	+0.27	0.02	+0.11	0.02	+0.29	0.02
10 Bray 등 b	10	-1.09	0.02	.	.	+0.34	0.02	+0.36	0.02	+0.58	0.02
11 Bray 등 c	15	-1.41	0.03	.	.	+0.33	0.02	+0.24	0.02	+0.59	0.02
12 Bray 등 d	20	-1.71	0.03	.	.	+0.45	0.02	+0.47	0.02	+0.69	0.02
13 Bray 등 e	30	-1.91	0.03	.	.	+0.39	0.02	+0.34	0.02	+0.51	0.02
14 Hansen 등	15	-1.70	0.17	.	.	.	.	+0.73	0.14	+1.29	0.15
15 Cuellar 등	15	-1.50	0.08	-1.55	0.08	.	.	.	.	.	.
16 Fanghanel 등	10	-0.98	0.05	-0.98	0.05	+0.21	0.05	+0.27	0.05	+0.19	0.05
17 Finer 등	15	-1.18	0.05	-0.67	0.05	-0.04	0.04	-0.04	0.04	+0.55	0.05
18 Fujioka 등	20	-0.36	0.03	.	.	+0.16	0.03	+0.28	0.03	+0.81	0.04
19 Hazenberg 등	10	-0.55	0.04	-0.45	0.04	+0.03	0.04	+0.33	0.04	.	.
20 McMahan 등	20	-0.28	0.02	-0.28	0.02	+0.11	0.02	+0.28	0.02	+0.28	0.02
21 박철영 등	10	-1.33	0.05	.	.	+0.60	0.05	+0.63	0.05	+0.42	0.05
22 Dujovne 등	20	-1.01	0.02	-0.99	0.02	+0.19	0.01	+0.35	0.01	+0.24	0.01
23 Gokcel 등	20	-1.52	0.10	-1.58	0.10	.	.	.	.	.	.
24 Smith 등 a	10	-0.51	0.01	-0.36	0.01	+0.14	0.01	+0.18	0.01	+0.18	0.01
25 Smith 등 b	15	-0.90	0.01	-0.36	0.01	+0.08	0.01	+0.11	0.01	+0.18	0.01
26 Wirth 등	15	-0.67	0.01	.	.	.	.	.	.	.	.
27 Faria 등	10	-1.30	0.06	.	.	-0.38	0.05	+0.43	0.05	+0.46	0.05
28 McMahan 등	20	-0.39	0.04	-0.39	0.04	+0.27	0.04	+0.54	0.04	+0.67	0.04
29 SerranoRios 등	15	-0.67	0.03	-0.79	0.03	-0.15	0.03	.	.	.	.
30 Sramek 등	20	-1.30	0.08	-1.36	0.08	+0.10	0.07	.	.	+0.68	0.07
31 Zannad 등 a	10	-0.93	0.04	-0.96	0.04	-0.11	0.03	-0.11	0.03	+0.62	0.03
32 Zannad 등 b	20	-1.25	0.04	-1.29	0.04	+0.17	0.03	+0.13	0.03	+0.58	0.04
종합적 효과크기 (Δ) (95% 신뢰구간)		-1.01 (-1.17~-0.85)		-0.88 (-1.12~-0.64)		+0.17 (+0.10~+0.25)		+0.26 (+0.19~+0.33)		+0.48 (+0.38~+0.58)	
Fail-safe N		9782.9		1640.9		99.6		340.5		1548.5	

