



and -9.6 for placebo ($P=.26$ vs baseline); however, the comparison between capsaicin and vehicle did not reach significance ($P=.4$), possibly because of the small number of patients. Similarly, for jabbing pain the mean change from the baseline VAS was -34 for capsaicin ($P=.01$ vs baseline) and -0.3 for placebo ($P=.98$ vs baseline). Here, the difference between treatments was significant ($P<.05$). Twelve of the 13 patients using capsaicin had a burning sensation from the ointment and 1 stopped the trial due to this adverse effect.⁴

In a general review of postsurgical neuropathic pain, 1 expert recommended tricyclic antidepressants, gabapentin, or pregabalin as first-line agents, with serotonin norepinephrine reuptake inhibitors or topical lidocaine as second-line agents for pharmacologic treatment.¹ Tramadol, opioids, valproic acid, lamotrigine, combination therapy, and electrical stimulation of the spinal cord were also mentioned as third- or fourth-line treatments.

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What is the single best empiric antibiotic treatment for acute traveler’s diarrhea in adults?

Evidence-Based Answer

Fluoroquinolones remain the single best empiric antibiotic treatment for traveler’s diarrhea (SOR: **C**, consensus guideline). Rifaximin appears as effective as ciprofloxacin but is dosed 3 times a day versus twice a day for ciprofloxacin (SOR: **B**, RCT). Azithromycin is more effective than levofloxacin in areas where common pathogens demonstrate fluoroquinolone resistance, such as Southeast Asia and India (SOR: **B**, RCT).

A 2000 Cochrane systematic review of 20 RCTs (N=3,157) covering Latin America, Africa, and Asia from 1983 through 1997 evaluated antibiotic treatment for traveler’s diarrhea.¹ Ten double-blinded, placebo-controlled RCTs (N=1,935) all reported a reduction in illness duration for the antibiotic treatment group

compared with placebo, but a pooled data analysis between antibiotics was not performed due to the different types of reported data.

The antibiotic group had more participants with resolution of diarrhea symptoms by 72 hours compared with placebo (6 trials, N=697; OR 5.9; 95% CI, 4.1–8.6). The antibiotic group also had a reduction in the number of unformed stools per 24-hour period for up to 72 hours (2 trials, N=223; day 1 mean difference in unformed stools -1.6 ; 95% CI, -2.7 to -0.52 ; day 2 MD -2.1 ; 95% CI, -2.8 to -1.4 ; day 3 MD -1.4 ; 95% CI, -1.9 to -0.82). Patients taking antibiotics experienced more adverse effects than patients taking placebo (5 trials, N=862; OR 2.4; 95% CI, 1.5–3.8).¹

A 2006 double-blinded RCT randomized 399 adults with traveler’s diarrhea across multiple centers in Latin America and India to 1 of 3 treatment groups for 3 days: rifaximin 200 mg TID, ciprofloxacin 500 mg BID with an additional placebo dose, and placebo TID.² Both rifaximin and ciprofloxacin were statistically better than placebo in reducing the time to last unformed stool (rifaximin=32 hours, placebo=66 hours; risk ratio [RR] 1.6; 95% CI, 1.2–2.2; ciprofloxacin=29 hours, placebo=66 hours, RR 1.9; 95% CI, 1.3–2.7). No statistical difference was noted between rifaximin and ciprofloxacin for time to last unformed stool (RR 0.88; 95% CI, 0.66–1.2).

A 2007 double-blinded RCT with 156 adults compared azithromycin 1 g in a single dose, azithromycin 500 mg daily for 3 days, and levofloxacin 500 mg daily for 3 days in Thailand, where fluoroquinolone resistance has exceeded 85% in some isolates.³ *Campylobacter* predominated (64% of patients), with levofloxacin resistance in 50% of isolates.

