6. 부록

부록 1. The 2007 Oxford league table of analgesic efficacy (Oxford 2007)

Analgesic	Number of patients in comparison	Percent with at least 50% pain relief	NNT	Lower confidence interval	Higher confidence interval
Etoricoxib 180/240	248	77	**1.5**	1.3	1.7
Etoricoxib 120	500	70	**1.6**	1.5	1.8
Valdecoxib 40	473	73	**1.6**	1.4	1.8
Dipyrone 1000	113	79	**1.6**	1.3	2.2
Ibuprofen 600/800	165	86	**1.7**	1.4	2.3
Valdecoxib 20	204	68	**1.7**	1.4	2.0
Ketorolac 20	69	57	**1.8**	1.4	2.5
Ketorolac 60 (intramuscular)	116	56	**1.8**	1.5	2.3
Diclofenac 100	545	69	**1.8**	1.6	2.1
Piroxicam 40	30	80	**1.9**	1.2	4.3
Celecoxib 400	298	52	**2.1**	1.8	2.5
Paracetamol 1000 + Codeine 60	197	57	**2.2**	1.7	2.9
Oxycodone IR 5 + Paracetamol 500	150	60	**2.2**	1.7	3.2
Bromfenac 25	370	51	**2.2**	1.9	2.6
Rofecoxib 50	675	54	**2.3**	2.0	2.6
Oxycodone IR 15	60	73	**2.3**	1.5	4.9
Aspirin 1200	279	61	**2.4**	1.9	3.2
Bromfenac 50	247	53	**2.4**	2.0	3.3
Dipyrone 500	288	73	**2.4**	1.9	3.2
Ibuprofen 400	5456	55	**2.5**	2.4	2.7
Bromfenac 100	95	62	**2.6**	1.8	4.9
Oxycodone IR 10 + Paracetamol 650	315	66	**2.6**	2.0	3.5
Diclofenac 25	502	53	**2.6**	2.2	3.3
Ketorolac 10	790	50	**2.6**	2.3	3.1
Paracetamol 650 + tramadol 75	679	43	**2.6**	2.3	3.0
Oxycodone IR 10+Paracetamol 1000	83	67	**2.7**	1.7	5.6
Naproxen 400/440	197	51	**2.7**	2.1	4.0
Piroxicam 20	280	63	**2.7**	2.1	3.8
Lumiracoxib 400	370	48	**2.7**	2.2	3.5
Naproxen 500/550	784	52	**2.7**	2.3	3.3
Diclofenac 50	1296	57	**2.7**	2.4	3.1
Ibuprofen 200	3248	48	**2.7**	2.5	2.9
Dextropropoxyphene 130	50	40	**2.8**	1.8	6.5
Paracetamol 650 + tramadol 112	201	60	**2.8**	2.1	4.4
Bromfenac 10	223	39	**2.9**	2.3	4.0
Pethidine 100 (intramuscular)	364	54	**2.9**	2.3	3.9
Tramadol 150	561	48	**2.9**	2.4	3.6
Morphine 10 (intramuscular)	946	50	**2.9**	2.6	3.6
Naproxen 200/220	202	45	**3.4**	2.4	5.8
Ketorolac 30 (intramuscular)	359	53	**3.4**	2.5	4.9
Paracetamol 500	561	61	**3.5**	2.2	13.3
Celecoxib 200	805	40	**3.5**	2.9	4.4
Paracetamol 1500	138	65	**3.7**	2.3	9.5
Ibuprofen 100	495	36	**3.7**	2.9	4.9
Oxycodone IR 5 + Paracetamol 1000	78	55	**3.8**	2.1	20.0
Paracetamol 1000	2759	46	**3.8**	3.4	4.4
Paracetamol 600/650 + Codeine 60	1123	42	**4.2**	3.4	5.3
Paracetamol 650 + Dextropropoxyphene (65 mg hydrochloride or 100 mg napsylate)	963	38	**4.4**	3.5	5.6
Aspirin 600/650	5061	38	**4.4**	4.0	4.9
Paracetamol 600/650	1886	38	**4.6**	3.9	5.5
Ibuprofen 50	316	32	**4.7**	3.3	8.0
Tramadol 100	882	30	**4.8**	3.8	6.1
Tramadol 75	563	32	**5.3**	3.9	8.2
Aspirin 650 + Codeine 60	598	25	**5.3**	4.1	7.4
Oxycodone IR 5 + Paracetamol 325	149	24	**5.5**	3.4	14.0
Ketorolac 10 (intramuscular)	142	48	**5.7**	3.0	53.0
Paracetamol 300 + Codeine 30	379	26	**5.7**	4.0	9.8
Bromfenac 5	138	20	**7.1**	3.9	28.0
Tramadol 50	770	19	**8.3**	6.0	13.0
Codeine 60	1305	15	**16.7**	11.0	48.0
Placebo	>10,000	18	**N/A**	N/A	N/A