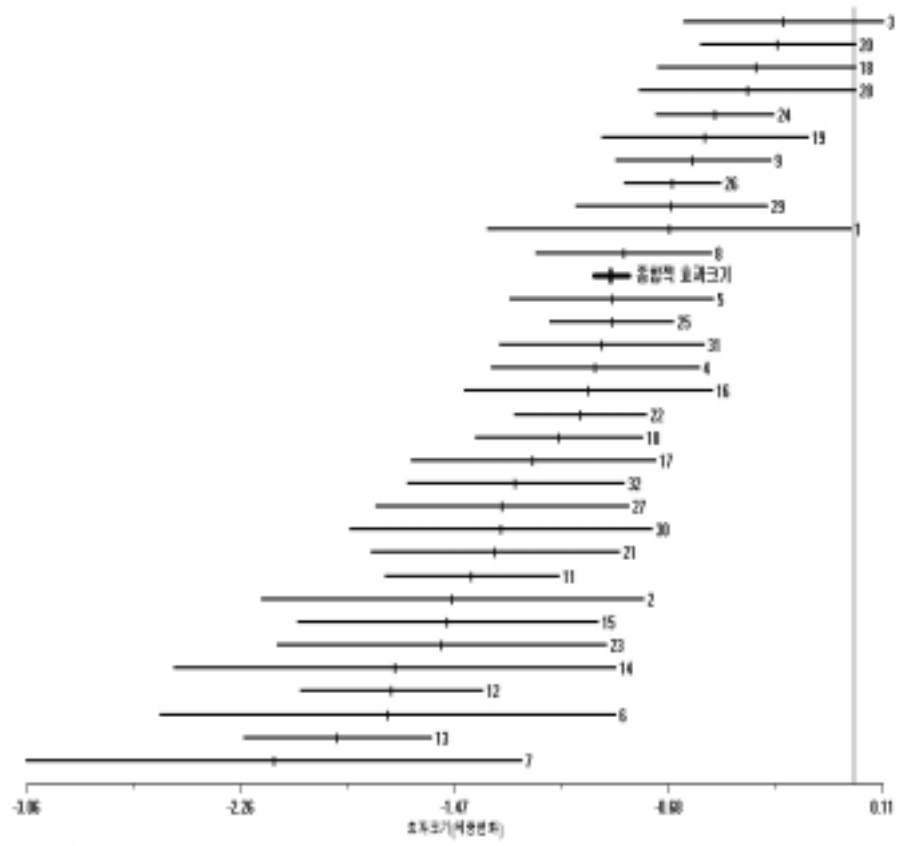
\* 효과크기: 표준화된 평균 변화의 차

† ES : 효과크기

‡ Var: 분산

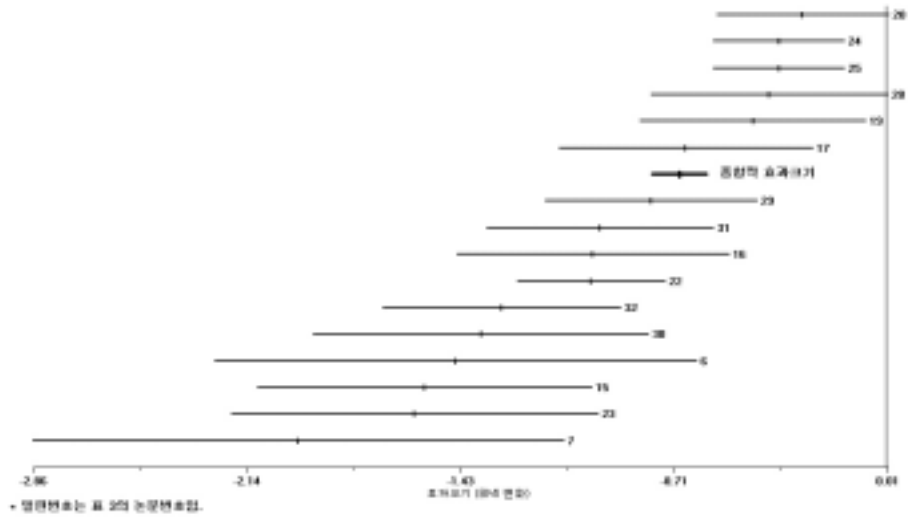
\*\*고혈압군



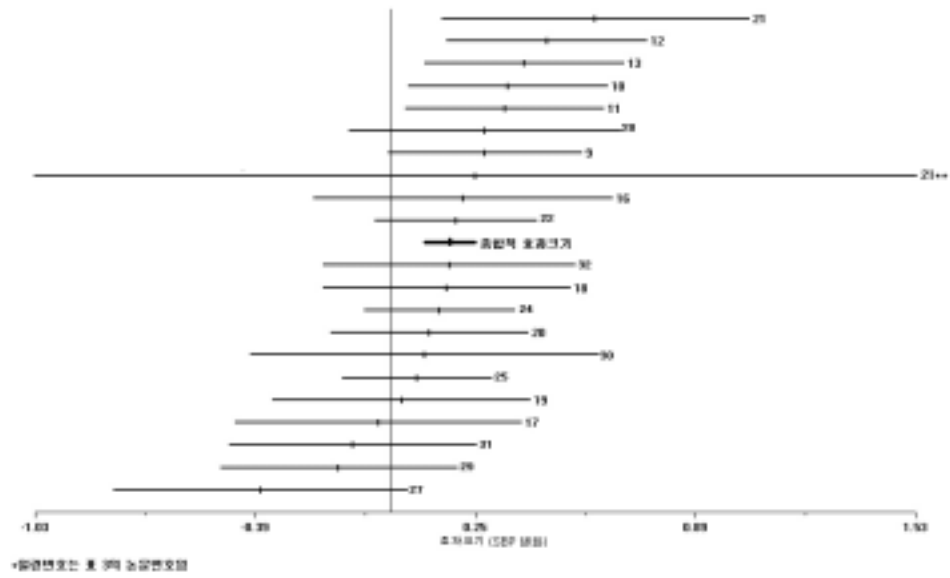


•실선은 0.05의 유의수준을 나타낸다.

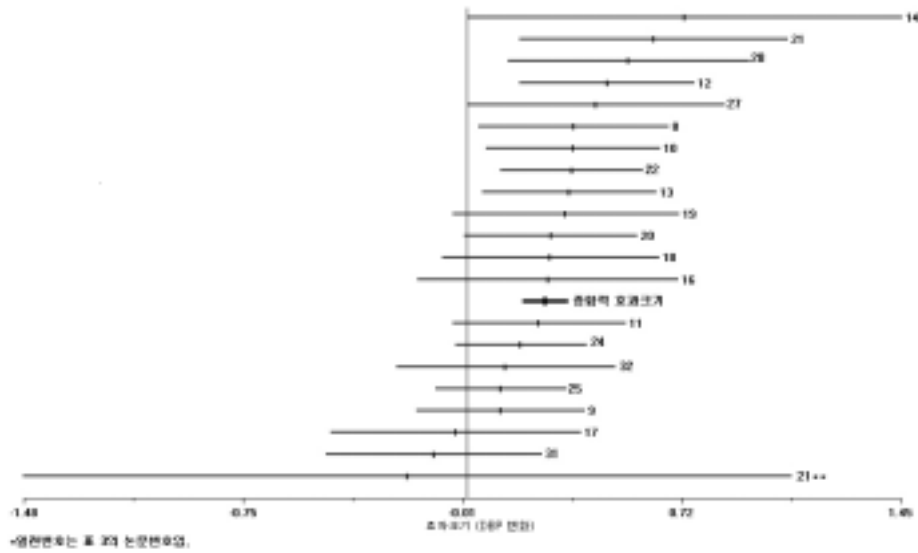
1.