Cure rates with single-dose and 3-day regimens of azithromycin were greater than those for levofloxacin at both 48 hours (53%–65% vs 38%; $P=.02$) and 72 hours (85%–95% vs 71%; $P=.01$). The rate of pathogen eradication in the azithromycin groups was higher than with levofloxacin (96%–100% vs 38%; $P=.001$).³

Consensus guidelines from the Infectious Disease Society of America recommend first-line empiric therapy with fluoroquinolones (“based on good evidence from at least 1 RCT”) unless the destination is Southeast Asia, India, or known to have a significant burden of fluoroquinolone-resistant *Campylobacter*.⁴ Alternative empiric treatment for all destinations

is azithromycin 1,000 mg as a single dose (“based on moderate evidence from at least one non RCT”). Rifaximin 200 mg 3 times daily is a second alternative, specifically in the treatment of afebrile, nondysenteric traveler’s diarrhea.

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the US Army at large, or the Department of Defense.

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Is induction of labor indicated for suspected fetal macrosomia?

Evidence-Based Answer

No. Induction of labor is not indicated for suspected fetal macrosomia, as induction does not decrease associated fetal or maternal morbidity (SOR: **A**, systematic review of RCTs and cohort trials and Cochrane review). Induction may also increase the cesarean section rate (SOR: **C**, inconsistent RCTs and retrospective cohort trials).

A 2002 systematic review of 2 RCT and 9 observational trials compared maternal and neonatal outcomes among women with suspected fetal macrosomia (3,600–4,500 g) who were induced (N=1,051) or managed expectantly (N=2,700).¹ None showed a significant difference in shoulder dystocia, 5-minute Apgar scores <7, or instrumental vaginal delivery. The observational trials (n=3,438) had a significantly lower incidence of cesarean sections with expectant management than with induction (8.4% vs 17%; OR 0.39; 95% CI, 0.30–0.50), although this difference was not found in the RCTs (n=313) (24% vs 21%; OR 1.2; 95% CI, 0.69–2.0).

A 1998 Cochrane review of 3 RCTs (N=372) also compared expectant management and induction of labor for suspected fetal macrosomia: one by estimated fetal weight 4,000 to 4,500 g, a second by estimated fetal weight 4,000 to 4,750 g, and a third by estimated fetal weight of more than the 97th percentile for gestational age.² Perinatal morbidities occurred

with expectant management (4 clavicular fractures and 2 brachial plexus injuries) but were rare and not statistically significant compared with induction. Across all 3 RCTs, no difference was noted in rates of shoulder dystocia (RR 1.1; 95% CI, 0.44–2.6), instrumental vaginal delivery (RR 1.0; 95% CI, 0.60–1.7), or cesarean section (RR 0.96; 95% CI, 0.67–1.4).

A 2012 retrospective cohort trial (N=130,000) examined the labor management for macrosomic newborns (4,000–4,500 g).³ No statistically significant trends were noted between the induction group and the expectant management group for Apgar scores <7 or neonatal injury. Labor induction was associated with statistically significantly lower cesarean rates than expectant management at 39 to 41 weeks’ gestational age (39 weeks: OR 1.3; 95% CI, 1.2–1.3; 40 weeks: OR 1.3; 95% CI, 1.2–1.4; and 41 weeks: OR 1.2; 95% CI, 1.1–1.3). A weakness of this study was the context of suspected macrosomia, as the trial reviewed only known macrosomia cases.

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Are thiazolidinediones effective in the treatment of nonalcoholic steatohepatitis (NASH)?

Evidence-Based Answer

Yes, thiazolidinediones do appear to be effective in the treatment of NASH, with pioglitazone improving histological parameters including steatosis and fibrosis in patients with biopsy-proven nonalcoholic fatty liver disease (NAFLD) (SOR: **C**, meta-analysis using histopathologic outcomes).

NAFLD is thought to be due in part to insulin resistance, suggesting insulin sensitizers as a possible treatment. A meta-analysis of 7 RCTs (N=489), 4 of which were placebo controlled (n=355), assessed the effect of