대한의학회 임상진료지침 교육 워크숍

자료추출 · 근거수준 평가 실습자료

대한의학회
Korean Academy of Medical Sciences

[실습자료] 자료추출

WORKSHEET 자료추출양식

1. 연구의 특성

연구ID						

2. 연속형 변수: 변수명( )

연구ID												

변수명( )

연구ID												

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변수명( )

연구ID												

The effects of caffeine on alertness: a randomized trial

Morrocona MM, Smith A, Jones FH

TRIAL DESIGN

A randomized controlled trial was employed in which participants were randomly allocated to either an experimental group (n=15) or a control group (n=17) using a computer generated random number table. Treatment allocation was concealed in opaque envelopes. Decaffeinated plunger coffee with 100 mg caffeine for the experimental group and decaffeinated plunger coffee for the control group was prepared from 2 single identical packs of coffee with the same taste.

PARTICIPANTS

Adults aged between 18 and 60 years (mean 42 (10.5)) who reported experiencing day time drowsiness (defined by trial personnel as experiencing any of mild-moderately severe fatigue, drowsiness or tiredness during the day, difficulty concentrating or sustaining attention, irritability or low mood).

Participants were all coffee and/or tea drinkers who drank between 1-6 caffeinated beverages each day. All participants were asked to abstain from coffee for the 12 hours prior to the ingestion of experimental or control cup of coffee.

INTERVENTION AND CONTROL

One cup of decaffeinated plunger coffee was prepared for each participant in both groups. For the experimental group, 100 mg caffeine was added to their coffee before ingestion. The administration of coffee took place at 10am.

OUTCOMES

The primary outcome was alertness, measured by a reaction time test. Secondary measures included fatigue and drowsiness using the Line Analogue Rating Scales (LARS), (0 not fatigued/drowsy; 100 extremely fatigued/drowsy), measures of irritability using the Irritability Negative Affectivity Subscale (INAS) of the Workplace Mood Scale (scale from 1-50, higher score is more irritable) and the Beck Irritability Scale (scale from 1-30, higher score is less irritable), a measure of depression, and adverse outcomes. A questionnaire was used as a method for the evaluation of all outcomes, and participants were asked to fill in the questionnaire.

RESULTS

The outcomes were reported in tables.

Table 1 | Primary and secondary outcome measures for caffeinated versus decaffeinated coffee

	Measurement Time Period							
	Pre-ingestion		10 minutes		30 minutes		60 minutes	
	Caffeine (n=15)	Decaf (n=17)	Caffeine (n=15)	Decaf (n=17)	Caffeine (n=15)	Decaf (n=17)	Caffeine (n=15)	Decaf (n=17)
RT	0.1865 (0.0212)	0.1792 (0.0211)	0.1702 (0.0167)	0.1660 (0.0184)	0.1441 (0.0114)	0.1439 (0.0077)	0.1385 (0.0116)	0.1393 (0.0057)
INAS	35 (16.3)	33 (15.3)	19 (15.2)	27 (17.1)	18 (13.2)	31 (16.1)	23 (15.1)	31 (15.2)
BDI-II	9 (2.3)	7 (2.2)	9 (2.4)	7 (2.1)	10 (2.2)	7 (2.1)	9 (2.3)	8 (2.4)
BII	10 (4.2)	11 (4.5)	24 (3.2)	13 (4.2)	21 (3.2)	10 (4.2)	20 (3.4)	10 (4.1)
LARS fatigue	87 (35.8)	83 (37.7)	68 (30.4)	70 (35.6)	38 (28.3)	63 (31.5)	40 (32.0)	67 (36.5)
LARS drowsiness	57 (28.5)	65 (27.6)	46 (25.5)	57 (26.5)	25 (16.7)	58 (28.3)	26 (18.6)	59 (28.6)

Means and Standard Deviations are presented

RT: Reaction Time Test (milliseconds); INAS: Irritability Negative Affectivity Subscale; BDI-II: Beck Depression Inventory II; BII: Beck Irritability Inventory; LARS: Line Analogue Rating Scales (100mm)

Table 2 | Adverse outcome measures for caffeinated versus decaffeinated coffee

	Caffeine (n=15)	Decaf (n=17)
Headache	3	1
Gastrointestinal Irritation	2	0
Sleep Disruption	3	4
Anxiety	1	0
Heart Palpitations	1	0

Caffeine for daytime drowsiness

Norscafe W, Santina X, Neebergen F

TRIAL DESIGN

Each participant was randomly to an experimental group or control group using concealed envelopes. Caffeinated and decaffeinated coffee was not distinguishable by taste or texture.

PARTICIPANTS

132 adults aged between 18 and 65 years (mean 37 (12.5)) who responded to advertisements asking for coffee or tea drinkers who experienced fatigue or tiredness during the day, even after a normal night's sleep. Those with chronic fatigue syndrome were excluded. Participants were all coffee and/or tea drinkers who drank caffeinated beverages daily. All participants were asked to abstain from coffee from 6pm the previous night before the trial took place.

INTERVENTION AND CONTROL

A cup of decaffeinated plunger coffee was prepared for participants in both groups.
For the experimental group, 100 mg of caffeine was added to the coffee before ingestion. The administration of coffee took place in the morning.

OUTCOMES

The primary outcome was alertness, measured by a Reaction Time Test. Secondary measures included a mood questionnaire measuring energetic arousal and tense arousal, psycho physiological measures of arousal, Visual Analogue Scales (VAS) measuring fatigue; and a measure of irritability using the Irritability Negative Affectivity Subscale (INAS) of the Workplace Mood Scale.

Participants were asked to record if they experienced any side effects, in particular headache, and the time from ingestion to headache.

Results were reported in the text of the article. Data on adverse outcomes was also collected.