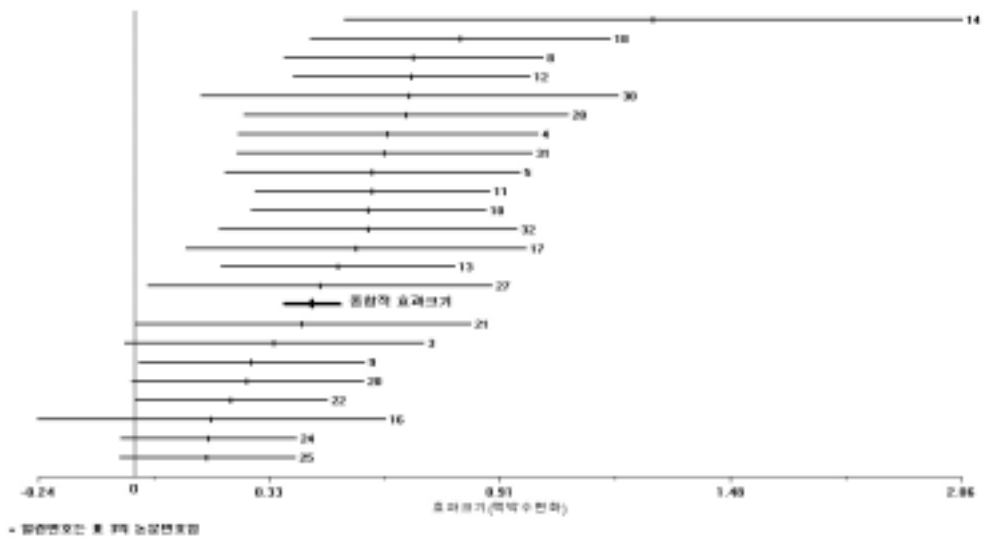
2.



3.



4.



5.

### 3. Subgroup

가.

	92kg	14		-0.81
(-0.97~-0.71)	, 92kg	15	-0.88 (-0.97~-0.78)	
	가	가		(p=0.004,
0.04)	( 4, 5).			

	가 34kg/m <sup>2</sup>	9		
-0.57 (-0.70~-0.43),	34kg/m <sup>2</sup>	6	-0.87 (-1.06~-	
0.68)				
	( 4, 5).			

	44	20		-0.95 (-1.03~-
0.87), 44	12		-0.77 (-0.89~-0.64)	
		44	+0.22 (+0.12 ~+0.33), 44	
+0.06(-0.07~+0.20)	가		가가	
(p=0.01)	( 4, 5).			

80% 15  
-0.81 (-0.91~-0.71), 80% 17 -0.97 (-1.07~-0.88)  
( 4, 5).

24 12 -0.95 (-  
1.11~-0.79), 24 20 -0.88 (-0.95~-0.81)  
( 4, 5).

15mg 13 -0.78 (-0.97~-  
0.89), 15mg 19 -0.97 (-1.05~-0.88) , ,  
가  
( 4, 5).

가 120 8 -  
1.02 (-1.24~-0.80), 120 8 -0.59 (-0.72~-0.47) 가  
가 (p=0.02). 가 120 5  
-0.02 (-0.29~+0.25), 120  
14 +0.19 (+0.11~0.28) 가 가가

( $p=0.05$ ). , ,  
( 4, 5).

15mg 가 120 가  
( $p<0.05$ ). 92kg , 44  
가가 ( $p<0.05$ ), 92kg  
가가 ( $p<0.05$ )( 6, 7).

4. Subgroup

( )

변수	집단	체중 변화(kg)				체질량지수변화(kg/m <sup>2</sup> )			
		n	Δ	95% CI	p	n	Δ	95% CI	p
체중 (kg)	<92	14	-0.81	-0.97 ~ -0.71	0.96	13	-0.61	-0.74 ~ -0.49	0.83
	≥92	15	-0.88	-0.97 ~ -0.78		15	-0.84	-1.04 ~ -0.65	
BMI (kg/m <sup>2</sup> )	<34	15	-0.79	-0.90 ~ -0.68	0.56	9	-0.57	-0.70 ~ -0.43	0.65
	≥34	14	-0.98	-1.07 ~ -0.89		6	-0.87	-1.06 ~ -0.68	
연령 (세)	<44	20	-0.95	-1.03 ~ -0.87	0.14	8	-0.67	-0.82 ~ -0.52	0.27
	≥44	12	-0.77	-0.89 ~ -0.64		8	-0.72	-0.87 ~ -0.56	
여성 비율 (%)	<80	15	-0.81	-0.91 ~ -0.71	0.21	7	-0.68	-0.84 ~ -0.51	0.08
	≥80	17	-0.97	-1.07 ~ -0.88		9	-0.71	-0.85 ~ -0.56	
투여기간 (주)	<24	12	-0.95	-1.11 ~ -0.79	0.3	5	-0.86	-1.19 ~ -0.53	0.29
	≥24	20	-0.88	-0.95 ~ -0.81		11	-0.66	-0.77 ~ -0.56	
용량 (mg)	<15	13	-0.78	-0.97 ~ -0.89	0.13	5	-0.59	-0.81 ~ -0.37	0.54
	≥15	19	-0.97	-1.05 ~ -0.88		11	-0.74	-0.86 ~ -0.62	
대상자수 (명)	<120	15	-1.04	-1.19 ~ -0.90	0.06	8	-1.02	-1.24 ~ -0.80	0.02
	≥120	17	-0.85	-0.93 ~ -0.78		8	-0.59	-0.72 ~ -0.47	

n : 논문수

Δ : 종합적 효과크기

5. Subgroup

( )

