| Study Date Country | Design | Inclusion criteria | Abortion regimen | Intervention/Comparison | Results |
|-------------------|--------|--------------------|------------------|-------------------------|---------|
| Andersson, 2016 Sweden | RCT | N=102 women ≥ 18 years, with gestations between 13-22 weeks | Day 0: Mifepristone (dose not specified) Day 2: Repeat doses of misoprostol (dose and interval not specified) | Intervention (n=52): paracervical block with 20mL 0.25% bupivacaine (2 injection sites, deep injection) administered 1 h after first misoprostol dose Comparison (n=50): paracervical block with 20mL normal saline (2 injection sites, deep injection) administered 1 h after first misoprostol dose | Direct measurement of pain N (%) with pain score > 7 on 10cm VAS Intervention: 39 (75) Comparison: 32 (65) Risk ratio: 1.1 (95% CI 0.9, 1.5) P=0.292 |
| Winkler, 1997 Germany | Comparative Trial | N=20 women between 16-42 year of age with pregnancies between 16-23 gestational weeks seeking abortion for fetal indications | Gemeprost 1mg PV q6hr with IV oxytocin augmentation as needed | Intervention (n=10): Paracervical block with 10mL of 0.5% bupivacaine (2 injection points) Comparison (n=10): no paracervical block | Direct measurement of pain Maximum pain score on 11-point VAS, median (range) Intervention: 8.5 (5-10) Comparison: 7.0 (1-10) P=not significant |

**Safety and Side Effects**
No differences in side effects between two groups. One adverse event (sensory loss and weakness 30 mins after bupivacaine PCB, resolved)

**Induction to abortion interval**
Median minutes (IQ range) Intervention: 435 (320-748) Comparison: 398 (260-540) Risk ratio: 80 (95% CI -5, 180) P=0.075

**Indirect measurement of pain**
Median mg (IQ range) of additional meperidine Intervention: 5 (1.3-10.5) Comparison: 6 (1-10) Risk ratio: 0 (95% CI -2, 2.5) P=0.772

**Induction to abortion interval**
Median hours (range) Intervention: 13 (8-36) Comparison: 20 (8-44) P=not significant
| Study          | Country   | Sample Size | Gestation Range | Treatment Details | Pain Management                                      | Primary Pain Outcome | Secondary Pain Outcome | Safety and Side Effects |
|---------------|-----------|-------------|-----------------|-------------------|-----------------------------------------------------|----------------------|------------------------|------------------------|
| Tintara, 2018 | Thailand  | 56 women    | 14-24 weeks     | Misoprostol SL 400mcg every 6 hours | Intervention (n=28): celecoxib 400mg po x 1<br>Comparison (n=28): placebo<br>All: morphine 3mg IV every 3 hours if pain score ≥ 7 | Direct measurement of pain: Mean (SD) pain score on 10cm VAS at time of complete abortion<br>Intervention: 4.6 (2.8)<br>Comparison: 7.3 (2.2)<br>P=0.01<br>Mean difference (SD) in hourly pain score: -0.5 (0.15), p<0.001 | Indirect measurement of pain: N (%) requiring additional IV morphine<br>Intervention: 12 (43)<br>Comparison: 12 (43)<br>P=1<br>Median mg (IQ range) of additional IV morphine<br>Intervention: 3 (3-3.8)<br>Comparison: 7.5 (3-12)<br>P=0.08 | Safety and Side Effects: No differences in rates of fever, chills, nausea/vomiting, itching, or diarrhea between groups. No adverse events reported. |
| Velipasaoglu, 2016 | Turkey   | 60 women    | 13-22 weeks     | Misoprostol 400mcg PV every 4hr for 48 hours | Acetaminophen (n=20): 500mg PO at first miso, then every 6hr x 2, then every 12hr<br>Diclofenac (n=20): 75mg PO at first miso, then every 6hr x 2, then every 12hr | Direct measurement of pain: Mean (SD) pain scores on 10-cm VAS<br>Acetaminophen: 3.31 (1.34)<br>Diclofenac: 4.02 (2.02)<br>HnBB: 3.17 (1.65)<br>P=0.352 | Median (IQ range) pain score at final misoprostol administration<br>Acetaminophen: 7 (5-8.5) | - |
Hyoscine N-butylbromide (HnBB, n=20): 10mg po at first miso, then q6hr x 2, then q12hr

All: Meperidine IV as needed

Diclofenac: 8 (4-9)
HnBB: 6 (4-9)
P=0.288

**Indirect measurement of pain**
N (%) requiring additional IV meperidine
Acetaminophen: 5 (25)
Diclofenac: 8 (40)
HnBB: 4 (20)
P=0.344

**Induction to abortion interval**
Median (IQ range) hours
Acetaminophen: 21.5 (11.25-32)
Diclofenac: 28 (20.25-34.5)
HnBB: 16 (12.5-27.5)
P=0.611