RESULTS

68 participants were allocated to the caffeine group and 64 participants to the decaffeinated group. Analysis of the irritability measure (INAS) showed a significant decrease in mean scores in irritability in the group administered caffeinated coffee (mean 19, SD 15.5) compared to those administered decaffeinated coffee (mean 36, SD 17.3) 30 minutes after administration (p=0.008). The response was maintained at 60 minutes. Of the adverse outcomes, headache occurred in more than 5 participants in each group (caffeine group 19; decaf group 9). The risk of headache (HR) in the caffeinated group was 0.94 times that of the decaffeinated group with a 95% CI (0.60, 1.48).

Journal of

Drowsiness

Caffeine as a stimulant for entertainment industry employees

Oohlahlazza JE, Sorentina ML, Ribisi G

Accepted 11 October **1998**

1. Trial design

Participants were randomly assigned to the experimental group (n=35) or control group (n=37) using a random number table. Concealed opaque serially numbered envelopes were used. Participants consumed either a cup of decaffeinated plunger coffee with 100 mg caffeine or a cup of decaffeinated plunger coffee with the same taste from the same company.

2. Participants

Adults working in the entertainment industry were asked to participate due to their high use of caffeine. They were aged between 18 and 50 years (mean 29 (12.5)) and reported day time drowsiness (defined by trial personnel as experiencing any of mild-moderately severe fatigue or drowsiness or tiredness during the day, difficulty concentrating or sustaining attention, irritability or low mood). They were all coffee drinkers. All participants were asked to abstain from coffee for the 12 hours prior to the ingestion of the experimental or control cup of coffee.

3. Intervention and control

A cup of decaffeinated plunger coffee was prepared for participants in both groups. For the experimental group, 100 mg caffeine was added to their coffee before ingestion. Administration of caffeinated and decaffeinated coffee took place between 10am and 11am.

4. Outcomes

The primary outcome was alertness measured by a Reaction Time Test. Secondary measures included Visual Analogue Scales measuring fatigue and drowsiness, measures of irritability including the Irritability Negative Affectivity Subscale (INAS) of the Workplace Mood Scale, self-rated level of sleepiness as measured by the C-Esta Sleepiness Scale (CESS) and adverse outcomes. Fatigue, drowsiness, irritability and adverse outcomes were obtained by self-evaluation questionnaire, except for the level of sleepiness (CESS) which was assessed by trial personnel using an interview. The trial personnel were not aware whether participants had been assigned to the experimental or control group.

5. Results

Secondary outcomes were reported in tables.

Table 1: Irritability, tiredness and drowsiness

	Measurement Time Period					
	Pre-ingestion		30 minutes		60 minutes	
	Caffeine (n=35)	Decaf (n=37)	Caffeine (n=35)	Decaf (n=37)	Caffeine (n=35)	Decaf (n=37)
INAS	37 (25.3)	37 (24.3)	20 (22.2)	30 (22.1)	22 (23.2)	33 (24.1)
VAS fatigue	87 (35.8)	83 (37.7)	68 (30.4)	70 (35.6)	38 (28.3)	63 (31.5)
VAS drowsiness	57 (28.5)	65 (27.6)	46 (25.5)	57 (26.5)	25 (16.7)	58 (28.3)

Note: Means and Standard Deviations are presented
INAS: Irritability Negative Affectivity Subscale; VAS: Visual Analogue Rating Scales (100mm)

Table 2: Sleepiness

	C-Esta Sleepiness Scale				
	Alert/ focused	A little sleepy	Sleepy	Very sleepy	Dozing off
Decaf with 100 mg of Caffeine (n=35)	21	6	3	3	2
Decaf (n=37)	19	8	4	2	4

Note: C-ESS: C-Esta Sleepiness Scale – as measured at 30 minutes after ingestion of coffee

Table 3: Adverse outcome measures

	Caffeine (n=35)	Decaf (n=37)
Headache	4	2
Gastrointestinal Irritation	0	0
Sleep Disruption	6	3

Abstracts of the Fourth International Conference on Daytime Drowsiness

To be presented November 17-22, 2004, Sydney, Australia.

1 Caffeine improves attention and irritability in adults

Deliciozza S, Markus T, Philips N

Study Objective: The aim of the study was to investigate the effect of a caffeinated beverage (brewed coffee) compared to a decaffeinated beverage on alertness, fatigue and irritability in adults (>18 years) who regularly used caffeine to eliminate these symptoms. 80 participants were randomized to either a cup of coffee (100 mg) (n=40) or to decaffeinated coffee (n=40) using a computer generated random number sequence.

Results: Results at 30 minutes following ingestion of coffee (at 10 am) indicated that caffeine was useful for reducing fatigue, as measured on a visual analogue scale (caffeine group 55 (15.5), decaffeinated group 70 (16.8)) and irritability measured on the INAS (caffeine group 20 (2.4); decaffeinated group 30 (3.2)). There was no statistically significant effect on alertness at 30 minutes as measured by a reaction time test. Furthermore, there was no statistically significant difference in the level of sleepiness between the two groups as measured on the C-Esta Sleepiness Scale by trial personnel (caffeine group: 19 alert/focused 21 sleepy ; decaffeinated group: 17 alert/focused 23 sleepy). 10 participants in the caffeinated group reported headache and 9 participants in the decaffeinated group reported headache. The risk of headache was lower in the caffeinated group but this was not statistically significant (HR 0.89, 95% CI (0.69, 1.14)).

Conclusions: The authors conclude that caffeinated beverages may be effective in reducing subjective feelings of fatigue and irritability but may not have a significant effect on cognitive correlates.

Vol 447| 31 May **1999**| doi:10.1038/05837

ARTICLES

An investigation of the effects of caffeine

Mama-Kaffa D, Otomune SL, Partridge D

Trial design
One hundred and nineteen participants were assigned into two groups whereby participants born on even days were assigned to the experimental group and participants born on odd days were assigned to the control group. Caffeinated and decaffeinated coffee administered to the participants was identical in appearance, colour and taste.

Participants
Adult volunteers were recruited by advertisements in local newspapers and on radio networks. They were aged between 18 and 58 years (mean 39 (12.5)) and reported daily use of caffeine to alleviate symptoms of fatigue and drowsiness. All participants were asked to abstain from coffee for the 12 hours prior to the ingestion of the experimental or control cup of coffee.