변수	집단	수축기혈압변화(mmHg)				이완기혈압변화(mmHg)				맥박수변화(회/분)			
		n	Δ	95% CI	p	n	Δ	95% CI	p	n	Δ	95% CI	p
체중 (kg)	<92	7	+0.09	-0.05 ~ +0.23	0.09	7	+0.14	-0.002 ~ +0.27	0.004	11	+0.35	+0.24 ~ +0.46	0.04
	≥92	11	+0.23	+0.12 ~ +0.34		11	+0.33	+0.22 ~ +0.45		11	+0.54	+0.42 ~ +0.66	
BMI (kg/m <sup>2</sup> )	<34	8	+0.11	-0.02 ~ +0.25	0.46	8	+0.21	+0.07 ~ +0.34	0.99	12	+0.43	+0.32 ~ +0.54	0.3
	≥34	10	+0.22	+0.12 ~ +0.33		11	+0.29	+0.18 ~ +0.39		11	+0.46	+0.35 ~ +0.56	
연령 (세)	<44	10	+0.22	+0.12 ~ +0.33	0.01	12	+0.23	+0.13 ~ +0.32	0.63	16	+0.44	+0.36 ~ +0.53	0.97
	≥44	9	+0.06	-0.07 ~ +0.20		7	+0.32	+0.16 ~ +0.47		7	+0.44	+0.28 ~ +0.61	
여성 비율 (%)	<80	9	+0.15	+0.02 ~ +0.28	0.72	9	+0.35	+0.22 ~ +0.48	0.19	10	+0.52	+0.40 ~ +0.65	0.07
	≥80	10	+0.17	+0.06 ~ +0.28		10	+0.19	+0.09 ~ +0.30		13	+0.40	+0.30 ~ +0.50	
투여 기간 (주)	<24	3	+0.02	-0.51 ~ +0.56	0.78	3	+0.24	-0.33 ~ +0.81	0.93	7	+0.56	+0.36 ~ +0.76	0.14
	≥24	16	+0.18	+0.10 ~ +0.26		16	+0.26	+0.18 ~ +0.34		16	+0.42	+0.34 ~ +0.50	
용량 (mg)	<15	7	+0.13	-0.02 ~ +0.27	0.82	8	+0.22	+0.09 ~ +0.36	0.45	10	+0.41	+0.27 ~ +0.53	0.17
	≥15	12	+0.19	+0.09 ~ +0.29		11	+0.28	+0.17 ~ +0.38		13	+0.47	+0.37 ~ +0.57	
대상자 수(명)	<120	5	-0.02	-0.29 ~ +0.25	0.05	5	+0.28	+0.007 ~ +0.25	0.42	8	+0.49	+0.31 ~ +0.68	0.53
	≥120	14	+0.19	+0.11 ~ +0.28		14	+0.25	+0.17 ~ +0.33		15	+0.43	+0.35 ~ +0.51	

n : 논문수

Δ : 종합적 효과크기



6. ( )

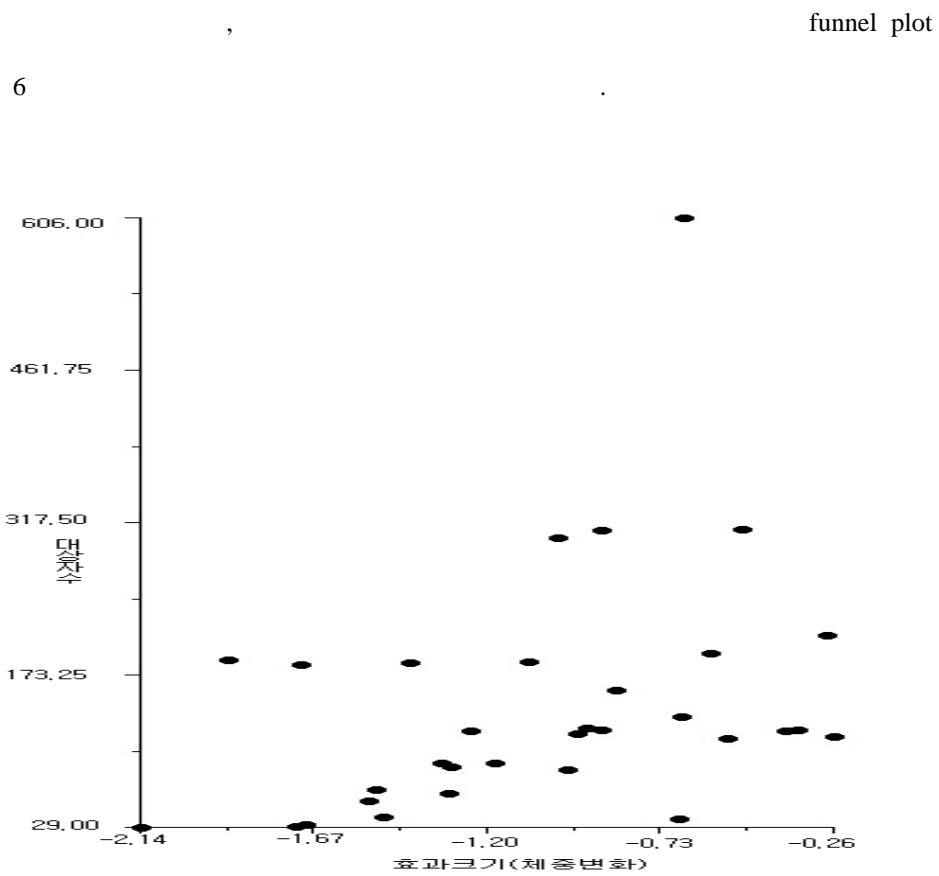
변수	기준집단	체중 변화 (kg)		체질량지수변화 (kg/m <sup>2</sup> )	
		회귀계수	p	회귀계수	p
연령 (세)	<44	0.29	0.14	-0.22	0.80
여성비율 (%)	<80	-0.16	0.38	-0.31	0.72
투여기간 (주)	<24	-0.22	0.42	-0.31	0.58
용량 (mg)	<15	-0.44	0.01	-0.25	0.37
대상자수 (명)	<120	0.57	0.05	0.65	0.18

