Cochrane Library

Cochrane Database of Systematic Reviews

Midazolam for sedation before procedures (Review)

Conway A, Rolley J, Sutherland JR

Conway A, Rolley J, Sutherland JR.
Midazolam for sedation before procedures.
Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD009491.
DOI: 10.1002/14651858.CD009491.pub2.

www.cochranelibrary.com

WILEY

[Intervention Review]

Midazolam for sedation before procedures

Aaron Conway[1], John Rolley[2], Joanna R Sutherland[3]

[1]Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia. [2]School of Nursing and Midwifery, Deakin University, Geelong, Australia. [3]UNSW Rural Clinical School, Coffs Harbour Health Campus, Coffs Harbour, Australia

Contact address: Aaron Conway, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Queensland, Australia. Aaron.conway@qut.edu.au.

Editorial group: Cochrane Anaesthesia, Critical and Emergency Care Group.
Publication status and date: New, published in Issue 5, 2016.

Citation: Conway A, Rolley J, Sutherland JR. Midazolam for sedation before procedures. *Cochrane Database of Systematic Reviews* 2016, Issue 5. Art. No.: CD009491. DOI: 10.1002/14651858.CD009491.pub2.

ABSTRACT

Background

Midazolam is used for sedation before diagnostic and therapeutic medical procedures. It is an imidazole benzodiazepine that has depressant effects on the central nervous system (CNS) with rapid onset of action and few adverse effects. The drug can be administered by several routes including oral, intravenous, intranasal and intramuscular.

Objectives

To determine the evidence on the effectiveness of midazolam for sedation when administered before a procedure (diagnostic or therapeutic).

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL to January 2016), MEDLINE in Ovid (1966 to January 2016) and Ovid EMBASE (1980 to January 2016). We imposed no language restrictions.

Selection criteria

Randomized controlled trials in which midazolam, administered to participants of any age, by any route, at any dose or any time before any procedure (apart from dental procedures), was compared with placebo or other medications including sedatives and analgesics.

Data collection and analysis

Two authors extracted data and assessed risk of bias for each included study. We performed a separate analysis for each different drug comparison.

Main results

We included 30 trials (2319 participants) of midazolam for gastrointestinal endoscopy (16 trials), bronchoscopy (3), diagnostic imaging (5), cardioversion (1), minor plastic surgery (1), lumbar puncture (1), suturing (2) and Kirschner wire removal (1). Comparisons were: intravenous diazepam (14), placebo (5) etomidate (1) fentanyl (1), flunitrazepam (1) and propofol (1); oral chloral hydrate (4), diazepam (2), diazepam and clonidine (1); ketamine (1) and placebo (3); and intranasal placebo (2). There was a high risk of bias due to inadequate reporting about randomization (75% of trials). Effect estimates were imprecise due to small sample sizes. None of the trials reported on allergic or anaphylactoid reactions.

Intravenous midazolam versus diazepam (14 trials; 1069 participants)

There was no difference in anxiety (risk ratio (RR) 0.80, 95% confidence interval (CI) 0.39 to 1.62; 175 participants; 2 trials) or discomfort/pain (RR 0.60, 95% CI 0.24 to 1.49; 415 participants; 5 trials; I^2 = 67%). Midazolam produced greater anterograde amnesia (RR 0.45; 95% CI 0.30 to 0.66; 587 participants; 9 trials; low-quality evidence).

Intravenous midazolam versus placebo (5 trials; 493 participants)

One trial reported that fewer participants who received midazolam were anxious (3/47 versus 15/35; low-quality evidence). There was no difference in discomfort/pain identified in a further trial (3/85 in midazolam group; 4/82 in placebo group; P = 0.876; very low-quality evidence).

Oral midazolam versus chloral hydrate (4 trials; 268 participants)

Midazolam increased the risk of incomplete procedures (RR 4.01; 95% CI 1.92 to 8.40; moderate-quality evidence).