Intervention and control
A cup of coffee was prepared for each participant in both groups. For the experimental group, 100 mg caffeine was added to coffee before ingestion. The ingestion of coffee took place in the morning.

Outcomes
The primary outcome was alertness, measured by a Reaction Time Test. Secondary measures included fatigue, measured by the Visual Analogue Scales, irritability, measured by the Irritability Negative Affectivity Subscale (INAS) of the Workplace Mood Scale and adverse outcomes. Participants were asked to complete a self-reported questionnaire in order to assess their fatigue, irritability and adverse outcomes.

Results
Secondary outcomes were reported in tables.

Table 1 Change scores of secondary outcomes at 30 and 60 minutes

	Measurement Time Period					
	Pre-ingestion		30 minutes		60 minutes	
	Caffeine (n=58)	Decaf (n=61)	Caffeine (n=58)	Decaf (n=61)	Caffeine (n=58)	Decaf (n=61)
INAS	37 (35.3)	37 (34.3)	-17 (9.2)	-7 (5.1)	-15 (10.2)	-4 (5.2)
VAS fatigue	87 (35.8)	83 (37.7)	-19 (15.4)	-13 (35.6)	-25 (18.3)	-18 (31.5)
VAS drowsiness	57 (28.5)	65 (27.6)	-10 (8.5)	-7 (7.5)	-12 (10.7)	-6 (8.3)

Note: Means and Standard Deviations are presented
INAS: Irritability Negative Affectivity Subscale; VAS: Visual Analogue Rating Scales

Table 2 Adverse outcomes

	Caffeine (n=58)	Decaf (n=61)
Headache	12	9
Gastrointestinal Irritation	4	1
Sleep Disruption	7	4
Anxiety	1	0
Heart Palpitations	1	0

Original Article

Volume 3 Issue 10 **2003** doi: 10.1111/j. 2796.2003.01780.x

Randomized controlled trial of the effects of caffeine on alertness and irritability

Piazza-Allerta MI, Certa HL

Trial design: A randomized controlled trial was performed which allocated participants into two groups using concealed opaque envelopes. Treatment coffee was not different from placebo coffee by texture or taste. Intention to treat analysis was not reported (no drop outs).

Participants: Adults aged between 18 and 65 years (mean 42 (10.5)) who reported experiencing day time drowsiness and had scores of over 60 on the VAS measure of drowsiness. All participants were coffee and/or tea drinkers who drank caffeinated beverages every day. All participants were asked to abstain from coffee for the 12 hours prior to the ingestion of experimental or control cup of coffee.

Intervention and control: A cup of decaffeinated plunger coffee was prepared for participants in both groups. For the experimental group, 100 mg of caffeine was added to the coffee before ingestion. The ingestion of coffee took place in the morning.

Outcomes: The primary outcome was of alertness measured by a reaction time test. Secondary measures included a Visual Analogue Scale of fatigue (0 no fatigue; 100 extremely fatigued), irritability measured by the Beck Irritability Scale (scale from 1-30, higher score is less irritable) and adverse outcomes.

Results: Outcomes were reported in tables.

Table 1 Outcome measures for caffeinated versus decaffeinated coffee

	Measurement Time Period							
	Pre-ingestion		10 minutes		30 minutes		60 minutes	
	Caffeine	Decaf	Caffeine	Decaf	Caffeine	Decaf	Caffeine	Decaf
	(n=35)	(n=37)	(n=35)	(n=37)	(n=35)	(n=37)	(n=35)	(n=37)
RT	0.1625 (0.0276)	0.1603 (0.0207)	0.1541 (0.0188)	0.1590 (0.0103)	0.1261 (0.0176)	0.1481 (0.0083)	0.1352 (0.0179)	0.1385 (0.0181)
BII	10 (4.2)	11 (4.5)	24 (3.2)	13 (4.2)	21 (3.2)	10 (4.2)	20 (3.4)	10 (4.1)
VAS fatigue	87 (35.8)	83 (37.7)	68 (30.4)	70 (35.6)	38 (28.3)	63 (31.5)	40 (32.0)	67 (36.5)

Note: Means and Standard Deviations are presented
RT: Reaction Time Test (milliseconds); BII: Beck Irritability Inventory; VAS: Visual Analogue Rating Scales (100mm)

Table 2 Adverse outcome measures for caffeinated versus decaffeinated coffee

	Caffeine (n=35)	Decaf (n=37)
Headache	8	6
Gastrointestinal Irritation	4	1
Sleep Disruption	7	4
Anxiety	1	0
Heart Palpitations	1	0

TREATMENT

The effects of caffeine on alertness in nurses

Kahve-Paradiso Caffeine Research Group 2002

METHODS

	Trial design: Nurses (N=132) were allocated to the two groups by whether they had an odd or even employee number. A cup of decaffeinated plunger coffee with 100 mg caffeine administered to the treatment group was identical to a cup of decaffeinated plunger coffee administered to the control group in terms of taste and texture.
	Participants: Nurses who regularly worked night shifts as well as day shifts (i.e. a mixture) in rural hospitals were asked to participate due to their high use of caffeine. They were aged between 18 and 40 years (mean 23 (12.5)) and reported day time drowsiness (defined by trial personnel as scores of over 60 on a VAS measure of tiredness and drowsiness). Most of the participants were female (female 100, male 32). All participants were caffeine drinkers who drank at least 5 cups of coffee or tea a day (range 5-12) and were asked to abstain from coffee for the 12 hours prior to the ingestion of experimental or control cup of coffee. Participants were all required to have undertaken at least two night shifts within 5 days of the administration of the trial dose of caffeine. They were all working on a day shift that began at 7am.
	Intervention and control: A cup of decaffeinated plunger coffee was prepared for participants in both groups. For the experimental group, 100 mg of caffeine was added to their coffee before ingestion. Administration of coffee was within the first hour of the work shift.
	Outcomes: The primary outcome was alertness measured by a Reaction Time Test. Secondary measures included Visual Analogue Scales measuring fatigue and drowsiness, measures of irritability including the Irritability Negative Affectivity Subscale (INAS) of the Workplace Mood Scale and self-rated level of sleepiness as measured by the C-Esta Sleepiness Scale (CESS). Fatigue, drowsiness and irritability were evaluated by a self-assessment questionnaire. Each participant was interviewed and rated their level of sleepiness (CESS) by an investigator who was not aware whether the participant was allocated to the experimental group or control group.