7. ( )

변수	기준집단	수축기혈압변화 (mmHg)		이완기혈압변화 (mmHg)		맥박수 변화 (회/분)	
		회귀계수	p	회귀계수	p	회귀계수	p
체중 (kg)	<92	0.17	0.01	0.15	0.03	0.19	0.07
연령 (세)	<44	-0.30	0.03	-0.09	0.39	-0.19	0.21
여성비율 (%)	<80	-0.16	0.22	-0.17	0.09	-0.18	0.22
대상자수 (명)	<120	0.03	0.73	0.01	0.92	-0.13	0.30

#### 4. 가

가. Funnel plot



6. funnel plot

. Fail-safe N

, , , , Rosenthal Fail-safe N 3 .



EMBASE

가

(Egger ,2001), Smith (1992)

MEDLINE EMBASE

34%

KMBASE

1

(

, , ), , ,

가

가

(Harris,

2001).

cross-over

(carry-over effect)가

,

가

5mg

20-30mg

5mg

가

(2000) 10mg 4 가  
 15mg 가 2/3  
 10mg 10mg  
 . ,  
 .  
 , LOCF(last  
 observation carried forward : ) LOCF  
 . LOCF  
 가 가  
 가 가  
 . ,  
 . ,  
 . 32 가  
 가 가  
 . 가 12 가  
 .  
 가

22

가



,  
 가  
 ( , 2000; , 2000; Egger ,2001).  
 ,  
 subgroup  
 . , ,  
 ,  
 .  
 가 가  
 (publication bias) . 가  
 가 가  
 . Rosenthal(1979) 가  
 가  
 “file drawer problem” .  
 funnel plot . Funnel plot  
 , 가  
 가 가  
 . 가  
 가  
 (Egger ,2001). fail-safe  
 N , 가





1.01

가

가

가 +0.17 (95% CI: +0.10~+0.25),  
+0.26(+0.19~+0.33), +0.48(+0.38~+0.58)

가 . Cohen (1977)

가 ,

가 .

가 .

가 가

가 10mmHg

가

가 .

James (2000) 10mg 6

20mg 18

43% , 16% 80%

(p<0.001).

4

(1999) 10mg 12 Apfelbaum  
5.2kg , 0.5kg  
가 (p=0.004)  
가 .  
. Gockel (2002)  
2  
15.76mg/dl 124.88mg/dl  
(p<0.001), 28.08mg/dl, LDL 20.92 mg/dl .  
가 .  
subgroup  
, , , , , , ,  
. -1.01  
92kg -0.81, -0.88  
3 (Faria , 2002; Weintraub, 1991  
a,b) 가 .  
t-test p 0.3  
. 15mg , 가  
120 가 . -  
(Bray ,1996) .  
가 ,

가가 . 가 ,  
가 가  
가 가  
가 .  
가 가 .  
가 가 .  
가 .  
1 가  
가  
가 .  
가 .  
가 .  
가 .

가

가

가

가

# VI.

가

가

가

가

1966

2002 9

MEDLINE, EMBASE

22

, 32

subgroup

가

-1.01 (95% CI : -

1.17~ -0.85),

-0.88 (-1.12~ -0.64)

+0.17

(+0.10~+0.25), +0.26 (+0.19~+0.33), +0.48 (+0.38~+0.58)



. , 1999; 42(11): 1106-1111  
 가 . 가 . ; 2002  
 . ; 2000  
 . 2 . ; 2001  
 . ;  
 2000  
 . 가 .  
 2000:25-36  
 . 2002; 45(5): 907-611  
 , , (Reductil®)  
 가 3 .  
 2001;10(4):336-47  
 . Sibutramine. 2001; 10(1): 37-78  
 . '95 . 1997  
 . '98 . 1999  
 . ; 2000

Apfelbaum M, Vague P, Ziegler O, et al. Long-term maintenance of weight loss after a very-  
 low-calorie diet: a randomized blinded trial of the efficacy and tolerability of  
 sibutramine. Am J Med 1999 ;106(2):179-84

Arterburn D, Noel PH. Extracts from "Clinical Evidence". Obesity. BMJ

2001;322(7299):1406-9

Bach DS, Rissanen AM, Mendel CM, et al. Absence of cardiac valve dysfunction in obese patients treated with sibutramine. *Obes Res* 1999 ;7(4):363-9

Bray GA, Blackburn GL, Ferguson JM, et al. Sibutramine produces dose-related weight loss. *Obes Res* 1999;7(2):189-98

Bray GA, Ryan DH, Gordon D, et al. A double-blind randomized placebo-controlled trial of sibutramine. *Obes Res* 1996 ;4(3):263-70

