

INPLASY PROTOCOL

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None declared.

Lidocaine and oncologic outcomes— a systematic review from in vivo animal studies and clinical trials

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Review question / Objective: In vitro experiments have shown that lidocaine can inhibit cancer cellular viability, proliferation and migration, and induce cancer cell apoptosis, these cancer cells include breast cancer cell, hepatic cancer cell, gastric cancer cell, colon cancer cell, glioma cell, retinoblastoma, ovarian cancer and other cancer cells. whether lidocaine has the same anticancer efficacy in surgical patients is still unclear. Thus, we searched literatures to identify studies and conducted a systematic review on oncologic outcomes that examined: 1) lidocaine versus placebo or no treatment in exnograf models in vivo, 2) lidocaine versus placebo in surgical patients.

Information sources: The Pubmed, Cochrane Library, and Embase were searched from Jan 2000 to April 2022. The key terms included "lidocaine" or "lignocaine", "cancer" or "carcinoma", "oncologic outcome" or "recurrence" or "metastasis" or "survival", "in vivo" or "animal", "surgery", "clinical trials" or "clinical".

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 April 2022 and was last updated on 28 April 2022 (registration number INPLASY202240161).

INTRODUCTION

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exnograff models in vivo, 2) lidocaine versus placebo in surgical patients.

Condition being studied: Lidocaine, an amide local anesthetic agent, exerts its local anesthetic efficacy by blocking voltage-gated sodium channels. Perioperative intravenous administration of lidocaine can reduce intraoperative opioids usage, postoperative acute and chronic pain, perioperative inflammation, and postoperative complications such as PONV and POD[1-4]. It is becoming more and more popular in the perioperative period and contributing to more clinical benefits beyond local anesthetics. In vitro experiments have shown that lidocaine can inhibit cancer cellular viability, proliferation and migration, and induce cancer cell apoptosis, these cancer cells include breast cancer cell, hepatic cancer cell, gastric cancer cell, colon cancer cell, glioma cell, retinoblastoma, ovarian cancer and other cancer cells[5-11]. Lidocaine inhibits endothelial cell proliferation and angiogenesis[12], and enhances natural killer(NK) cell activity[13]. It has been confirmed that voltage-gated sodium channels are expressed in cancer cells and involved in cancer metastasis[14]. Therefore, lidocaine has a potential anticancer efficacy, and it is of a great promising prospect in cancer surgeries. The intravenous administration of lidocaine in the perioperative period can cause an average blood concentration of 1.5 uM[15], which is a very safe range and much lower than that in intoxication(21 uM)[16]. In vitro experiments, the concentration of lidocaine for causing significant anticancer effect ranges from 1 to 10 mM[5-11], that for increasing NK activity is about 50 uM[13], which are much higher than in clinical administration. This big difference makes it urgent to elucidate whether systemic administration of lidocaine can produce the similar anticancer effects in in vivo animals and in surgical patients to in vitro cancer cells. Thus, we searched literatures to identify studies and conducted a systematic review on oncologic outcomes that examined: 1) lidocaine versus placebo or no treatment in exnograff models in vivo,

2) lidocaine versus placebo in surgical patients.

METHODS

Participant or population: Animals inoculated with cancer cell lines and patients undergoing cancer surgery.

Intervention: Lidocaine intravenous administered.

Comparator: Placebo.

Study designs to be included: RCTs, prospective or retrospective observational studies.

Eligibility criteria: The inclusion criteria included 1) studies comparing lidocaine with placebo or no treatment in animals inoculated with cancer cell lines, 2) lidocaine was administered ip. or iv. in vivo studies after inoculation or during surgery, 3) studies comparing lidocaine with placebo in patients undergoing cancer surgery, 4) lidocaine was administered iv. or sb. intraoperatively with or without postoperatively, 5) RCTs, prospective or retrospective observational studies, 6) conference abstracts or correspondence with enough data were considered for eligibility. The exclusion criteria included 1) studies comparing lidocaine with other agents, 2) studies reporting lidocaine combined with other agents versus placebo or no treatment, 3) studies without full text, review articles or case reports.

Information sources: The Pubmed, Cochrane Library, and Embase were searched from Jan 2000 to April 2022. The key terms included "lidocaine" or "lignocaine", "cancer" or "carcinoma", "oncologic outcome" or "recurrence" or "metastasis" or "survival", "in vivo" or "animal", "surgery", "clinical trials" or "clinical".

Main outcome(s): Oncologic outcomes including OS (overall survival), DFS(disease-free survival), and recurrence in clinical studies, OS, metastasis, and tumor growth in in vivo animal studies.

Data management: The methodological quality was evaluated by the Newcastle-Ottawa Scale(NOS) for cohort studies and by the Jadad score for RCTs. The maximum NOS score was of 9 stars and the maximum Jadad score was 7.

Quality assessment / Risk of bias analysis: The methodological quality was evaluated by the Newcastle-Ottawa Scale(NOS) for cohort studies and by the Jadad score for RCTs. The maximum NOS score was of 9 stars and the maximum Jadad score was 7.

Strategy of data synthesis: The effect size for continuous data was expressed as the mean difference (MD) with 95% confidence interval (CI). The effect size for dichotomous outcomes was expressed as odds ratio (OR) with 95% CI. The between-study heterogeneity was qualified with the I² value, a fixed effect model was used in the case of homogeneity (I² < 50%), and a random effect model was chosen in the case of heterogeneity (I² ≥ 50%).

Subgroup analysis: Subgroup comparisons were performed when necessary to identify the sources.

Sensitivity analysis: Sensitivity analysis was also performed to test the robustness of the meta-analysis results.

Country(ies) involved: China.

Keywords: Lidocaine; cancer; oncologic outcomes; surgery.

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