

Supplementary Material for: “Comparative efficacy of traditional non-selective NSAIDs and selective cyclooxygenase-2 inhibitor in patients with acute gout: a systematic review and meta-analysis”

Journal: BMJ Open

Authors: Mengtao Li, PhD, Chen Yu, PhD, Xiaofeng Zeng, PhD

Corresponding author: Prof Xiaofeng Zeng, Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

Table of content

Figure S1. Risk of bias summary

Figure S2. Risk of bias graph

Table S1. Detailed search strategy

Table S2. Summary of findings: COXIBs vs traditional NSAIDs for acute gout

Table S3. Summary of findings: one COXIB vs another COXIB for acute gout

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cui M 2016	+	?	?	?	+	?	+
Gao C 2018	+	?	?	?	+	?	+
Gao Q 2013	+	?	?	?	+	?	+
Guo D 2014	+	?	?	?	+	?	+
Guo M 2014	+	?	?	?	+	?	+
Hong J 2013	+	?	?	?	+	?	+
Kuang L 2015	+	?	?	?	+	?	+
Lan T 2018	+	?	?	?	+	?	+
Li S 2016	+	?	?	?	+	?	+
Li T 2013	+	+	+	+	+	+	+
Liu C 2015	+	?	?	?	+	?	+
Li Y 2017	-	?	?	?	+	?	+
Lu J 2014	+	?	?	?	+	?	+
Ming H 2016	+	?	?	?	+	?	+
Pan Q 2016	+	?	?	?	+	?	+
Rubin B 2004	+	+	+	+	+	+	+
Schumacher H 2002	+	+	+	+	+	+	+
Sheng J 2019	+	?	?	?	+	?	+
Wu L 2019	+	?	?	?	+	?	+
Xia H 2015	+	?	?	?	+	?	+
Ye Q 2010	+	?	?	?	+	?	+
Zhang J 2012	+	?	?	?	+	?	+
Zhou S 2016	+	?	?	?	+	?	+
Zhu H 2015	+	?	?	?	+	?	+

Figure S1. Risk of bias summary

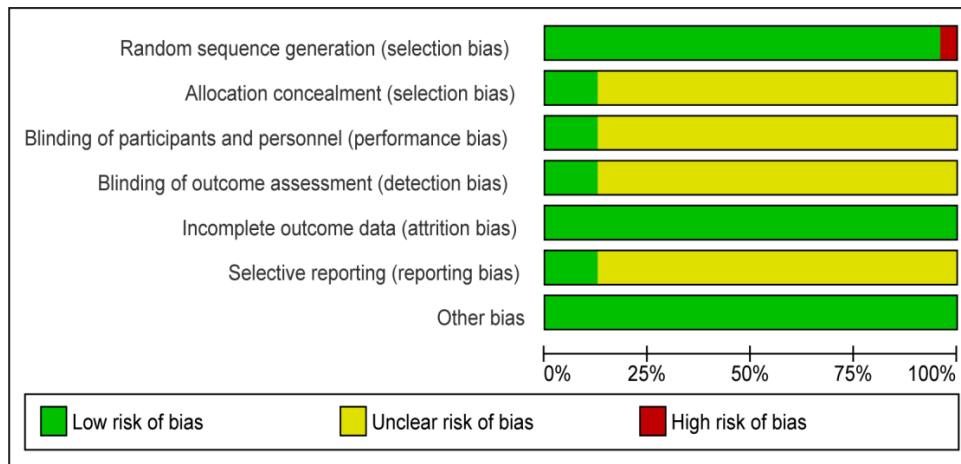


Figure S2. Risk of bias graph

Table S1. Detailed search strategy

PubMed		
Search	Query	Number
#3	Search (((gout) OR gouty arthritis) OR acute gout) AND (((Etoricoxib) OR Celecoxib) OR Meloxicam)	61
#2	Search ((gout) OR gouty arthritis) OR acute gout	18847
#1	Search ((Etoricoxib) OR Celecoxib) OR Meloxicam	9404
Web of Science		
# 3	#2 AND #1 Databases = WOS, BIOSIS, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO. Timespan=All years; Search language=Auto	183
# 2	TOPIC: (gout) OR TOPIC: (gouty arthritis) OR TOPIC: (acute gout) Databases = WOS, BIOSIS, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO. Timespan=All years; Search language=Auto	36,548
# 1	TOPIC: (Etoricoxib) OR TOPIC: (Celecoxib) OR TOPIC: (Meloxicam) Databases = WOS, BIOSIS, CSCD, DIIDW, INSPEC, KJD, MEDLINE, RSCI, SCIELO. Timespan=All years; Search language=Auto	19,277
Embase		
# 3	#2 AND #3	308
# 2	'gout'/exp OR gout OR 'gouty arthritis'/exp OR 'gouty arthritis' OR (gouty AND ('arthritis'/exp OR arthritis)) OR 'acute gout'/exp OR 'acute gout' OR (acute AND ('gout'/exp OR gout))	28,967
# 1	'etoricoxib'/exp OR etoricoxib OR 'celecoxib'/exp OR celecoxib OR 'meloxicam'/exp OR meloxicam	29,285
CNKI		
	(依托考昔 and 痛风) OR (塞来昔布 and 痛风) OR (美洛昔康 and 痛风)	214
	(Etoricoxib and Gout) OR (Celecoxib and Gout) OR (Meloxicam and Gout)	214
Wangfang		
	主题:(痛风)*主题:(美洛昔康) Etoricoxib and Gout	97
	主题:(痛风)*主题:(塞来昔布) Celecoxib and Gout	121
	主题:(痛风)*主题:(依托考昔) Meloxicam and Gout	107
	(依托考昔 and 痛风) OR (塞来昔布 and 痛风) OR (美洛昔康 and 痛风)	325
	(Etoricoxib and Gout) OR (Celecoxib and Gout) OR (Meloxicam and Gout)	325