Cohen J. *Statistical Power Analysis for the Behavior Science*. Academic press; 1977

Conolly HM, Crary JL, McGoon MD, et al. Valvular heart disease associated with fenfluramine-phentermine. *N Eng J Med* 1997;337:581-8

Cuellar GE, Ruiz AM, Monsalve MC, et al. Six-month treatment of obesity with sibutramine 15 mg; a double-blind, placebo-controlled monocenter clinical trial in a Hispanic population. *Obes Res* 2000 ;8(1):71-82

DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986 Sep;7(3):177-88

Dujovne CA, Zavoral JH, Rowe E, et al. Effects of sibutramine on body weight and serum lipids: a double-blind, randomized, placebo-controlled study in 322 overweight and obese patients with dyslipidemia. *Am Heart J* 2001 ;142(3):489-97

Egger M, Smith GD, Altman DG. *Systematic reviews in health care: meta-analysis in context*. BMJ books; 2001

Fanghanel G, Cortinas L, Sanchez-Reyes L, et al. A clinical trial of the use of sibutramine for the treatment of patients suffering essential obesity. *Int J Obes Relat Metab Disord*



2000 ;24(2):144-50

Fanghanel G, Cortinas L, Sanchez-Reyes L, et al. Second phase of a double-blind study clinical trial on Sibutramine for the treatment of patients suffering essential obesity: 6 months after treatment cross-over. *Int J Obes Relat Metab Disord* 2001 ;25(5):741-7

Faria AN, Ribeiro Filho FF, Lerario DD, et al. Effects of sibutramine on the treatment of obesity in patients with arterial hypertension. *Arq Bras Cardiol* 2002 ;78(2):172-80

Finer N, Bloom SR, Frost GS, et al. Sibutramine is effective for weight loss and diabetic control in obesity with type 2 diabetes: a randomised, double-blind, placebo-controlled study. *Diabetes Obes Metab* 2000 Apr;2(2):105-12

Flegal KM, Carroll MD, Ogden CL, et al .Prevalence and trends in obesity among US adults, 1999-2000. *JAMA* 2002 ;288(14):1723-7

Fujioka K, Seaton TB, Rowe E, et al. Weight loss with sibutramine improves glycaemic control and other metabolic parameters in obese patients with type 2 diabetes mellitus. *Diabetes Obes Metab* 2000 ;2(3):175-87

Gardin JM, Schumacher D, Constantine G, et al. Valvular abnormalities and cardiovascular status following exposure to dexfenfluramine or phentermine/fenfluramine. *JAMA* 2000;283(13):1703-9

Glass GV. Primary, secondary and meta-analysis of research. *Educational Researcher* 1976;5:3-8

Glazer G. Long-term pharmacotherapy of obesity 2000: a review of efficacy and safety. *Arch Intern Med* 2001;161(15):1814-24

Gokcel A, Gumurdulu Y, Karakose H, et al. Evaluation of the safety and efficacy of

- sibutramine, orlistat and metformin in the treatment of obesity. *Diabetes Obes Metab* 2002;4(1):49-55
- Gokcel A, Karakose H, Ertorer EM, et al. Effects of sibutramine in obese female subjects with type 2 diabetes and poor blood glucose control. *Diabetes Care* 2001;24(11):1957-60
- Goldstein DJ. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992 ;16(6):397-415
- Grunstein RR, Wilcox I. Sleep-disordered breathing and obesity. *Baillieres Clin Endocrinol Metab* 1994 Jul;8(3):601-28
- Haddock CK, Poston WS, Dill PL, et al. Pharmacotherapy for obesity: a quantitative analysis of four decades of published randomized clinical trials. *Int J Obes Relat Metab Disord* 2002 ;26(2):262-73
- Hanotin C, Thomas F, Jones SP, et al. A comparison of sibutramine and dexfenfluramine in the treatment of obesity. *Obes Res* 1998 ;6(4):285-91
- Hanotin C, Thomas F, Jones SP, et al. Efficacy and tolerability of sibutramine in obese patients: a dose-ranging study. *Int J Obes Relat Metab Disord* 1998 ;22(1):32-8
- Hansen D, Astrup A, Toubro S, et al. Predictors of weight loss and maintenance during 2 years of treatment by sibutramine in obesity. Results from the European multi-centre STORM trial. Sibutramine Trial of Obesity Reduction and Maintenance. *Int J Obes Relat Metab Disord* 2001 ;25(4):496-501
- Hansen DL, Toubro S, Stock MJ, et al. The effect of sibutramine on energy expenditure and appetite during chronic treatment without dietary restriction. *Int J Obes Relat Metab Disord* 1999 ;23(10):1016-24

- Hansen DL, Toubro S, Stock MJ, et al. Thermogenic effects of sibutramine in humans. *Am J Clin Nutr* 1998 ;68(6):1180-6
- Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med* 2001;20(3 Suppl):21-35
- Hazenbergh BP. Randomized, double-blind, placebo-controlled, multicenter study of sibutramine in obese hypertensive patients. *Cardiology* 2000;94(3):152-8
- Hedges LV & Olkins I. *Statistical methods of Meta-analysis*. Academic Press; 1985
- Hodge AM, Dowse GK, Gareeboo H, et al. Dramatic increase in the prevalence of obesity in Western Samoa over the 13 years period 1978-1991. *Int J Obes* 1994; 18:419-28
- Horwitz Ri, Brass LM, Kernan WN, et al. Phenylpropanolamine and risk of hemorrhagic stroke: final report of the hemorrhagic stroke project.  
[http://www.fda.gov/ohrms/dockets/ac/00/backgrd/3647b1\\_tab19.doc](http://www.fda.gov/ohrms/dockets/ac/00/backgrd/3647b1_tab19.doc)  
<http://www.nhlbi.nih.gov/about/oei/index.htm>
- Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials* 1996 ;17(1):1-12
- James WP, Astrup A, Finer N, et al. Effect of sibutramine on weight maintenance after weight loss: a randomised trial. STORM Study Group. Sibutramine Trial of Obesity Reduction and Maintenance. *Lancet* 2000;356(9248):2119-25
- Kannel WB, D'Agostine RB, Cobb JL. Effect of weight on cardiovascular disease. *Am J Clin Nutr* 1996; 63(Suppl 4):19S-22S
- Kelly F, James SP, Lee IK. Sibutramine weight loss in depressed patients. *Int J Obes* 1995;19:145

- Ko GTC, Chan JCN, Cockram CS, et al. Prediction of hypertension, diabetes, dyslipidemia or albuminuria using simple anthropometric in Hong kong Chinese. *Int J Obes* 1999;23(ii):1136-42
- Lake JK, Power C, Cole TJ. Women's reproductive health the role of body mass index in early and adult lif. *Int J Obes* 1997;12T:432-8
- Lee IM, Manson JE, Hennekens CH, et al. Body weight and mortality. A 27-year follow-up of middle-aged men. *JAMA* 1993 Dec 15;270(23):2823-8
- Lew EA, Garfinkel L. Variations in mortality by weight among 750,000 men and women *J Chron Dis* 1979;32:563-76
- Luque CA, Rey JA. The discovery and status of sibutramine as an anti-obesity drug. *Eur J Pharmacol* 2002 ;440(2-3):119-28
- McMahon FG, Fujioka K, Singh BN,et al. Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. *Arch Intern Med* 2000 ;24;160(14):2185-91
- McMahon FG, Weinstein SP, Rowe E et al. Sibutramine is safe and effective for weight loss in obese patients whose hypertension is well controlled with angiotensin-converting enzyme inhibitors.*J Hum Hypertens* 2002;16(1):5-11
- McNeely W, Goa KL. Sibutramine. A review of its contribution to the management of obesity. *Drugs* 1998 ;56(6):1093-124
- Munro JF, MacCuish Acn Wilson EM, et al. Comparison of continuous and intermittent anorectic therapy in obesity. *BMJ* 1968; 1:352-4
- National Heart, Lung, and Blood Institute. The Practical Guideline. Identification, evaluation

- and treatment of overweight and obesity in adults. North American Association for the Study of Obesity. 1998
- Nisoli E, Carruba MO. An assessment of the safety and efficacy of sibutramine, an anti-obesity drug with a novel mechanism of action. *Obes Rev* 2000 ;1(2):127-39
- O'Meara S, Riemsma R, Shirran L, et al. The clinical effectiveness and cost-effectiveness of sibutramine in the management of obesity: a technology assessment. *Health Technol Assess* 2002;6(6):1-97
- Pi-Sunyer XF. Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults the evidence report. *Obes Res* 1998; 6:515
- Pi-Sunyer XF. Medical hazards of obesity. *Ann Intern Med.* 1993; 119: 655-60
- Rodrigues AM, Radominski RB, Suplicy Hde L, et al. The cerebrospinal fluid/serum leptin ratio during pharmacological therapy for obesity. *J Clin Endocrinol Metab* 2002 ;87(4):1621-6
- Rolls BJ, Shide DJ, Thorwart ML, et al. Sibutramine reduces food intake in non-dieting women with obesity. *Obes Res* 1998 ;6(1):1-11
- Rosenthal R. The "file drawer problem" and tolerance for null results. *Psychol Bull* 1979;86:638-41
- Schuh LM, Schuster CR, Hopper JA, Mendel CM. Abuse liability assessment of sibutramine, a novel weight control agent. *Psychopharmacology* 2000 ;147(4):339-46
- Seagle HM, Bessesen DH, Hill JO. Effects of sibutramine on resting metabolic rate and weight loss in overweight women. *Obes Res* 1998 ;6(2):115-21
- Seidell JC, Flegal KM. Assessing obesity: classification and epidemiology. *British Medical*

Bulletin 1997;53(2):238-52

Serrano-Rios M, Melchionda N, Moreno-Carretero E. Role of sibutramine in the treatment of obese Type 2 diabetic patients receiving sulphonylurea therapy. *Diabet Med* 2002 ;19(2):119-24

Sjostrom L, Rissanen A, Andersen T, et al; Randomized placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. *Lancet* 352:167-173, 1998

Smith BJ, Darzins PJ, Quinn M, et al. Modern methods of searching the medical literature. *Med J Aust* 1992;157:603-11

Smith IG, Goulder MA. Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. *J Fam Pract* 2001 ;50(6):505-12

Spector TD, Hart DJ, Doyle DV. Incidence and progression of osteoarthritis in women with unilateral knee disease in the general population: the effect of obesity. *Ann Rheum Dis* 1994 Sep;53(9):565-8

Sramek JJ, Leibowitz MT, Weinstein SP, et al. Efficacy and safety of sibutramine for weight loss in obese patients with hypertension well controlled by beta-adrenergic blocking agents: a placebo-controlled, double-blind, randomised trial. *J Hum Hypertens* 2002 ;16(1):13-9

Stampfer MJ, Maclure KM, Colditz GA, et al. Risk of symptomatic gallstones in women with severe obesity. *Am J clin Nutr* 1992;55:652-8