부록 2. Acute Coronary Syndrome의 치료효과크기 자료추출 결과

1. Initial management

Antiplatelet therapy	P	I	C	O	ARR	RRR	n	NNT	Utility
Aspirin	unstable angina	aspirin 300mg	placebo	the rate of vascular events(cardiovascular death, non-fatal MI, non-fatal stroke)	5.3%	46.0%	15,828	19	0.7
	acute MI	aspirin 300mg	placebo	the rate of vascular events	3.8%	30.0%	19,288	26	0.7
Combination aspirin and clopidogrel therapy	NSTE-ACS	aspirin 300mg +Clopidogrel 300mg	aspirin	cardiovascular death, stroke, MI	2.1%	20.0%	12,562	48	0.3
	STE-ACS	aspirin 300mg +Clopidogrel 300mg	aspirin	the rate of death, reinfarction, stroke	0.9%	9.0%	45,852	111	0.7
				the rate of death	0.6%	7.0%	45,852	167	0
Glycoprotein IIB/IIIA receptor antagonists	NSTE-ACS	Glycoprotein IIB/IIIA receptor antagonists	placebo	the odds of death or MI at 30days	1.0%	9.0%	31,402	100	0.3

Anticoagulant therapy	P	I	C	O	ARR	RRR	n	NNT	Utility
Unfractionated heprin	NSTE-ACS	Unfractionated heprin(UFH)	placebo	the combined end point of death or MI	2.5%	33.0%	1,353	40	0.3
	STE-ACS	Unfractionated heprin(UFH)	aspirin	the rate of re-infarction	0.3%		33,968	333	0.5
		Unfractionated heprin(UFH)	aspirin	the rate of death	0.5%		33,686	200	0
Low Molecular weight heparin (enoxaparin)	NSTE-ACS	LowMolecularweightheparin (enoxaparin)	unfractionated heparin (UHF)	to prevent one MI	0.8%	17.0%	11,128	125	0.6
				to prevent one extra revascularisation procedure	2.0%	12.0%	11,128	50	0.7
	STE-ACS	Low Molecular weight heparin(enoxaparin)	unfractionated heparin	MI	2.3%	41.0%	6,069	43	0.5
				recurrent ischemia	2.0%	30.0%	6,069	50	0.5

Anticoagulant therapy	P	I	C	O	ARR	RRR	n	NNT	Utility
				death or MI	2.9%	26.0%	6,069	34	0.3
				death, MI or recurrent ischemia	4.8%	28.0%	6,069	21	0.3
		with alteplase or tenecteplase		increase major bleeding	1.0%	44.0%	1,639	100	0.7
		Low Molecular weight heparin(enoxaparin)	unfractionated heparin	death of recurrent MI	2.1%	17.0%	20,506	48	0
				increase major bleeding at 30 days	0.7%	53.0%	20,506	143	0.7
Direct Thrombin inhibitors		Direct Thrombin inhibitors	unfractionated heparin	re-infarction at seven days	0.7%	20.0%	17,073	143	0.5
Synthetic pentasaccharides	NSTE-ACS	Synthetic pentasaccharide, fondaparinux	enoxaparin	reduced risk of major bleeding	1.9%	48.0%	20,078	53	0.7
				short(30day) term mortality	0.6%	17.0%	20,078	167	0
				long term(180day) mortality	0.7%	11.0%	20,078	143	0
	STE-ACS	fondaparinux (subcutaneous inj. 2.5mg/day)	placebo or UFH	death or recurrent MI at 30days	1.5%	14.0%	12,092	67	0.3
				death rate at all times(9, 30, 180days)	1.1%	13.0%	12,092	91	0
		fondaparinux (subcutaneous inj. 2.6mg/day)	placebo or UFH	death	3.2%	21.0%	2,666	31	0
				death or recurrent MI	4.1%	23.0%	2,666	24	0.3

other therapy	P	I	C	O	ARR	RRR	n	NNT	Utility
Beta Blockers	NSTE-ACS	Beta Blocker		rate of progression to MI	3.0%	13.0%	4,700	33	0.6
	STE-ACS	intravenous beta blocker therapy		early(7 day) benefit in cardivascular mortality	0.7%	15.0%	16,027	147	0.3
		oral beta blockade		re-infarction	0.5%	18.0%	45,852	200	0.5
				arrhythmic death	0.5%	17.0%	45,852	200	0
				motality	0.7%	13.0%	52,645	143	0
				re-infarction	0.5%	22.0%	52,645	200	0.5
				cardiac arrest	0.7%	15.0%	52,645	143	0.5
Glycaemic Control		intensive metabolic control using insulin and glucose infusion	placebo	marked mortality benefit at one year	7.5%	29.0%	620	13	0

2. Early pharmacological intervention

Antiplatelet tx	P	I	C	O	ARR	RRR	n	NNT	Utility
Aspirin	Co		placebo	long term secondary preventive benefit	2.7%	37%		37	0.7
Clopidogrel	Non-ST elevation		placebo	CV Death/MI/stroke	2.1%	18%	12,562	48	0.3
	Medical therapy only		placebo	CV Death/MI/stroke	1.9%	19.0%	7,985	53	0.3
	revascularization		placebo	CV Death/MI/stroke	2.4%	17.3%	4,577	42	0.3

Anticoagulant tx	P	I	C	O	ARR	RRR	n	NNT	Utility
	Coronary Heart Disease	warfarin : High-Intensity Oral Anticoagulant (OA)	no-aspirin	mortality	3.3%	19.4%		30	0
				MI	5.6%	34.1%		18	0.5
				thromboembolic complications	5.9%	59.6%		17	0.7
				Stroke	1.7%	44.7%		59	0.5
				Death, MI or Stroke	9.8%	32.6%		10	0.3
		warfarin :Moderate-Intensity OA	no-aspirin	mortality	2.6%	10.7%		38	0
				MI	10.4%	42.8%		10	0.5
				Stroke	2.9%	50.9%		34	0.5
				Death, MI or Stroke	2.4%	7.1%		42	0.3
		High- or Moderate-Intensity OA	aspirin	major bleeding	-2.7%	-270.0%		(37)	0.7

Anticoagulant tx	P	I	C	O	ARR	RRR	n	NNT	Utility
		high- or moderate-intensity OA and Aspirin	aspirin	death, MI, stroke	5.4%	50.0%		19	0.3
		high- or moderate-intensity OA and Aspirin	aspirin	major bleeding	-1.6%	-94.1%		(63)	0.7
		warfarin+aspirin	aspirin	MI	1.9%	44.0%		53	0.5
				ischemic stroke	0.4%	54.0%		250	0.5
				coronary revascularisation	2.0%	20.0%		50	0.7
				major bleeding	-0.9%	150.0%		(111)	0.7

Statin tx	P	I	C	O	ARR	RRR	n	NNT	Utility
	CHD		placebo	CHD mortality	1.3%	29%	30,817	75	0
	healthy population		placebo	major coronary events in the primary prevention		34%	13,200		0.6
	CHD		placebo	major coronary events in the secondary prevention		30%	17,617		0.7
	healthy population	(WOSCOP)	placebo	major coronary event	2.5%	29%	6,595	40	0.5
	healthy population	(WOSCOP)	placebo	coronary mortality	0.6%	33%	6,595	167	0
	healthy population	(AFCAPS/TexCAPS)	placebo	major coronary event	4.1%	37%	6,605	24	0.5
	healthy + CHD	(CTT META)	mainly placebo	5 year, major vascular event	3.7%	79%	90,056	27	0.5

Beta Blocker tx & Antianginal tx	P	I	C	O	ARR	RRR	n	NNT	Utility
BetaBlockertx	ACS without clinical MI		(control)	MI	3.0%	9.4%		33	0.5
	ACS with clinical MI			2 year death			24,974	42	0
	clinical MI with LVF	Carvedilol	placebo	all-cause mortality	3.0%	23%	1,959	33	0
Nitrates and calcium channel blockers	acute MI	Captopril	placebo	5wk mortality	0.5%	6.5%	58,050	200	0
	acute MI	Mononitrate	placebo	5wk mortality	0.2%	2.7%	58,050	500	0
	acute MI	Magnesium	placebo	5wk mortality	-0.4%	-5.5%	58,050	(250)	0
	acute MI	transdermal GTN	open control	6wk mortality	0.8%	11.3%	19,394	125	0

Beta Blocker tx & Antianginal tx	P	I	C	O	ARR	RRR	n	NNT	Utility
	MI	diltiazem(calcium channel blocker)	placebo	death	0.1%	0.0%	2,466	1689	0
				1st recurrent cardiac event	1.9%	0.0%	2,466	52	0

ACE Inhibitors	P	I	C	O	ARR	RRR	n	NNT	Utility
	ACS without clinical MI :highriskpatientswithvasculardisease	ramipril	placebo	all cause mortality, MI, stroke	3.8%	21.3%	9,297	26	0.3
				death from cardiovascular cause	2.0%	24.7%	9,297	50	0
				MI	2.4%	19.5%	9,297	42	0.5
				Stroke	1.5%	30.6%	9,297	67	0.5
	stable CHD	Perindopril 8mg	placebo	cardiovascular death, MI, cardiac arrest	1.9%	19.2%	12,218	53	0.3
	stable CHD	trandolipril	placebo	Primary : death from cardiovascular causes, nonfatal MI, CABG, PCI	0.6%	2.7%	8,290	167	0.3
				Death from cardiovascular causes	0.2%	5.4%	8,290	500	0
				nonfatal MI	0.0%	0.0%	8,290		
				CABG	0.6%	8.5%	8,290	167	0.7
				PCI	−0.4%	−3.3%	8,290	(250)	0.7
	acute MI	ACE inhibitor	mainly placebo	death	0.5%	6.3%	98,483	208	0
				nonfatalcardiacfailure	0.6%	3.9%	98,483	167	0.7
				ventricular	0.2%	6.1%	98,483	500	0.6

ACE Inhibitors	P	I	C	O	ARR	RRR	n	NNT	Utility
				fibrillation					
	hear faiure or left-ventricular dysfunction	ACE inhibitor	placebo	death	3.8%	14.2%	12,763	26	0
				re-infarction	2.1%	19.1%	12,763	48	0.5
				readmission for CHF	5.2%	27.5%	12,763	19	0.7
				death/MI/readmission for CHF	7.2%	17.6%	12,763	14	0.3
				stroke	0.2%	5.1%	12,763	500	0.5