Oral midazolam versus placebo (3 trials; 176 participants)

Midazolam reduced pain (midazolam mean 2.56 (standard deviation (SD) 0.49); placebo mean 4.62 (SD 1.49); P < 0.005) and anxiety (midazolam mean 1.52 (SD 0.3); placebo mean 3.97 (SD 0.44); P < 0.0001) in one trial with 99 participants. Two other trials did not find a difference in numerical rating of anxiety (mean 1.7 (SD 2.4) for 20 participants randomized to midazolam; mean 2.6 (SD 2.9) for 22 participants randomized to placebo; P = 0.216; mean Spielberger's Trait Anxiety Inventory score 47.56 (SD 11.68) in the midazolam group; mean 52.78 (SD 9.61) in placebo group; P > 0.05).

Intranasal midazolam versus placebo (2 trials; 149 participants)

Midazolam induced sedation (midazolam mean 3.15 (SD 0.36); placebo mean 2.56 (SD 0.64); P < 0.001) and reduced the numerical rating of anxiety in one trial with 54 participants (midazolam mean 17.3 (SD 18.58); placebo mean 49.3 (SD 29.46); P < 0.001). There was no difference in meta-analysis of results from both trials for risk of incomplete procedures (RR 0.14, 95% CI 0.02 to 1.12; downgraded to low-quality evidence).

Authors' conclusions

We found no high-quality evidence to determine if midazolam, when administered as the sole sedative agent prior to a procedure, produces more or less effective sedation than placebo or other medications. There is low-quality evidence that intravenous midazolam reduced anxiety when compared with placebo. There is inconsistent evidence that oral midazolam decreased anxiety during procedures compared with placebo. Intranasal midazolam did not reduce the risk of incomplete procedures, although anxiolysis and sedation were observed. There is moderate-quality evidence suggesting that oral midazolam produces less effective sedation than chloral hydrate for completion of procedures for children undergoing non-invasive diagnostic procedures.

PLAIN LANGUAGE SUMMARY

Midazolam for sedation before procedures

Review question

We wanted to find out whether midazolam makes medical procedures more comfortable for children and adults, as well as whether it makes the procedure easier to perform.

Background

Children and adults can become anxious during medical procedures and the procedures can be painful. Pain and anxiety can sometimes make the procedure more difficult to perform for the medical staff, due to movement or a lack of co-operation from the patient. Sedative medications, including midazolam, are used to reduce pain and anxiety. They can be injected directly into the bloodstream (with an almost immediate effect), injected into muscle tissue, given as a nasal spray, or swallowed as a tablet or solution.

Study characteristics

The evidence is up-to-date to January 2016. We included 30 trials involving 2319 participants. We looked at trials that compared midazolam with no active treatment ('dummy' treatment/placebo) or a different medication for sedation before a procedure. The trials

involved children and adults having procedures to diagnose medical problems rather than procedures for treatment of a disease. We disregarded trials where people received a general anaesthetic or other medications for sedation or pain relief in addition to midazolam during their procedure.

Key results

Midazolam administered into the bloodstream compared with other medications did not seem to make the participants more drowsy, reduce anxiety or pain, or make the procedure easier to perform. This is based on the low-quality evidence currently available. A potential benefit is that children and adults who received midazolam compared with no active treatment did not remember as much about the procedures. Midazolam made them drowsy, reduced anxiety and made it easier to perform a procedure. There is moderate-quality evidence that a solution of midazolam given to children to drink before a procedure was not as effective as a different medication called chloral hydrate. A nasal spray of midazolam before a procedure made the participants drowsy and reduced their anxiety, but this did not make it easier to perform procedures on them. This review cannot be used to assess the harms of midazolam for sedation before a procedure.

Quality of the evidence

We rated the evidence, in the main, as being of low quality. Particularly concerning was that many trials did not explain how participants were randomized to either midazolam or to a different treatment, and that the results did not give us a very clearly defined answer.