Starling RD, Liu X, Sullivan DH. Influence of sibutramine on energy expenditure in African American women. *Obes Res* 2001 ;9(4):251-6

- Stock MJ. Sibutramine: a review of the pharmacology of a novel anti-obesity agent. *Int J Obes Relat Metab Disord* 1997;21 Suppl 1:S25-9
- Van Gaal LF, Wauters MA, Peiffer FW, et al. Sibutramine and fat distribution: is there a role for pharmacotherapy in abdominal/visceral fat reduction? *Int J Obes Relat Metab Disord* 1998 ;22 Suppl 1:S38-40; discussion S41-2
- Wadden TA, Berkowitz RI, Sarwer DB, et al. Benefits of lifestyle modification in the pharmacologic treatment of obesity: a randomized trial. *Arch Intern Med* 2001;161(2):218-27
- Wadden TA, Berkowitz RI, Womble LG, et al. Effects of sibutramine plus orlistat in obese women following 1 year of treatment by sibutramine alone: a placebo-controlled trial. *Obes Res* 2000;8(6):431-7
- Walsh KM, Leen E, Lean ME. The effect of sibutramine on resting energy expenditure and adrenaline-induced thermogenesis in obese females. *Int J Obes Relat Metab Disord* 1999 ;23(10):1009-15
- Weintraub M, Rubio A, Golik A, et al. Sibutramine in weight control: a dose-ranging, efficacy study. *Clin Pharmacol Ther* 1991;50(3):330-7
- Wirth A, Krause J. Long-term weight loss with sibutramine: a randomized controlled trial. *JAMA* 2001 ;286(11):1331-9
- Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993 29;328(17):1230-5
- Zaadsstra BM, Seidell JC, Van Noord PAH et al. Fat and female fecundity prospective study of body fat distribution on conception rates. *BMJ* 1993;306:484-7

Zannad F, Gille B, Grentzinger A, et al. Effects of sibutramine on ventricular dimensions and heart valves in obese patients during weight reduction. *Am Heart J* 2002 ;144(3):508-15



# Data abstraction form

## 1. Background information

Authors \_\_\_\_\_

Title \_\_\_\_\_

Journal \_\_\_\_\_

Country \_\_\_\_\_

Publication year \_\_\_\_\_

## 2. Subjects (Treatment group/ Control group)

Number of subjects used in analysis (completed trial or LOCF)

% Female

Age

Hypertension patient (%)

Diabetes patient (%)

Baseline body weight (kg)

Baseline BMI ( $\text{kg}/\text{m}^2$ )

Baseline SBP (mmHg)

Baseline DBP (mmHg)

Baseline heart rate (beat/min)

### 3. Intervention

run-in period: \_\_\_\_\_ week

Diet intervention : Yes No

Exercise intervention : Yes No

Dosage: \_\_\_\_\_ mg

Duration: \_\_\_\_\_ week

### 4. Outcome (After - Before) mean, SD, p-value

Weight change \_\_\_\_\_ kg

BMI change \_\_\_\_\_ kg / m<sup>2</sup>

SBP change \_\_\_\_\_ mmHg

DBP change \_\_\_\_\_ mmHg

Heart rate change \_\_\_\_\_ beat/min

## ABSTRACT

### **Effect of sibutramine on weight loss and blood pressure : a meta-analysis of the randomized controlled trials.**

Su-Hyun Kim

Graduate School of

Health Science and Management

Yonsei University

(Directed by Prof. Chung Mo Nam, Ph. D)

**Background:** Obesity, which is associated with high mortality and co-morbidity, is on the increase worldwide including Korea. It should be taken as a major public health problem since even modest weight reduction brings much health benefit.

**Objectives :** Sibutramine is recently developed pharmacologic agents used in the treatment of obesity. It can bring weight loss by suppressing appetite and promoting energy expenditure but it can also raise blood pressure through norepinephrine effect. This study is aimed to provide a comprehensive meta-analysis of randomized controlled trials for the effect of sibutramine on weight loss and blood pressure.

**Methods :** We founded 22 double-blind, randomized, placebo-controlled trials of sibutramine by the MEDLINE,EMBASE(1966-2002.9) and a manual search. A total

number of 22 studies were divided into 32 individual studies by the dosage. The effect sizes for weight, BMI, SBP, DBP and heart rate change were calculated through meta-analysis. We performed subgroup analysis to explore the difference of the effect sizes for initial weight, BMI, age, sex, dosage, duration and sample size.

**Results:** Sibutramine showed a large effect on weight loss compared with the placebo : the overall effect sizes for weight change and BMI change were -1.01 (95% CI : -1.17~ -0.85) and -0.88 (-1.12~ -0.64), while those for SBP, DBP and heart rate change were +0.17(+0.10~+0.25), +0.26 (+0.19~+0.33) and 0.48 (+0.38~+0.58) , respectively. In subgroup analysis, the effect sizes for weight loss were significantly larger when dosage 15 mg and sample size was < 120 ( $p<0.05$ ). The effect sizes for increased SBP were significantly larger when initial weight 92 kg and age < 44 ( $P<0.05$ ) and so were the effect sizes for increased DBP when initial weight 92 kg ( $P<0.05$ ).

**Conclusion:** Sibutramine showed a large effect on weight loss. Since blood pressure and heart rate were increased slightly but significantly, it might be used cautiously in patients with borderline or high blood pressure. Additional studies focused on its effect on blood pressure are needed.

---

**Keywords :** obesity, sibutramine, weight loss, blood pressure, meta-analysis