This is a response from the SBU's Enquiry Service November 11, 2015

Disclaimer: Responses from SBU's Enquiry Service presents conclusions solely as interpreted by the authors of the individual studies included. SBU's Enquiry Service makes no attempt to combine or interpret the body of evidence, as there has been no formal quality control by SBU nor statistical processing to weight and synthesize the data provided.

Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk for bleeding after gastrointestinal surgery

NSAIDs are a class of drugs that are anti-inflammatory, analgesic and antipyretic but which also leads to an increased risk of bleeding.

Question

Can NSAIDs intake during stomach and bowel surgery lead to an increased risk of bleeding?

Summary

SBU's Enquiry Service identified four systematic reviews and seven randomised controlled studies (RCT) which addressed the effect of NSAID on surgery-related bleeding compared to placebo or any other medication. The four systematic reviews identified included studies that examined surgery-related bleeding for a range of surgeries not restricted to gastrointestinal surgery. The seven RCTs identified examined the risks of gastrointestinal surgery-related bleeding, including gallbladder and gastrointestinal tumour removal.

The authors of the two identified systematic reviews that examine COX-2 selective inhibitors draw the conclusion that there is no difference in surgery-related bleeding risks for any of the examined treatments. The authors of the remaining two reviews draw the conclusions that NSAID can lead to a slightly increased risk for surgery-related bleeding.

The authors of the identified RCTs draw the conclusion that there are no meaningful differences in the tendency for bleeding, duration of bleeding, or blood loss in patients treated with NSAIDs compared to controls. One study found that ketorolac administered during the surgery increased the bleeding duration compared to placebo. All seven RCTs were double blinded, but included relatively few patients (n=16 to 60).

SBU's Enquiry Service has not itself drawn any conclusions in this matter as no attempt has been made to assess the quality nor to appropriately weight and combine the conclusions.

Methods

We searched Embase, Medline, The Cochrane Library, various HTA-databases, as well as web sites of various Swedish government agencies in June 2015. The complete search strategy is presented in the section "Literature search." In addition, the reference lists of relevant articles were screened and Scopus was used.

Only systematic reviews or RCT that presented the effects of NSAID treatment on gastrointestinal surgery-related bleeding were included in this answer. We excluded RCTs that evaluated bleeding associated with orthopaedic or gynaecological procedures as well as organ

transplantation. We have also excluded treatments that combined NSAIDs with other medications, for example acetylsalicylic acid.

Identified abstracts and articles were largely read by only one person. No attempt has been made to judge the quality of the included articles. It is likely that some of the included articles are of a lower quality than SBU usually includes in their assessments.

Results

The abstracts of all 1219 articles identified by the literature search were read. Of these, 33 were judged to be potentially relevant and read in full text. In total eleven articles, four systematic reviews and seven RCTs, met the inclusion criteria. See section "Included articles".

Literature search

PubMed via NLM 8 June 2015 **Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk for bleeding after gastrointestinal surgery**		
	Search terms	**Items found**
Population:		
1.	Search ("Digestive System Surgical Procedures"[Mesh]) OR ((((intestine[Title/Abstract]) OR abdominal[Title/Abstract])) AND surgical[Title/Abstract])	317 332
Intervention:		
2.	Search ("Anti-Inflammatory Agents, Non-Steroidal"[Mesh]) OR NSAID[Title/Abstract]	71 293
Study types:		
3.	Search ("Hemorrhage"[Mesh]) OR bleeding[Title/Abstract]	356 376
Final	#1 AND #2 AND #3	331

The search result, usually found at the end of the documentation, forms the list of abstracts

[MeSH] = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
[Title/Abstract] = Title or abstract
" " = Citation Marks; searches for an exact phrase

Cohrane Library via Wiley 8 June 2015 **Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk for bleeding after gastrointestinal surgery**		
	Search terms	**Items found**
Population:		
1.	"surgery":ti,ab,kw (Word variations have been searched)	79 588
Intervention:		
2.	MeSH descriptor: [Anti-Inflammatory Agents, Non-Steroidal] explode all trees	6 587
3.	NSAID:ti,ab,kw (Word variations have been searched)	1 746
Outcome:		
4.	"bleeding":ti,ab,kw (Word variations have been searched)	18 204

Cohrane Library via Wiley 8 June 2015 **Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk for bleeding after gastrointestinal surgery**		
Final	#1 AND (#2 OR #3) AND #4	98(2CDSR, 90 CENTRAL and 1 CRM)

The search result, usually found at the end of the documentation, forms the list of abstracts

[MeSH] = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
[TI, AB, KW] = Title, abstract or keyword
CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies

Embase via embase.com 9 juni 2015 **Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk for bleeding after gastrointestinal surgery**		
	Search terms	**Items found**
Population:		
1.	'abdominal surgery'/exp OR 'abdominal surgery':ab,ti OR 'gastrointestinal surgery'/exp OR 'gastrointestinal surgery':ab,ti OR 'intestinal surgery':ab,ti OR 'intestinal surgery'/exp	598 737
2.	'bleeding'/exp OR 'bleeding':ab,ti	697 520
Intervention:		
3.	'nonsteroid antiinflammatory agent'/exp OR nonsteroid NEAR/2 'anti inflammatory' OR nsaid:ab,ti OR nsaids:ab,ti	471 076
Study types:		
4.	'systematic review'/exp OR systematic:ab,ti OR meta:ab,ti OR 'randomized controlled trial'/exp OR (randomized AND controlled) OR 'observational study'/exp OR 'controlled study'/exp	5,132,194
Final	#1 AND #2 AND #3 AND #4	711

/exp= Includes terms found below this term in the EMTREE hierarchy
:ti:ab = Title or abstract
' ' = Citation Marks; searches for an exact phrase

CDR DATUM 8 juni 2015 **Nonsteroidal anti-inflammatory drugs (NSAIDs) and risk for bleeding after gastrointestinal surgery**		
	Search terms	**Items found**
Population:		
1.	MeSH DESCRIPTOR Gastrointestinal Hemorrhage EXPLODE ALL TREES	261
2.	(bleeding) AND (surgical)	547
Intervention:		
3.	MeSH DESCRIPTOR Anti-Inflammatory Agents, Non-Steroidal EXPLODE ALL TREES	989
4.	(NSAID)	238
Final	(#1 OR #2) AND (#3 OR #4)	65

The search result, usually found at the end of the documentation, forms the list of abstracts

Included articles

1. Elia N, Lysakowski C, Tramèr MR. Does multimodal analgesia with acetaminophen, nonsteroidal antiinflammatory drugs, or selective cyclooxygenase-2 inhibitors and patient-controlled analgesia morphine offer advantages over morphine alone? Meta-analyses of randomized trials. Anesthesiology 2005;103:1296-1304.
2. Maund E, McDaid C, Rice S, Wright K, Jenkins B, Woolacott N. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs for the reduction in morphine-related side-effects after major surgery: A systematic review. British Journal of Anaesthesia 2011;106:292-297.
3. McDaid C, Maund E, Rice S, Wright K, Jenkins B, Woolacott N. Paracetamol and selective and non-selective non-steroidal anti-inflammatory drugs (nsaids) for the reduction of morphine-related side effects after major surgery: A systematic review. Health Technology Assessment 2010;14:1-196.
4. Straube S, Derry S, McQuay HJ, Moore RA. Effect of preoperative Cox-II-selective NSAIDs (coxibs) on postoperative outcomes: a systematic review of randomized studies. Acta Anaesthesiologica Scandinavica 2005;49:601-613.
5. Zemmel MH. The role of COX-2 inhibitors in the perioperative setting: efficacy and safety. A systematic review. AANA Journal 2006;74:49-60.
6. Varrassi G, Panella L, Piroli A, Marinangeli F, Varrassi S, Wolman I, et al. The effects of perioperative ketorolac infusion on postoperative pain and endocrine-metabolic response. Anesthesia and Analgesia 1994;78:514-519.
7. Cheng PGB, Lim MJ, Onsiong MK, Chiu KYW, Chan MK, Li KWM, et al. Celecoxib premedication in post-operative analgesia for laparoscopic cholecystectomy. Acute Pain 2004;6:23-28.
8. Oberhofer D, Skok J, Nesek-Adam V. Intravenous ketoprofen in postoperative pain treatment after major abdominal surgery. In: World journal of surgery; 2005. p 446-9.
9. Power I, Noble DW, Douglas E, Spence AA. Comparison of i.m. ketorolac trometamol and morphine sulphate for pain relief after cholecystectomy. Br J Anaesth 1990;65:448-55.
10. Puura A, Puolakka P, Rorarius M, Salmelin R, Lindgren L. Etoricoxib pre-medication for post-operative pain after laparoscopic cholecystectomy. In: Acta anaesthesiologica Scandinavica; 2006. p 688-93.
11. Sandhu T, Paiboonworachat S, Ko-iam W. Effects of preemptive analgesia in laparoscopic cholecystectomy: a double-blind randomized controlled trial. Surg Endosc 2011;25:23-7.
12. Saravanan P, Badhe A, Rajendran KM, Sahai A. A clinical trial of perioperative ketorolac infusion on postoperative pain relief. Journal of Anaesthesiology Clinical Pharmacology 1999;15:271-278.