Angiotensin Receptor Blockers	P	I	C	O	ARR	RRR	n	NNT	Utility
	acute MI	Losartan	Caprtopril	all-cause mortality	-1.8%	-11.0%	5,477	(56)	0
				MI	-0.1%	-0.7%	5,477	(1000)	0.5
				sudden cardiac death/resuscitated cardiac arrest	-1.3%	-17.6%	5,477	(77)	0
	MI	Valsartan	Caprtopril	Death from cardivascular causes(A)	0.1%	0.6%	9,818	1000	0
				A or MI	0.7%	3.0%	9,818	143	0.3
				A or heart failure	0.2%	0.7%	9,818	500	0.4
				A, MI, heart failure	0.8%	2.5%	9,818	125	0.3
				A, MI, HF, resuscitation after cardiac arrest, stroke	0.6%	1.8%	9,818	167	0.3
	chronic heart failure	candesartan	placebo	Cardiovascular death or	4.3%	12.5%	7,599	23	0.3

Angiotensin Receptor Blockers	P	I	C	O	ARR	RRR	n	NNT	Utility
				hospital admission for CHF					
				cardiovasculardeath	2.1%	10.3%	7,599	48	0
				hospital admission for CHF	4.3%	17.8%	7,599	23	0.7
	CHF	candesartan	placebo	Cardiovascular death or hospital admission for CHF	7.0%	17.5%	2,028	14	0.3
				cardiovascular death	3.2%	12.9%	2,028	31	0
				hospital admission for CHF	7.8%	27.7%	2,028	13	0.7
	CHF	candesartan	placebo	Cardiovascular death or hospital admission for CHF	4.4%	10.4%	2,548	23	0.3
				cardiovasculardeath	3.6%	13.2%	2,548	28	0
				hospital admission for CHF	3.8%	13.6%	2,548	26	0.7

3. Reperfusion therapy for ST elevation ACS (within the first 12 hours – focusing on both primary PCI

P	I	C	O	ARR(%)	RRR(%)	n	NNT	Utility	comment
ST elevation ACS	Primary PCI	thrombolysis	short term mortality	3.0%	36%	1,778	33	0	
			long term mortality	3.0%	38%	828	33	0	
			Stroke	2.0%	64%	1,778	50	0.5	
			Re-infarction	5.0%	59%	1,570	20	0.5	
			Recurrent ischaemia	11.0%	59.0%	1,156	9	0.7	
			Death or non-fetal re-infarction	5.0%	44.0%	1,494	20	0.3	
			Need for CABG	5.0%	36.0%	892	20	0.7	
	Adjuvant therapies for primary PCI								
ST elevation ACS treated with primary PCI	Glycoprotein IIb/IIIarec eptorantagonists(abcixi mab)	placebo	30-day of death, reinfarction, or urgent or ischemia-driven TVR	3.6%	46.0%	3,266	28	0.3	A논문
		placebo	6 month of death, reinfarction, or urgent or ischemia-driven TVR	3.2%	20.0%	3,266	31	0.3	A논문
		placebo or none = control	30-day mortality	1.0%	29.0%	27,115	100	0	A논문

P	I	C	O	ARR(%)	RRR(%)	n	NNT	Utility	comment
		placeboornone = control	6-12 month mortality	1.8%	29.0%	27,115	56	0	B논문
		placeboornone = control	30-day reinfarction	0.9%	38.1%	27,115	111	0.5	B논문
	Intracoronary stenting								
ST elevation ACS treated with primary PCI	Intracoronary stenting	Isolated balloon angioplasty	reinfarction at 12 months	1.2%	33.0%		83	0.5	
			Target vessel revascularization at 12 months	14.4%	52.0%		7	0.5	
	Thrombolytic therapy								
STelevationACS	Thrombolytic therapy	placebo	35-day mortality	1.9%	18.0%		53	0	
	Thrombolytictherapyintheveryealryphase(≤2hrs)	placebo (Tx >2hrs)	35-day mortality	24.0%			4	0	
	Service delivery								
acute MI	Transfer of pts to interventional centres	thrombolysis	death, re-infarction, stroke at 30 days	6.0%	40.0%		17	0.3	A
			primarily driven by a reduction in re-infarction	4.7%	75.0%		21	0.5	A
			death, re-infarction, stroke at 30 days	7.0%	45.0%		14	0.3	B
			primarily driven by a reduction in re-infarction	1.7%	55.0%		59	0.5	B
	Choice of thrombolytic agent	Choice of thrombolytic agent	Choice of thrombolytic agent			40,539			