Table S2: Summary of findings: COXIBs vs traditional NSAIDs for acute gout**COXIBs compared to traditional NSAIDs for acute gout****Patient or population:** acute gout**Setting:****Intervention:** COXIBs**Comparison:** traditional NSAIDs

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with traditional NSAIDs	Risk difference with COXIBs
Pain Likert scale	593 (4 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.15 SD lower (0.31 lower to 0.01 higher)
Pain Likert scale - Etoricoxib 120 mg qd vs Indomethacin 50 mg tid	513 (3 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.09 lower (0.27 lower to 0.08 higher)
Pain Likert scale - Etoricoxib 120 mg qd vs Diclofenac 75 mg qd	80 (1 RCT)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.53 lower (0.98 lower to 0.09 lower)
Pain VAS scale	741 (6 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 1.95 SD lower (3.46 lower to 0.044 lower)
Pain VAS scale - Etoricoxib 120 mg qd vs Diclofenac 75 mg bid	426 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 1.63 SD lower (460 lower to 1.34 higher)

COXIBs compared to traditional NSAIDs for acute gout**Patient or population:** acute gout**Setting:****Intervention:** COXIBs**Comparison:** traditional NSAIDs

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with traditional NSAIDs	Risk difference with COXIBs
Pain VAS scale - Etoricoxib 120 mg qd vs Diclofenac 75 mg qd	155 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 1.82 SD lower (5.18 lower to 1.53 higher)
Pain VAS scale - Celecoxib 200 mg qd vs Diclofenac 100 mg qd	160 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 2.41 lower (5.91 lower to 1.09 higher)
Response rate	382 (3 RCTs)	⊕⊕⊕⊕ HIGH	OR 6.71 (2.88 to 15.64)	805 per 1,000	160 more per 1,000 (118 more to 180 more)
C-reactive protein	674 (5 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.88 SD lower (1.63 lower to 0.12 lower)
C-reactive protein-Pain VAS scale - Etoricoxib 120 mg qd vs Diclofenac 75 mg bid	426 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 1.15 SD lower (3.09 lower to 0.79 higher)

COXIBs compared to traditional NSAIDs for acute gout**Patient or population:** acute gout**Setting:****Intervention:** COXIBs**Comparison:** traditional NSAIDs

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with traditional NSAIDs	Risk difference with COXIBs
C-reactive protein-Pain VAS scale - Etoricoxib 120 mg qd vs Diclofenac 75 mg qd	249 (3 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.69 SD lower (1.35 lower to 0.04 lower)
Patient's global assessment of response	511 (3 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.1 SD lower (0.27 lower to 0.07 higher)
Investigator's global assessment of response	509 (3 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.29 SD lower (0.46 lower to 0.11 lower)
Inflammation swelling	321 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.25 lower (0.74 lower to 0.24 higher)
Onset of efficacy (h) - Etoricoxib 120 mg qd vs Diclofenac 75 mg qd	113 (1 RCT)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.94 lower (1.33 lower to 0.55 lower)

COXIBs compared to traditional NSAIDs for acute gout

Patient or population: acute gout

Setting:

Intervention: COXIBs

Comparison: traditional NSAIDs

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with traditional NSAIDs	Risk difference with COXIBs

***The risk in the intervention group** (and the associated 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and the associated 95% CI).

CI: Confidence interval; **SMD:** Standardized mean difference; **OR:** Odds ratio

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Table S3: Summary of findings: one COXIB vs another COXIB for acute gout**Another COXIBs compared to one COXIBs for acute gout****Patient or population:** acute gout**Setting:****Intervention:** another COXIBs**Comparison:** one COXIBs

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with one COXIBs	Risk difference with another COXIBs
Pain Likert scale	292 (3 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 0.56 lower (1.1 lower to 0.02 lower)
Pain VAS scale	436 (6 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 2.82 SD lower (4.01 lower to 1.62 lower)
Pain VAS scale - Etoricoxib 120 mg qd vs Celecoxib 200 mg tid	312 (4 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 2.36 lower (3.36 lower to 1.37 lower)
Pain VAS scale - Etoricoxib 120 mg qd vs Meloxicam 15 mg qd	124 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 4.02 SD lower (10.28 lower to 2.24 higher)
Response rate-Etoricoxib 120 mg qd vs Celecoxib 200 mg bid	216 (3 RCTs)	⊕⊕⊕⊕ HIGH	OR 4.84 (2.19 to 10.72)	694 per 1,000	222 more per 1,000 (138 more to 266 more)

Another COXIBs compared to one COXIBs for acute gout

Patient or population: acute gout

Setting:

Intervention: another COXIBs

Comparison: one COXIBs

Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with one COXIBs	Risk difference with another COXIBs
C-reactive protein	140 (2 RCTs)	⊕⊕⊕⊕ HIGH	-	-	SMD 1.98 SD lower (4.9 lower to 0.95 higher)
Onset of efficacy (h)-Etoricoxib 120 mg qd vs Meloxicam 15 mg qd	84 (1 RCT)	⊕⊕⊕⊕ HIGH	-	-	SMD 1.57 lower (2.07 lower to 1.08 lower)

***The risk in the intervention group** (and the associated 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and the associated 95% CI).

CI: Confidence interval; **SMD:** Standardized mean difference; **OR:** Odds ratio

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect