# Caffeine for asthma

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## Background

-Caffeine has been widely consumed throughout the world for centuries.It is used for both non-medical and medical purposes.It is ubiquitous,being found in coffee,tea,cola-flavoured soft drinks and compound containing cocoa

-Caffeine has a variety of pharmacological effects; Caffeine belongs to a group of chemicals called methylxanthines

+Methylxanthines is possibly due to their inhibition of the enzyme phosphodiesterase which is a messenger within the cell that regulates many functions including the contraction and relaxation of smooth muscle.

+Methylxanthines are also competitive antagonists for adenosine receptors. One of the effects of adenosine, a chemical regulator, is that of bronchoconstriction

+ Methylxanthines are known to be weak bronchodilators and they also interact with respiratory muscles to reduce respiratory muscle fatigue, along with the bronchodilator drug theophylline.

- <u>There are two major reasons why it is important to know if caffeine is a bronchodilator</u>

+The first is because it may be beneficial for asthmatics to take caffeine in order to relieve the symtoms of asthma

+the second is because consuming caffeine may affect the results of important tests that determine how bad someone's asthma is

**O B J E C T I V E S**

1. To identify all published randomised controlled trials (RCT) of caffeine in the management of asthma.
2. To assess the methodological quality of these randomised controlled trials.
3. To estimate the overall effect of caffeine upon lung function and exhaled nitric oxide (FeNO).
4. To test whether there is a need to control for caffeine consumption prior to lung function testing and testing exhaled nitric oxide (FeNO).
5. To examine the need for further research into the effects of caffeine in asthma.

# M E T H O D S

## Criteria for considering studies for this review

### Types of studies

- We included randomised trials (RCTs) only.

### Types of participants

- We included adults (older than 18 years) with previously documented with mild to moderate asthma

### Types of interventions

- We included the following comparisons:

1. oral caffeine versus placebo; and
2. coffee versus decaffeinated coffee.

**Primary outcomes**

1. Lung function outcomes used were: forced expiratory volume in one second (FEV1), maximum mid-expiratory flow (FEF25-75) and specific airway conductance (Gaw/VL)
2. Exhaled nitric oxide concentration (FeNO)

**Secondary outcomes**

1. Forced vital capacity (FVC)
2. Maximal expiratory flow rates at 25% and 50% of vital capacity (Vmax50 and Vmax25 respectively)
3. Exercise-induced bronchoconstriction
4. Pulse
5. Blood pressure
6. Symptoms
7. Serum caffeine levels
8. Side effects and adverse effects.

**RESULTS**

Interventions

-Caffeine and matched placebos were administered orally (as solution = three studies, capsule = two studies , decaffeinated coffee plus caffeine = one study, caffeine versus decaffeinated coffee = one study)

-Two studies contributed to the 'low' dose comparison:

Bukowskyj 1987(5mg/kg) & Colacone 1990 (5 mg/kg).

-Four studies contributed to the high' dose comparison: Crivelli 1986 (6 mg/kg), Duffy 1991 (10 mg/kg), Gong 1986 (7.2 mg/kg) and Kivity 1990 (7 mg/kg).

-one study,Taylor 2004,assessed drinking a cup of coffee (prepared using a standard quantity-15 g-of either caffeine-containing)versus decaffeinated coffee

**Main results**

- We included seven trials involving people with mild to moderate asthma

- Six trials involving people showed that in comparison with placebo, caffeine, even at a 'low dose' (less than 5 mg/kg body weight), appears to improve lung function for up to two hours after consumption . FEV1 showed a small improvement up to two hours after caffeine ingestion (standardised mean difference 0.72; 95% confidence interval 0.25 to 1.20) which translates into a 5% mean difference in FEV1.

-However in two studies the mean differences in FEV1 were 12% and 18% after caffeine, FEF 25-75 also showed a small improvement with caffeine and this was sustained up to four hours

**Subgroup analysis: 'low' dose**

-All lung function parameters tended to improve post caffeine ingestion compared to placebo

+For FEV1, this effect was clear only at the 'short' time frame(up to 2 h)

+For FEF25-75, the difference was clear at all times

**Subgroup analysis: 'high' dose**

-Lung function was found to improve following a 'high' dose of caffeine compared to placebo for all measured outcomes.

+For FEV1 and FEF25-75 ,this effect was clear only at the 'short' time frame only.

+A clear improvement in Gaw/VL was also seen at the 'short' time frame(up to 2 h)

-The papers differed in their reporting of serum caffeine levels

<u>After a dose of caffeine (5 mg/kg)</u>

+Bukowskyj 1987 reported a peak serum level of 8.7 (SD= 1.7)µg/mL one hour after ingestion.

+Colacone 1990 used the same dose and reported a mean (but not peak) level of 5.4 (SD= 1.23) µg/mL at 1 hour 45 minutes

<u>After a dose of cafeine(10 mg/kg)</u>

+Duffy 1991 reported that peak serum levels of caffeine (mean 18.8; 95% CI 12.4 to 25.2 mg/L ) were observed 45 to 60 minutes

+Taylor 2004 reported that at 60 minutes, serum caffeine levels were higher after ingesting regular caffeine-containing coffee than after decaffeinated coffee at 60 minutes (3.9 versus 0.4 mg/mL respectively).

**Side effects and adverse effects**

-Five of the studies commented on side effects, including heart rate and blood pressure changes

+No side effects were reported after 'low' doses of caffeine.

+ After ingestion of a 'high' dose of caffeine some patients reported mild tremor (Kivity 1990), nervousness and gastrointestinal upset (Gong 1986), and some of them withdrew from the study because of nervousness and agitation (Duffy 1991), which was presumed to be due to the caffeine.

- Only one study (Gong 1986) reported significant changes in heart rate (a decrease up to 9%) and blood pressure (an increase up to 12%).

**Outcomes relating to exhaled nitric oxide**

-The impact of caffeine on FeNO was assessed in one study of Taylor2004.This study reported no significant difference in exhaled nitric oxide (data reported in the text as non significant (P=0.38) and presented graphically)

-Findings were not significantly different in subgroups for those treated with inhaled steroids and those not treated with steroids.

## A U T H O R S ' C O N C L U S I O N S

**Implications for practice**

-Caffeine, even at 'low' doses, has been found to improve lung

function for at least four hours after ingestion.

-The most sensitive outcome FEF25-75 showed that effects are sustained for over four hours post ingestion. It is therefore recommended that patients be advised to withhold caffeine for at least four hours prior to lung function testing

- Caffeine does not appear to have a significant effect on exhaled nitric oxide levels.

-This was not the purpose of trials examined in this review. It is not known if tolerance to the bronchodilatory effects of caffeine develops in habitual consumers

-The amount of dietary caffeine required and the true benefit of dietary caffeine intake would be difficult to calculate due to the varying levels of caffeine within different foods and beverages.It appears that a substantial intake of caffeinated products would be needed to achieve a beneficial bronchodilatory effect and that possible undesirable side effects may outweigh the benefits.

**Implications for research**

That caffeine has a bronchodilatory effect in asthma is clear from existing research. Future studies could address the following.

1. Patients' perception of the effect of caffeine on their asthma and quality of life, as this has not been systematically studied.
2. The maximum length of time at which bronchodilation is sustained, as this cannot be determined from existing trials.
3. Effects on patients with different levels of asthma severity, since existing trials have only studied people with mild to moderate asthma.
4. The response to caffeine of people with well-controlled asthmatics on anti-inflammatory agents. Asthmatics using inhaled steroids may be less responsive and this needs further evaluation.
5. Differences in the bronchodilator effects of caffeine between habitual consumers and non-consumers.
6. Whether caffeine ingestion alters management decisions in asthma (based on lung function measurements).

## REFERENCES

### References to studies included in this review


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Thank you for your attention and listening