RESULTS

The outcomes were reported in tables.

Table 1: Reaction time, irritability, tiredness and drowsiness

	Measurement Time Period					
	Pre-ingestion		30 minutes		60 minutes	
	Caffeine (n=65)	Decaf (n=67)	Caffeine (n=65)	Decaf (n=67)	Caffeine (n=65)	Decaf (n=67)
RT	0.1587 (0.0148)	0.1674 (0.0158)	0.1437 (0.0141)	0.1451 (0.0082)	0.1362 (0.0135)	0.1458 (0.0128)
INAS	37 (8.1)	37 (9.3)	20 (9.1)	30 (8.6)	22 (9.1)	33 (9.2)
VAS fatigue	87 (35.8)	83 (37.7)	68 (30.4)	70 (35.6)	38 (28.3)	63 (31.5)
VAS drowsiness	57 (28.5)	65 (27.6)	46 (22.3)	55 (20.8)	25 (16.7)	58 (28.3)

Note: Means and Standard Deviations are presented
RT: Reaction Time Test (milliseconds); INAS: Irritability Negative Affectivity Subscale; VAS: Visual Analogue Sales (0-100mm)

Table 2: Sleepiness

	C-Esta Sleepiness Scale				
	Alert/ focused	A little sleepy	Sleepy	Very sleepy	Dozing off
Decaf with 100 mg of Caffeine (n=65)	39	20	3	3	2
Decaf (n=67)	21	15	13	11	7

Note: C-ESS: C-Esta Sleepiness Scale – as measured at 30 minutes after ingestion of coffee

Caffeine and day time drowsiness in adults

Amore-Coffea JW

June 12 2000

Methods

65 participants who complained of regular day time drowsiness were recruited from a metropolitan area in Melbourne. They were all aged between 20 and 55 years and regularly drank coffee (>2 cups per day). Participants were excluded if they had scores of less than 50 on a VAS measure of fatigue. After consenting to the study they were randomized to two groups. One group received a café latte with 100 mg of caffeine added, and the other received an identical-tasting decaffeinated cafè latte. Outcome measures were fatigue (measured on a VAS scale) and irritability (measured on the Irritability Negative Affectivity Subscale (INAS)). Changes from baseline to 30 minutes post treatment on the VAS fatigue and INAS total scores were compared between treatment groups using an analysis of covariance model that included study treatment group, age group and baseline effects. Time to onset of headache was recorded if participants experienced this side effect.

Results

Participants who drank caffeinated café lattes experienced a statistically significant greater improvement in irritability than those who had decaffeinated cafè lattes [mean difference 15.10 (SE 8.64), $p < 0.01$].

Headaches were reported by 2 out of 31 participants from the caffeine group and 10 out of 34 participants from the decaffeinated group. There was no statistically significant difference in the time to onset of headache (HR 1.04, 95% CI (0.72, 1.51)).

[실습자료] 근거수준 평가

근거수준 **1** 임상질문 정의하기

Ⅰ. 임상질문을 정의하세요

□ 체계적 고찰 제목

난소암환자의 항암치료의 방법으로 복강내 투여와 정맥내 투여의 효과 비교

□ **PICO**로 정의해주세요

- **P**opulation _____
- **I**ntervention _____
- **C**omparator _____
- **O**utcomes _____

□ 최종질문을 완성하세요

근거수준 **2.** 결과의 중요성 평가하기

Ⅰ. 임상판단을 위한 결과값의 나열하기

□ 임상판단을 위한 가장 중요한 결과값을 선택하세요

□ 고려사항 :

- 결과값은 중재의 사용을 선택하기위해서 사용되기도 하며 사용하지 않기도 함
- 각 결과값은 중재에 미치는 영향정도 및 결과의 중요성에 따라 1에서 9점으로 점수화시킬 수 있음

1-3 : 중요하지 않음 4-6 : 중요함, 그러나 의사결정을 위해 사용되지 않음 7-9 : 중요함. 의사결정에 사용될 만큼 중요함

□ 결과값

결과값	중요성(1-9)	근거로 사용여부	
		예	아니오
		예	아니오
		예	아니오
		예	아니오
		예	아니오
		예	아니오
		예	아니오
		예	아니오

근거수준 **3.**

Ⅰ. 결과값에 따라 근거수준을 평가한다

(NO, Serious(-1), very Serious(-2))

결과값	연구수	출판편향	비뚫림위험	비일관성	비직접성	비정확성	근거수준	중요성
		0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )		
		0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )	0 ( ) -1 ( ) -2 ( )		

권고강도 **4.**

Ⅱ. 권고강도를 설정한다

고려항목	판단	이유
Balancing benefits and harms (이득과 위해)	YES( ) NO( )	사망률을 감소시키나, 통증 6명 중 1명(이중 3명 중 1명 극심한 통증) 발열 13명중 1명, 감염 9명 중 1명, 위장관 독성 3명 중 1명으로 위해가 이득에 비해 높음
Resources required(비용,자원 배분)	YES( ) NO( )	카테터 시술과 관련된 기술 및 비용의 소요
Confidence in estimates of effect(추정치의 확실성)	YES( ) NO( )	모든 항목에서 추정치에 대한 근거가 높음
Values and preferences(가치와 선호)	YES( ) NO( ) 명백하지 않음	환자의 가치와 선호도에대한 조사는 명백하지 않음
Acceptability/Feasibility(수용성/적용성)	YES( ) NO( )	모든 환자가 치료를 완료할 수 없음으모 명백하지 않음
권고의 방향	한다( ) 하지 않는다( )	
최종권고강도	STRONG( ) WEAK( )	

근거수준평가를 위한 실습자료

Intraperitoneal chemotherapy for the initial management of primary epithelial ovarian cancer

Background

Ovarian cancer tends to be chemosensitive and confine itself to the surface of the peritoneal cavity for much of its natural history. These features have made it an obvious target for intraperitoneal(IP) chemotherapy. Chemotherapy for ovarian cancer is usually given as an intravenous(IV) infusion repeatedly over five to eight cycles. Intraperitoneal chemotherapy is given by infusion of the chemotherapeutic agent directly into the peritoneal cavity. There are biological reasons why this might increase the anticancer effect and reduce some systemic adverse effects in comparison to IV therapy.

