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Review

Effect of paracetamol (acetaminophen) on body temperature in acute stroke: A meta-analysis

Junjie Fang [a], Chensong Chen [a], Hongsen Cheng [a], Ren Wang [a], Linhao Ma [b,*]

[a] Intensive Care Unit, Ningbo Fourth Hospital, Zhejiang, China
[b] Department of Critical Care & Emergency Medicine, Shanghai Changzheng Hospital, Shanghai, China

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ABSTRACT

Purpose: The objective of this study was to assess the efficacy of paracetamol (acetaminophen) on body temperature in acute stroke.

Methods: Medline, Cochrane Central Register of Controlled Trials, EMBASE, Chinese BioMedical Literature Database, China National Knowledge Infrastructure, and the World Health Organization (WHO) International Clinical Trials Registry Platform were searched electronically. Relevant journals and references of studies included were hand-searched for randomized controlled trials (RCT) and controlled clinical trials (CCT) regarding the efficacy of paracetamol (acetaminophen) on body temperature in acute stroke. Two reviewers independently performed data extraction and quality assessment. Data were analyzed using RevMan 5.3 software by the Cochrane Collaboration.

Results: Five studies were included. To compare the efficacy of paracetamol (acetaminophen) in acute stroke, the pooled RR (Risk Ratio) and its 95% CI of body temperature reduction at 24 h from the start of treatment were −0.3 (95% CI: −0.52 to −0.08), with statistical significance (P = 0.007). Consistently, the pooled RR (Risk Ratio) and its 95% CI of body temperature at 24 h from the start of treatment were −0.22 (−0.29, −0.15), with statistical significance (P < 0.00001). When analyzing the body temperature reduction after 5 days from the start of treatment, the pooled RR (Risk Ratio) and its 95% CI were 0.04 (95% CI: −0.20 to 0.29), with no statistical significance (P = 0.73). For functional outcome (mRS ≤ 2) analysis, the pooled RR and its 95% CI were 1.08 (0.88, 1.32), with no statistical significance (P = 0.45). In addition, the difference of serious adverse events between acetaminophen and placebo was 0.86 (95% CI: 0.62 to 1.2), with no statistical significance (P = 0.27).

Conclusion: Acetaminophen was revealed to have some favorable influence in body temperature reduction in acute stroke, but showed no important effect on improving functional outcome and reducing adverse events of patients.

What this paper adds: What is already known on this subject?
Paracetamol (acetaminophen) is one of the most commonly used antipyretic drugs and has some capability to reduce body temperature through acting on central nervous system.

What this study adds: Acetaminophen showed some capability to decrease body temperature for acute stroke.
Acetaminophen could not improve functional outcome and reduce adverse events of patients with acute stroke.

Contents

* Corresponding author.
E-mail addresses: drfangjunjie@163.com (J. Fang), ptccs@163.com (C. Chen), icuchs@126.com (H. Cheng), 75727646@qq.com (R. Wang), macro118@hotmail.com (L. Ma).

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1. Introduction

Many patients with acute stroke have fever or subfebrile body temperatures, and it has some association with case fatality and poor functional outcome [1-4]. Every degree increase of body temperature within 12 h of stroke onset indicates that the odds of poor outcome can be doubled [5]. Clinical outcome is associated with body temperatures measured in the first 12–24 h of stroke onset, but has no connection with initial stroke severity, lesion volume, age, sex, and stroke type [6-8]. And this relation may be mediated by the increased metabolic demands, an increased release of neurotransmitters, increased free-radical production, breakdown of the blood-brain barrier, and increased proteolysis caused by high body temperature [9].

Previous studies revealed that mitigation of even mild spontaneous hyperthermia had a favorable influence on neuroprotection in animal models of stroke, and was beneficial to have reduced infarct volume and improved functional outcome [10]. Reduction of body temperature and prevention of fever may have important potential in improving functional outcome after stroke onset. Indeed, guidelines for the treatment of acute ischaemic stroke and intracerebral haemorrhage have recommended antipyretic drugs to reduce body temperature in patients with fever or body temperature above 37.5 °C [11,12].

It is widely accepted that paracetamol (acetaminophen) is one of the most commonly used antipyretic drugs and is featured by potent inhibition of prostaglandin production in the CNS for reduction of body temperature [13-15]. In addition, paracetamol almost has no side-effects in doses up to 6 g per day [16]. One study reported that patients with acute ischaemic stroke obtained paracetamol at a daily dose of 6 g within 4 h, and the body temperature was reduced 0.3 °C within 4 h from start of treatment [17].

Clinically, several trials have focused on paracetamol (acetaminophen) for body temperature reduction in acute stroke. However, the evidence base for acetaminophen's reputation is not entirely obvious. The aim of this paper was to investigate the efficacy of acetaminophen in patients with acute stroke through a systematic review and meta-analysis.

2. Methods

2.1. Study eligibility criteria (PICOS)

2.1.1. Participants (P)

Patients with ischaemic stroke or intracerebral haemorrhage and body temperature >36 °C.

2.1.2. Intervention (I)

Intervention: paracetamol (acetaminophen).

2.1.3. Control (comparison) (C)

Control: placebo.

2.1.4. Outcome (O)

Primary outcomes:

- ◇ body temperature reduction at 24 h from the start of treatment
- ◇ body temperature at 24 h from the start of treatment
- ◇ body temperature reduction after 5 days from the start of treatment

Secondary outcomes:

- ◇ functional outcome (modified Rankin Scale, mRS ≤ 2)
- ◇ adverse events

2.1.5. Study design (S)

The studies selected for analysis were either randomized controlled trials (RCT) or controlled clinical trials (CCT). We did not use these terms as a restriction when searching the database, but filtered the articles by reading the abstract (and when necessary, the full-length article, or by contacting the authors) in order to classify the studies.

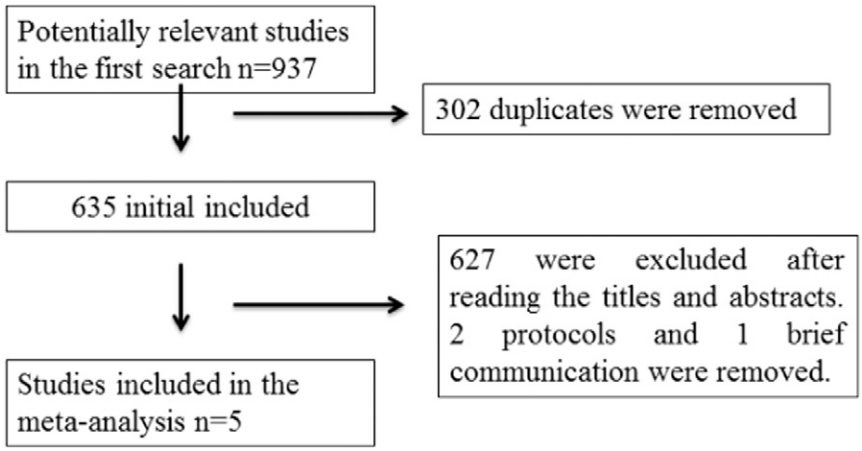

Fig. 1. Flow diagram of study searching and selection process.