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The effectiveness of prophylactic doses of intravenous nitroglycerin in preventing the incidence of myocardial ischaemia under general anaesthesia; A systematic review and meta-analysis

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Background and Goal of Study:

Nitroglycerin (TNG) has been shown to reverse myocardial ischaemia (MI). Observational studies have suggested that prophylactic doses of intravenous TNG is effective in reducing the incidence of intraoperative MI. However, the results of previous randomised controlled trials are not convincing. As a result, the effectiveness of prophylactic TNG in the prevention of intraoperative MI remains controversial. The purpose of this study was to evaluate whether prophylactic intravenous TNG can prevent the incidence of intraoperative MI. In addition, we also analysed haemodynamic changes (heart rate [HR], mean blood pressure [MBP], and pulmonary capillary wedge pressure [PCWP]) from in both pre and post anaesthesia induction as an indicator of the decrease in preload.

Materials and Methods:

This quantitative systematic review was performed according to the criteria outlined in the PRISMA statement. A comprehensive literature search was conducted to identify clinical trials which involved the administration of TNG in comparison to a placebo. The data from the individual trials were combined and the DerSimonian and Laird random-effects model was used to calculate either the pooled Relative Risk (RR) or the demonstrated weighted mean difference (WMD) in addition to the corresponding 95% confidence intervals (CI). The data was analyzsed to clarify differences in the incidence of MI. We also analyzsed haemodynamic changes (HR, MBP, and PWCP) between TNG and the placebo. The heterogeneity of the results was examined by Cochrane’s Q and I² test.

Results:

The result of selective data

Using electronic databases, we initially identified 174 articles for review. Of these, 138 studies were excluded because they were unrelated studies. The other 36 articles were thoroughly checked to meet our inclusion criteria. Of these, 28 studies were excluded because they involved different drugs (n = 20) or included results that were unavailable (n = 10). Ultimately, 8 studies were identified by the defined search strategy, fulfilled the inclusion criteria and contained the necessary data for the planned comparison. The process of identifying eligible studies is illustrated in Figure 1, and the details of selected trials are summarized in Table 1.

Figure 1 Flow chart

Table 1 Characteristics of assessed studies.

Author	Year	Age	Concentration of administration of nitroglycerin	Preoperative cardiac complication	Type of surgery	Anesthesia methods	Diagnosis methods of MI
Mutch WAC	1982	TNG; 56 Control; 54	0.5µg/kg/min	Stable angina	CABG	Premedication; diazepam 0.15 mg/kg po, morphine 0.1mg/kg im, atropine 0.007 mg/kg im	Holter ECG
Thomson IR	1984	TNG; 54 Control; 56	0.5µg/kg/min	Stable angina	CABG	Premedication; diazepam 0.15 mg/kg po, morphine 0.1mg/kg im, atropine 0.007mg/kg im Anesthesia for induction; fentanyl 125 µg/kg, pancuronium 0.1 mg/kg Anesthesia for maintenance; fentanyl 50 (±α) µg/kg	Holter ECG
Gallagher ID	1986	TNG; 57 Control; 61	1.0µg/kg/min	CAD	CABG	Premedication; diazepam 5-10 mg po, morphine 0.1mg/kg (maximum dose 10 mg) im, scopalamine 0.01 mg/kg (maximum dose 0.4 mg) im, Anesthesia for induction; fentanyl 50 µg/kg, pancuronium 0.1 mg/kg Anesthesia for maintenance; fentanyl 75 µg/kg	ECG, Serum creatine phosphokinase
Fusciardi J	1986	TNG; 68 Control; 62	0.9µg/kg/min	Stable angina	Vascular operation	Premedication; scopalamine 0.007 mg/kg im, morphine 0.1 mg/kg im Anesthesia; thiopental 5-7 mg/kg, fentanyl 13 µg/kg, pancuronium 0.1 mg/kg	ECG, Electrocardiographic
Dodds TM	1993	TNG; 65 Control; 68	0.9µg/kg/min	CAD	Noncardiac surgery	N/R	Holter ECG
Lell W	1993	TNG; 60 Control; 59	1.0µg/kg/min or 2.0µg/kg/min	CAD	Myocardial revascularization (=CABG)	Premedication; diazepam 0.1 mg/kg im, morphine 0.075 mg/kg im, scopalamine 0.3-0.4 mg im Anesthesia for induction; midazolam 0.3-0.5 mg/kg pancuronium or vecuronium 0.1mg/kg Anesthesia for maintenance; fentanyl 50-75 µg/kg pancuronium 0.03mg/kg	Holter ECG
Apostolidou IA	1999	TNG; 64 Control; 62	0.5-1.0µg/kg/min	CAD	CABG	Premedication; lorazepam 1-2 mg po, morphine 0.05-0.1 mg/kg im or subcutaneous, scopalamine 0.2-0.4 mg im or subcutaneous Anesthesia for induction; etomidate, fentanyl 5-10 µ g/kg, isoflurane, vecuronium 0.15mg/kg Anesthesia for maintenance; fentanyl 4 µg/kg/h, pancuronium 30 µg/kg/h, isoflurane (end-tidal concentration, 0.5-1%, lorazepam IV (2-4 mg)	Holter ECG
Zvara DZ	2000	TNG; 65 Control; 68	2.0µg/kg/min	CAD	CABG	Premedication; none or diazepam 0.1mg/kg PO Anesthesia; fentanyl up to 25 µg/kg or sufentanil up to 3 µg/kg (total dose, including induction), midazolam up to 0.15 mg/kg (total dose, including induction), inhalation anesthesia (halothane, enflurane, or isoflurane, as required), propofol infusion, 10-50 µg/kg/min, as required, titration of neuromuscular blocking drugs using nerve stimulator	Holter ECG, Serum creatine kinase isozymes, Serum troponin I

TNG: nitroglycerin, CAD: coronary artery disease, CABG; coronary artery bypass grafting, ECG; electrocardiogram, MI; myocardial ischemia, N/R; not recorded

The result of analyses:

Using electronic databases, we selected 8 trials for our review. Prophylactic intravenous TNG did not result in a decreased incidence of MI (RR= 0.61; 95% CI, 0.33 to 1.13; p=0.12; I²=55, Cochran’s Q = 13.3) (Fig 2). In terms of haemodynamic changes pre and post anaesthesia induction, intravenous TNG significantly reduced the MBP in comparison to the placebo. MBP; pre induction; WMD = -7.27; 95% CI -14.2 to -0.33; P = 0.04; I² = 97%; Cochrane’s Q = 136.9, post induction; WMD = -0.60; 95% CI -10.3 to -2.09; P = 0.003; I² = 68%; Cochrane’s Q = 9.48) (Fig 3, 4). In terms of haemodynamic changes (HR and PCWP), the effects of TNG were also similar to those of placebo during both before and after anaesthesia induction.

Conclusions:

Our analysis showed that prophylactic intravenous TNG does not reduce the incidence of intraoperative MI. Prophylactic doses of intravenous TNG significantly reduced the MBP both pre and post anaesthesia induction. From these results, prophylactic intravenous TNG provided little clinical benefit as it was not effective preventing the incidence of intraoperative MI.