Objectives

To determine if adding a component of the chemotherapy regime into the peritoneal cavity affects overall survival, progression-free survival, quality of life (QOL) and toxicity in the primary treatment of epithelial ovarian cancer.

Search methods

We searched the Gynaecological Cancer Review Group's Specialised Register, the Cochrane Central Register of Controlled Trials(CENTRAL) Issue 2, 2011,MEDLINE (1951 toMay 2011) and EMBASE (1974 toMay 2011).We updated these searches in February 2007, August 2010, May 2011 and September 2015. In addition, we handsearched and cascade searched the major gynaecological oncology journals up to May 2011.

Selection criteria

The analysis was restricted to randomised controlled trials (RCTs) assessing women with a new diagnosis of primary epithelial ovarian cancer, of any FIGO stage, following primary cytoreductive surgery. Standard IV chemotherapy was compared with chemotherapy that included a component of IP administration.

Data collection and analysis

We extracted data on overall survival, disease-free survival, adverse events and QOL and performedmeta-analyses of hazard ratios(HR) for time-to-event variables and relative risks (RR) for dichotomous outcomes using RevMan software.

Main results

Nine randomised trials studied 2119 women receiving primary treatment for ovarian cancer. We considered six trials to be of high quality. Women were less likely to die if they received an IP component to chemotherapy (eight studies, 2026 women; HR = 0.81; 95% confidence interval(CI): 0.72 to 0.90). Intraperitoneal component chemotherapy prolonged the disease-free interval (five studies,1311 women; HR = 0.78; 95% CI: 0.70 to 0.86). There was greater serious toxicity with regard to gastrointestinal effects, pain, fever and infection but less ototoxicity with the IP than the IV route.

Authors' conclusions

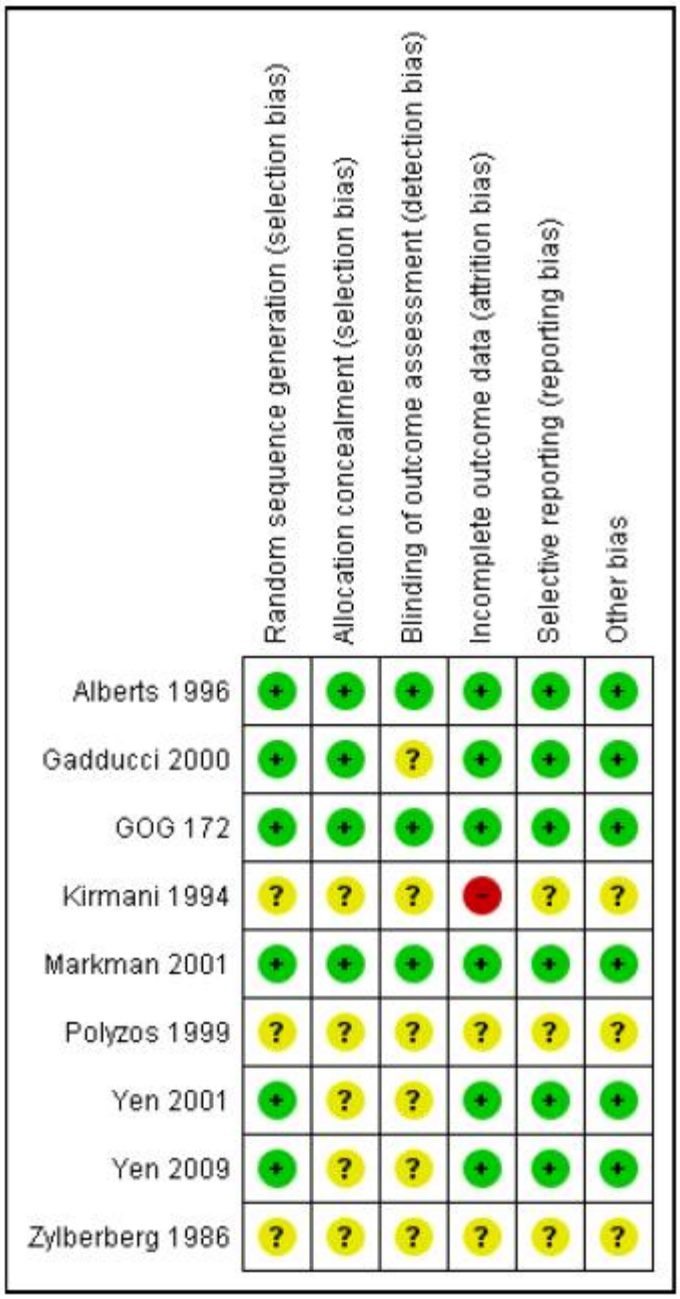
Intraperitoneal chemotherapy increases overall survival and progression-free survival from advanced ovarian cancer. The results of this meta-analysis provide the most

reliable estimates of the relative survival benefits of IP over IV therapy and should be used as part of the decision making process. However, the potential for catheter related complications and toxicity needs to be considered when deciding on the most appropriate treatment for each individual woman. The optimal dose, timing and mechanism of administration cannot be addressed from this meta-analysis. This needs to be addressed in the next phase of clinical trials.

모든 결과변수 목록

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Time to death	8		Hazard ratio (Fixed, 95% CI)	0.81 [0.72, 0.90]
1.1 High quality trials	6		Hazard ratio (Fixed, 95% CI)	0.80 [0.72, 0.90]
1.2 Low quality trials	2		Hazard ratio (Fixed, 95% CI)	1.09 [0.57, 2.11]
2 Time to death restricted to same dose trials	3		Hazard Ratio (Fixed, 95% CI)	0.79 [0.67, 0.92]
2.1 High quality trials	3		Hazard Ratio (Fixed, 95% CI)	0.79 [0.67, 0.92]
3 Time to recurrence	5		Hazard ratio (Fixed, 95% CI)	0.78 [0.70, 0.86]
3.1 High quality trials	4		Hazard ratio (Fixed, 95% CI)	0.77 [0.70, 0.85]
3.2 Low quality trials	1		Hazard ratio (Fixed, 95% CI)	1.26 [0.57, 2.78]
4 Adverse effects - anaemia (G3-4)	5	1110	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.78, 1.24]
4.1 High quality trials	4	1042	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.80, 1.28]
4.2 Low quality trials	1	68	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.14, 1.71]
5 Adverse effects - thrombocytopenia (G3-4)	8	2073	Risk Ratio (M-H, Random, 95% CI)	1.18 [0.43, 3.20]
5.1 High quality trials	6	1915	Risk Ratio (M-H, Random, 95% CI)	1.80 [0.59, 5.49]
5.2 Low quality trials	2	158	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.09, 0.81]
6 Adverse effects - leukopenia (G3-4)	8	2073	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.76, 1.16]
6.1 High quality trials	6	1915	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.80, 1.23]
6.2 Low quality trials	2	158	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.15, 2.19]
7 Adverse effects - renal (G3-4)	5	1339	Risk Ratio (M-H, Random, 95% CI)	1.52 [0.58, 4.00]
7.1 High quality trials	4	1271	Risk Ratio (M-H, Random, 95% CI)	1.81 [0.68, 4.84]
7.2 Low quality trials	1	68	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.01, 4.50]
8 Adverse effects - pulmonary (G3-4)	3	1220	Risk Ratio (M-H, Random, 95% CI)	1.22 [0.18, 8.26]
8.1 High quality trials	3	1220	Risk Ratio (M-H, Random, 95% CI)	1.22 [0.18, 8.26]
9 Adverse effects - cardiovascular (G3-4)	3	1152	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [0.85, 2.45]
9.1 High quality trials	3	1152	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [0.85, 2.45]
10 Adverse effects - fever (G3-4)	5	1797	Risk Ratio (M-H, Fixed, 95% CI)	1.64 [1.13, 2.38]
10.1 High quality trials	5	1797	Risk Ratio (M-H, Fixed, 95% CI)	1.64 [1.13, 2.38]
11 Adverse effects - fatigue (G3-4)	3	1171	Risk Ratio (M-H, Random, 95% CI)	2.32 [1.06, 5.07]
11.1 High quality trials	3	1171	Risk Ratio (M-H, Random, 95% CI)	2.32 [1.06, 5.07]
12 Adverse effects - gastrointestinal (G3-4)	5	1339	Risk Ratio (M-H, Random, 95% CI)	1.70 [1.28, 2.26]
12.1 High quality trials	4	1271	Risk Ratio (M-H, Random, 95% CI)	1.90 [1.57, 2.30]
12.2 Low quality trials	1	68	Risk Ratio (M-H, Random, 95% CI)	0.61 [0.26, 1.47]
13 Adverse effects - infection (G3-4)	3	1171	Risk Ratio (M-H, Fixed, 95% CI)	3.34 [2.06, 5.43]
13.1 High quality trials	3	1171	Risk Ratio (M-H, Fixed, 95% CI)	3.34 [2.06, 5.43]
14 Adverse effects - metabolic (G3-4)	2	873	Risk Ratio (M-H, Fixed, 95% CI)	4.45 [2.72, 7.26]
14.1 High quality trials	2	873	Risk Ratio (M-H, Fixed, 95% CI)	4.45 [2.72, 7.26]

RISK OF BIAS 평가 : 포함된 연구의 질평가



이질성 평가 : 포함된 연구의 동질성

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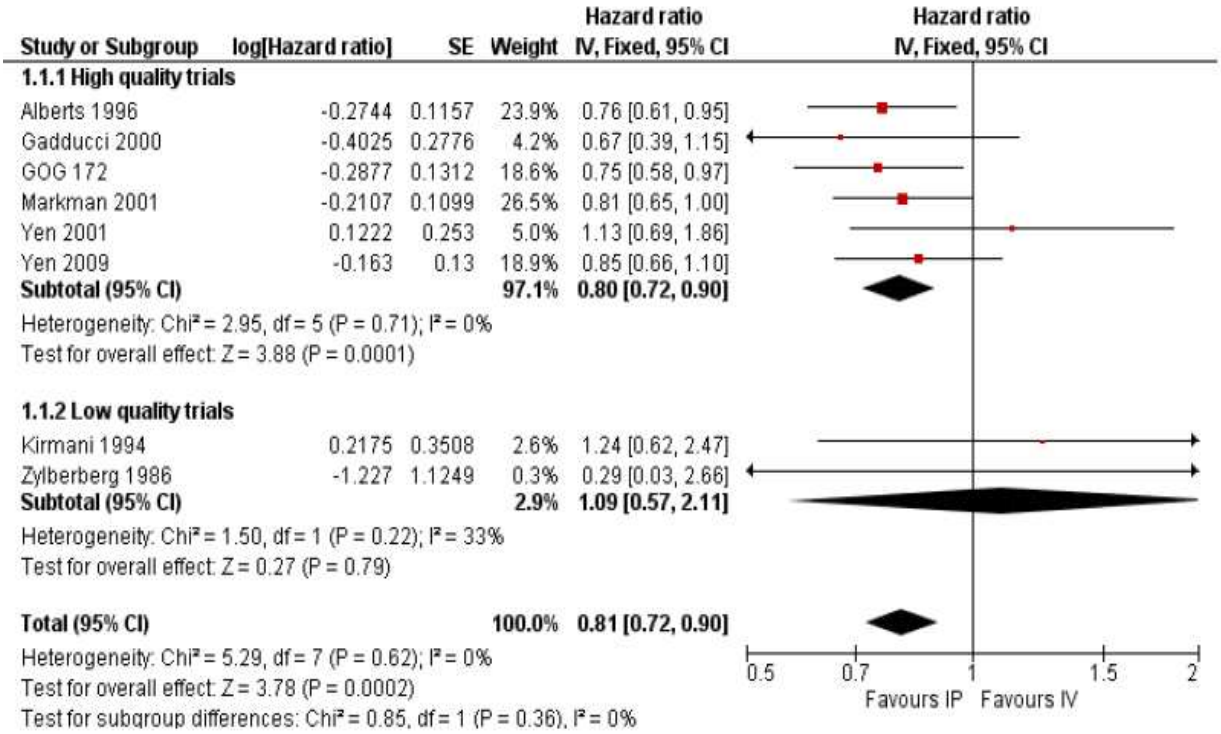

