



How to Slow the Flow: NSAIDs for Heavy Menstrual Bleeding

CLINICAL QUESTION

In premenopausal heavy menstrual bleeding without pathological cause, do nonsteroidal anti-inflammatory drugs (NSAIDs) improve patient outcomes?

BOTTOM LINE

Based on low-quality evidence, NSAIDs reduce relative mean menstrual blood loss by ~30%, and ~20-50% fewer sanitary products used than placebo. Effects on bleeding duration are inconsistent.

EVIDENCE

- Focused on randomized, placebo-controlled trials (RCTs). Menorrhagia, when defined: >80ml/cycle.
- Naproxen: 2 cross-over RCTs, 4 patients each. Baseline blood loss ~140ml. After 2 menstrual cycles of each treatment:¹⁻³
 - Mean blood loss decreased ~30% over placebo.¹⁻³
 - In 1 RCT, 79% felt naproxen better than placebo.³
 - No effect on bleeding duration.³
- Ibuprofen: 1 cross-over RCT, 13 patients.⁴ Baseline blood loss not stated. After 1 cycle of each treatment:
 - Ibuprofen 1200mg/day decreased mean blood loss ~25% over placebo.
 - Ibuprofen 600mg/day: not different from placebo.
 - No effect bleeding duration.

- Mefenamic acid: 5 RCTs:
 - Largest RCT: 80 women, 3 consecutive cycles.⁵
 - “Relief” of menorrhagia (not defined): 86% versus 20%, number needed to treat=2.
 - Number of pads per day: 15 at baseline, 7 on mefenamic acid (placebo not stated).
 - Number of bleeding days: 10 at baseline, 4 on mefenamic acid (placebo not stated).
 - 3 RCTs (2 cross-over, total 49 patients): mefenamic acid better than placebo.
 - Mean blood loss ~10-40% lower than placebo.⁶⁻⁸
 - “Responded” (not defined): 79% versus 18% (placebo).^{6,9}
 - 1 cross-over RCT, 15 patients: no difference in blood loss.¹⁰
- Mefenamic acid versus diclofenac:
 - 1 RCT, 68 women, only 1 completed all study follow-up.¹¹
 - Median number of pads used (baseline unknown): 21 versus 10 (diclofenac).
 - Number of bleeding days (baseline unknown): 6 versus 4 (diclofenac).
- Naproxen versus mefenamic acid:
 - 1 cross-over RCT, 35 women.¹²
 - Both groups decreased mean blood loss ~47% from baseline.
 - Days of bleeding in both groups decreased 0.8.
 - Number of tampons decreased from ~31 at baseline to ~24.

CONTEXT

- Volume of blood loss does not correlate with patient experience.¹³
- NSAIDs are used immediately before and during menses (example: mefenamic acid 500mg TID from menstruation onset to end⁶).
- Mefenamic acid costs ~\$20/cycle; naproxen and ibuprofen ~\$4 each.¹⁴⁻¹⁶

REFERENCES

1. Nygren GK, Rybo G. Acta Obstet Gynecol Scand Suppl. 1983; 113:101-3.
2. Rybo G, Nilsson S, Sikstrom B, Nygren KG. Lancet. 1981 Mar 14; 1(8220 Pt 1):608-9.
3. Ylikorkala O, Pekonen F. Obstet Gynecol. 1986; 10:10-12.
4. Mäkäräinen L, Ylikorkala O. Br J Obstet Gynaecol. 1986; 93:974-8.
5. Grover V, Usha R, Gupta U, *et al.* Asia-Oceania J Obstet Gynaecol. 1990; 16(3):255-9.
6. Fraser IS, Pearse C, Shearman RP, *et al.* Obstet Gynecol. 1981; 58:543-51.
7. Tsang BK, Domingo MT, Spence EH, *et al.* Can J Physiol Pharmacol. 1987; 65:2081-4.
8. Van Eijkeren MA, Christiaens GCML, Geuze HJ, *et al.* Am J Obstet Gynecol. 1992; 166:1419-28.
9. Bofill Rodriguez M, Lethaby A, Farquhar C. Cochrane Database Syst Rev. 2019; 9: CD000400.
10. Muggeridge J, Elder MG. Res Clin Forums. 1983; 5:83-8.
11. Kumar S, Tekur U, Singh B, *et al.* IJBCP. 2018; 7(10):1905-11.
12. Hall P, MacLachlan N, Thorn N, *et al.* Br J Obstet Gynaecol. 1987; 94:554-8.
13. Warner PE, Critchley HO, Lumsden MA *et al.* Am J Obstet Gynecol. 2004; 190:1224-1229.
14. Alberta Interactive Drug Benefit List. Available at: <https://idbl.ab.bluecross.ca/idbl/load.do>. Accessed October 5, 2020.
15. Well.ca online pharmacy. Available at: https://well.ca/products/rexall-extra-strength-ibuprofen_167575.html. Accessed October 2, 2020.
16. Well.ca online pharmacy. Available at: https://well.ca/products/rexall-naproxen-sodium-tablets-220_190531.html. Accessed October 2, 2020.

AUTHORS

Jennifer Potter MD
CCFP, Zainab Sari,
Adrienne J Lindblad
 BSP ACPR PharmD

Authors do not have any conflicts of interest to declare.