P	I	C	O	ARR(%)	RRR(%)	n	NNT	Utility	comment
acute MI	adminstration over 90 minunites :accelerated regimen of alteplase	streptokinase	mortality	1.1%	14%		91	0	
pts who fail to reperfuse after thrombolysis	**Rescue PCI after failed thrombolysis**	conservativetherapy	early severe heart failure	8.0%	68%		13	0.5	
		conservativetherapy	1-yearmortality	5.0%	38%		20	0	
		delayed PCI(at mean of 12 days post-infarction)	death, re-infarction, revascularization, ischaemic events at 6 months	25.0%	49%		4	0.3	

4. Invasive investigation and revascularization

P	I	C	O	ARR(%)	RRR(%)	n	NNT	Utility
Non-ST elevation ACS	routine coronary angiography and revascularization	coservative approach	death or MI after discharge	1.1%		9,212	91	0.3
			severe angina after discharge	2.8%	23%	9,212	36	0.5
			rehospitalization after discharge	8.8%	34%	9,212	11	0.8
			MI	3.0%	26%	2,457	33	0.5
			1 year mortality	1.7%	43.0%	2,457	59	0
moderateriskptswithNon-STelevation ACS	early invasive investigation and revascularisation		death, MI, refractory angina at 4 months	4.9%	59.0%	1,810	20	0.3
ST elevation ACS	PCI or CABG	conservative(ischaemia-driven) treatment	death, MI or revascularization	12.0%	56.0%	500	8	0.3

부록 3. 근거중심 의사결정 방법론 심포지엄

- Benefit & Harm, Its trade off -

2010년 2월 8일(월요일) 14:00-18:00

Session 1

치료적 중재 효과 측정의 올바른 이해

이상무 연구위원(한국보건의료연구원 보건의료분석실)

절대적, 상대적 치료효과 크기 지표의 장단점 분석, 제시된 치료효과 크기에 따른 의사결정자들의 효과에 대한 인식이 달라지는 것에 대한 사례발표

Session 2

의약품 허가에서의 Risk-benefit 상대비교 국제 동향

이의경 교수(숙명여자대학교 임상약학대학원)

Risk-Benefit의 상대 비교에 대한 개념에 대해 알아보고, WHO CIOMS Working groups의 약제 안전성 평가를 위한 주요 고려 항목 및 방법 제시, 유럽의 EMEA와 미국 FDA의 Benefit-risk analysis 동향 제시

Session 3

근거중심 의사결정에서의 trade-off

김수영 교수(한림대학교 의과대학)

근거중심 의사결정에서 이득과 위해의 연구결과에 대한 권고 statement 기술에 대한 설명, 체계적 문헌고찰에서의 근거의 종합요소(근거의 질, 이득과 유해의 balancing, 가치와 선호도, 자원이용), GRADE 과정에 대한 설명

Session 4

약제의 Risk-Benefit 평가 방법

RTI international (F. Reed Johnson)

이득과 위해의 trade-off 선호도를 계량적으로 측정하는 방법 및 8개 질환에 대한 Benefit-risk preference 연구에 대한 설명

2010년 2월 10일(수요일) 13:00-17:00

Session 1

Quantifying Patient and Physician Benefit-Risk Tradeoff Preferences Using Conjoint Analysis

RTI international (F. Reed Johnson)

Stated-Preference methods(conjoint analysis)를 이용한 환자와 임상의사의 이득과 위해간의 trade off preference를 계량적으로 측정하는 연구 방법론 설명 및 실제 연구 수행에 있어서 survey design, survey administration, data analysis에 대한 설명