**Abortion success**
N (%) achieving abortion within 24 hours
Acetaminophen: 11 (55)
Diclofenac: 11 (55)
HnBB: 14 (70)
p=0.535

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Fiala, 2005
Sweden
RCT

N=74 women with singleton pregnancies between 13-22 weeks

Day 0:
Mifepristone 600mg PO x 1

Day 2-3:
Misoprostol 800mcg PV x1, then 400mcg PO every 3 hours

**Intervention (n=36):**
diclofenac 100mg PO x 1

**Comparison (n=38):**
paracetamol 1000mg + codeine 20mg PO x 1

All: paracetamol, codeine, IV opiates or paracervical block as needed

**Direct measurement of pain**
Median (range) maximum pain score on 10cm VAS
Intervention: 7 (4-9)
Comparison: 7 (2-10)
P=0.7

**Indirect measurement of pain**
N (%) requiring additional IV opiates
Intervention: 29 (81)
Comparison: 31 (82)
P=0.91

Median mg (IQ range) of additional IV opiates
Intervention: 3.5 (0-25)
Comparison: 7 (0-53)
P=0.042

N (%) requiring additional oral pain medications
Intervention: 9 (25)
Comparison: 16 (42)
P=0.12

N (%) requiring additional paracervical block
Intervention: 4 (11)
Comparison: 2 (5)
P=0.42
Smith, 2016 Canada RCT

N=37 women > 18 years with gestations between 12-23+6 weeks

“Misoprostol per physician preference”

Intervention (n=17): Epidural patient-controlled analgesia with bupivacaine and fentanyl (5mL bolus of 0.0625% bupivacaine + fentanyl 2mg/mL with 10 minute lockout, then infusion of 10mL/hr)

Comparison (n=20): IV patient-controlled analgesia with fentanyl (25-50mcg bolus with 3-6 minute lockout)

Direct measurement of pain
Mean (SD) maximum pain score on 11-point verbal numeric pain scale during first 24 hours
Intervention: 4.2 (2.3)
Comparison: 5.9 (3.1)
P=0.07

Mean (SD) satisfaction score on 11-point verbal numeric scale
Intervention: 8.4 (1.4)
Comparison: 7.8 (1.8)
P=0.31

Indirect measurement of pain
N (%) requiring additional anxiolytic medication
Intervention: 0 (0)
Comparison: 3 (15)
P=not significant

Safety and Side Effects
No statistically significant differences in rates of retained products of conception or surgical evacuation of the uterus. No statistically significant differences in side effects (nausea, vomiting, pruritis, sedation, hypotension or need for bladder catheterization). One participant in the intervention group received a transfusion.

Induction to abortion interval
No statistically significant differences in induction to abortion interval (data not shown)
Maggiore, 2016
Italy
RCT

**N=104**
Women ≥ 18 years with “second trimester” pregnancies up to 24 weeks gestation (mean 19 weeks), request for analgesia with a baseline pain score ≥ 30mm

- **Gemeprost**: 1mg PV q3hr up to 5 doses, repeated for a second cycle if needed
- **In women with uterine scar**: gemeprost 1mg PV q6hr up to 5 doses for one cycle only

**Intervention (n=52):** Programmed intermittent epidural bolus technique: 10mL of 0.0625% levobupivacaine + sufentanil 0.5mcg/mL every 1 hour

**Comparison (n=52):** Continuous epidural infusion technique with 0.0625% levobupivacaine and sufentanil 0.5mcg/mL at a rate of 10mL/hr

**Direct measurement of pain**
“Visual analogue pain scores were similar between the study groups and they were at all times <20mm at the hourly assessments (p>0.05 for all comparisons).”

Mean (SD) satisfaction score on 10cm VAS
- **Intervention**: 8.4 (1.5)
- **Comparison**: 7.3 (2.0)
P=0.005

**Indirect measurement of pain**
Total consumption of levobupivacaine (mg), mean (SD)
- **Intervention**: 91 (36.5)
- **Comparison**: 107.3 (42.6)
P=0.038

Total consumption of sufentanil (mcg), mean (SD)
- **Intervention**: 72.8 (29.2)
- **Comparison**: 85.9 (34.1)
P=0.038

**Safety and Side Effects**
N (%) with at least one narcotic-related side effect
- **Intervention**: 21 (40.4)
- **Comparison**: 33 (63.5)
P=0.031

N (%) with nausea
- **Intervention**: 7 (13.5)
- **Comparison**: 18 (34.6)
P=0.022

No statistically significant differences in vomiting, pruritis, sedation or respiratory depression. No differences in epidural related adverse events (hypotension, dural puncture, neurologic complications, shivering) or abortion related adverse events (hemorrhage, transfusion, perforation).

V=intravenous; IQ=interquartile; Mg=milligram; Mcg=microgram; PO=per os; PV=per vaginum; PR=per rectum; VAS=visual analogue scale