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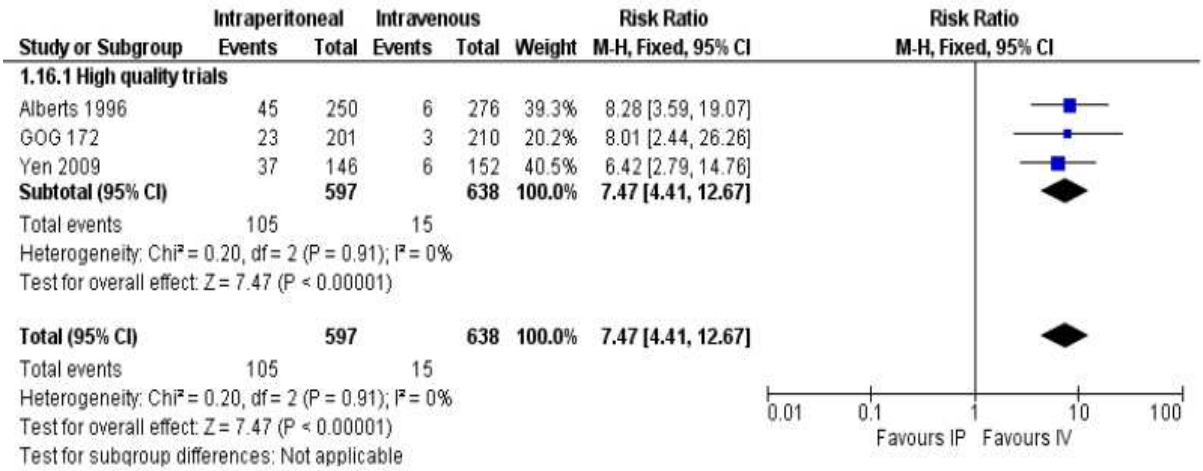
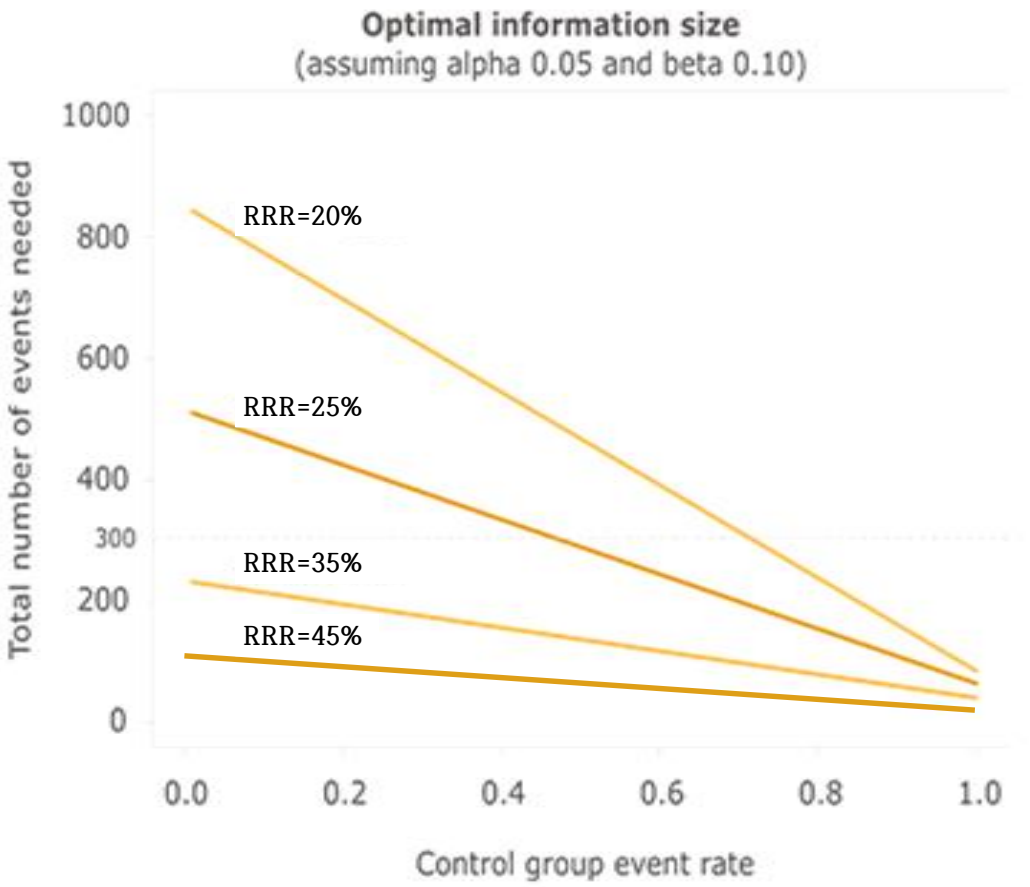


이질성 평가 : 포함된 연구의 동질성

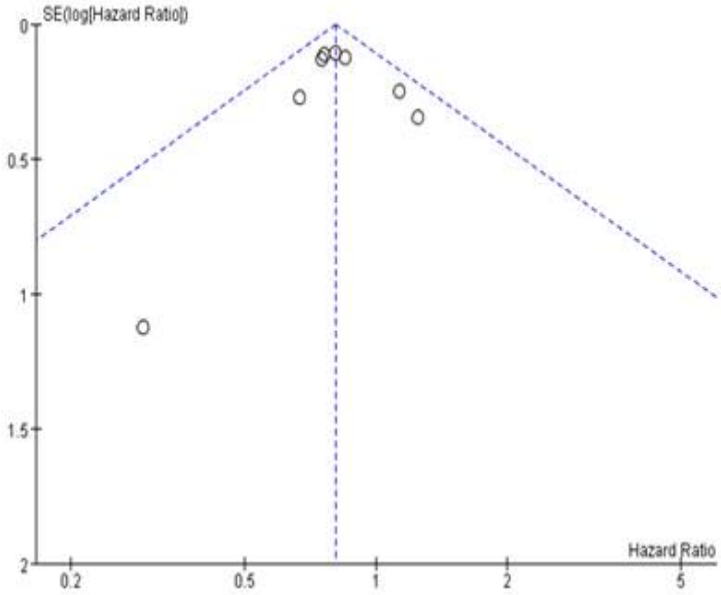
ID	Stage	intervention/comparison	cycles
Alberts 1996	III	Arm 1: IV cyclophosphamide(600mg/m²) + IV cisplatin(100mg/m²). Arm 2: IV cyclophosphamide(600mg/m²) + IP cisplatin(100mg/m²).	every three weeks for a total of six cycles
Gadducci 2000	II~IV	Arm 1: IV epidox 60mg/m² + IV CTX 600mg/m² + IV cisplatin 50mg/m². Arm 2: IV epidox 60mg/m² + IV CTX 600mg/m² + IP cisplatin 50mg/m².	every four weeks for a total of six cycles
GOG 172	III	Arm 1: IV paclitaxel 135mg/m² over 24h(day1) + IV cisplatin75 mg/m²(day2). Arm 2: IV paclitaxel 135mg/m² over 24h(day1) + IP cisplatin 100 mg/m² (day2) +IP paclitaxel 60 mg/m² (day8).	every three weeks for a total of six cycles
Kirmani 1994	IIC~IV	Arm 1: IV cisplatin 100mg/m² + IV cyclophosphamide 600mg/m². Arm 2: IP cisplatin 200mg/m² + IP etoposide 350mg/m².	three weeks for a total of six cycles
Markman 2001	III	Arm 1: IV paclitaxel 135mg/m²(day1) + IV cisplatin 75mg/m²(day2) Arm 2: IV carboplatin(AUC9) for two courses every 28 days, followed 4 weeks later by IV paclitaxel 135mg/m2 over 24 hours(day1) + IP cisplatin 100mg/m2(day2).	every three weeks for a total of six cycles
Yen 2001	III	Arm 1: IV cyclophosphamide 500mg/m² (day1)+ IV adriamycin or epirubicin50mg/m²(day1) + IV cisplatin50mg/m² (day1). Arm 2: IV cyclophosphamide 500mg/m²(day1) + IV adriamycin/epirubicin 50mg/m²(day1) + IP cisplatin100mg/m²(day 1).	every three weeks for a total of six cycles
Yen 2009	III	paclitaxel(day1) + IV cisplatin/carboplatin(day2) paclitaxel(day1) + IP cisplatin/carboplatin(day2)	every 3 weeks for 6 cycles
Zylberberg 1986	III	Arm1: IV adriamycin 35mg x 2 + fluorouracil 750mg x 2 + bleomycin 15mg + cisplatin 100mg + vincaleucoblastine 10mg + ifosfamide 1g x 2 Arm 2: IV adriamycin 20mg x 2 + fluorouracil 500mg x 2 + cisplatin 50mg + vincaleucoblastine 10mg + ifosfamide 1g x 2 + IP bleomycin 15mg + cisplatin 50mg + fluorouracil 500mg + adriamycin 30mg	

정확성 평가 : 포함된 연구의 충분한 사건수 평가



출판편향

사망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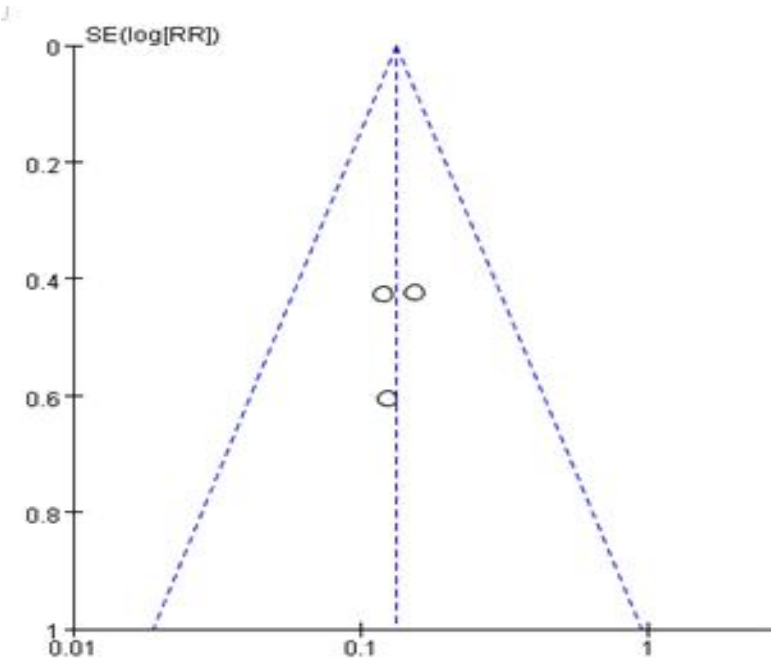
Hazard Ratio

통증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