

Timing of Blood Pressure Measurement Related to Caffeine Consumption

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Request

Should patients wait 30 minutes after consuming caffeine before having their blood pressure measured?

Response

BACKGROUND

Hypertension affects approximately 50–65 million Americans, leading to significant morbidity and mortality from associated conditions such as coronary artery disease, stroke, and heart failure.^{1,2} Blood pressure measurements are integral to the identification and effective management of hypertension¹; therefore, accurate measurements are needed.

Caffeine has been found to impact blood pressure acutely^{3,4}; this effect has brought into question the timing of caffeine consumption related to blood pressure measurement.¹ Caffeine's most important effect is inhibition of adenosine receptors.^{3–5} Adenosine causes vasodilation in various regions of the body.³ Inhibition of adenosine not only brings about a reduction in this vasodilation, but may lead to the release of neurotransmitters (eg, norepinephrine, dopamine, acetylcholine, glutamate, γ -aminobutyric acid), with the greatest impact on the excitatory neurotransmitters. Caffeine also increases the functioning of the sympathetic nervous system, adrenal cortex, and possibly renin-an-

OBJECTIVE: To determine whether patients should wait 30 minutes after caffeine consumption to have their blood pressure measured.

DATA SOURCES: Literature was obtained by searching MEDLINE (1980–September 2007), *International Pharmaceutical Abstracts* (1980–September 2007), and the Cochrane Database of Systematic Reviews (1994–September 2007). Search terms included caffeine and blood pressure. Literature was also obtained from citations in relevant articles.

STUDY SELECTION AND DATA EXTRACTION: Articles that examined caffeine's acute effect on blood pressure were reviewed, with additional focus on caffeine tolerance and hypertensive status.

DATA SYNTHESIS: Caffeine appears to affect blood pressure through adenosine receptor inhibition and an increased release of select neurotransmitters. Caffeine levels peak 30–120 minutes after oral intake and caffeine's half-life is 3–6 hours. The effect of caffeine on blood pressure has been examined for decades, with variable results depending on factors such as population examined (eg, hypertensive status, physical stressors, age) and study design (eg, acute effects, chronic ingestion, retrospective epidemiologic review). Caffeine tolerance diminishes the acute effect of caffeine on blood pressure, and hypertensive individuals are more susceptible to blood pressure changes. Reviews of caffeine's acute effect on blood pressure indicate changes of 3–15 mm Hg systolic and 4–13 mm Hg diastolic. Typically, blood pressure changes occur within 30 minutes, peak in 1–2 hours, and may persist for more than 4 hours.

CONCLUSIONS: Having a patient abstain from caffeine for 30 minutes prior to blood pressure monitoring is not adequate to avoid caffeine's potential effects. An alternative approach to blood pressure monitoring would be to ask the patient about recent caffeine consumption and interpret the blood pressure reading based on this information. In addition, healthcare practitioners should provide education regarding caffeine's effects.

KEY WORDS: blood pressure, caffeine, measurement.

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giotensin system. These actions may contribute to the overall propensity of caffeine to increase blood pressure. Inhibition of phosphodiesterase, the enzyme responsible for the inactivation of cyclic 3,5-adenosine monophosphate (cAMP),⁶ does not occur with the caffeine blood levels achieved from 2–3 cups of coffee and, therefore, does not typically pro-

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duce caffeine's pressor effect.³ Overall, caffeine's pharmacologic activity is consistent with blood pressure elevation.

Caffeinated beverages are consumed by 90% of the US population,⁷ with exposure typically beginning before birth and continuing throughout the person's life.⁴ Average caffeine consumption has been reported in the range of 2–4 cups (4 mg/kg) of coffee per day.⁷ Caffeine content varies greatly among beverages; the caffeine content in 6 ounces of brewed coffee is 100–150 mg, instant coffee 60–80 mg, tea 40–100 mg, and cola 17–55 mg.⁶

In their seventh report, the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommended that, "Caffeine...should be avoided for at least 30 minutes prior to measurement" (of blood pressure).¹ This is consistent with recommendations from the World Hypertension League⁸ and the American Academy of Family Physicians.⁹ Similarly, avoidance of all potentially complicating factors (including caffeine) for one hour before blood pressure monitoring is suggested by the American Society of Hypertension.¹⁰ Practitioners attempting to comply with these recommendations often have patients delay blood pressure monitoring for 30 minutes after caffeine intake. However, consideration of the pharmacokinetic features of caffeine^{6,11} brought this practice into question and prompted a review of the literature. Our literature searches yielded 33 articles whose titles appeared to focus solely on the acute effect of caffeine on blood pressure. However, on further review we discovered that the majority of these articles included examination of at least one additional variable. Based on these findings, we consulted review articles for summative information regarding caffeine's effect on blood pressure and used individual studies to discuss the issues of tolerance and the impact of underlying blood pressure on caffeine's blood pressure effects.

CAFFEINE PHARMACOKINETICS

When administered orally, caffeine is readily absorbed into the bloodstream, where it is quickly distributed into tissues, including the central nervous system.⁶ Peak plasma concentrations have been reported in the range of 30–120 minutes following administration.^{3,4,6,11–13} Caffeine is hepatically metabolized via CYP1A^{2,5,6} with minimal renal elimination of caffeine itself (1% excreted unchanged).^{6,11} The elimination half-life of caffeine is approximately 3–6 hours^{3,5,6,11,14} but may vary significantly^{3,5} and may be longer with larger doses. For example, one study demonstrated a half-life of 4 hours with a 250 mg dose versus a half-life of 4.7 hours with a 500 mg dose ($p < 0.05$).¹¹ This may be due in part to saturation of the enzyme system responsible for caffeine's metabolism.³ Various other factors have been found to influence metabolism, such as tobacco use, which increases caffeine clearance.⁵ Conversely, preg-

nant women and those taking oral contraceptives are reported to metabolize caffeine more slowly, leading to a prolonged half-life.^{3,5,11} Theobromine, theophylline, and paraxanthine are active metabolites of caffeine,¹¹ with the latter demonstrating a blood pressure-elevating effect.³ Therefore, based on caffeine's pharmacokinetic profile, we would expect caffeine to produce its maximum effect between 30 minutes and 2 hours after ingestion, and this effect would potentially persist for hours, based on the half-life. However, many factors may influence caffeine's clearance and produce a great deal of individual variation.^{3,11}

LITERATURE REVIEW

Caffeine's effect on blood pressure has been studied for many decades^{3,4} and, at times, the results from these studies have been contradictory.¹⁵ These differences may be due in part to the various ways that caffeine's effect on blood pressure has been examined. Studies have measured the response of blood pressure to variables such as chronic caffeine consumption, acute caffeine intake, caffeine combined with factors such as physical and psychological challenges (eg, exercise, mental arithmetic), and self-reported caffeine use evaluated via epidemiologic studies.^{3,4} In order to answer the question of caffeine consumption and timing of blood pressure monitoring, our review focused primarily on the acute effects of caffeine on blood pressure.

Timing of Blood Pressure Elevation

The time frame within which blood pressure becomes elevated after caffeine consumption is critical when making a recommendation regarding the timing of blood pressure monitoring in relation to caffeine intake. Research has shown that blood pressure values begin to increase 30 minutes after caffeine ingestion and peak between 1 and 2 hours.³ This is consistent with caffeine's pharmacokinetic profile,^{3,6,11} although there is a great deal of pharmacokinetic heterogeneity among individuals.^{3,15} Regarding the persistence of caffeine's acute effect on blood pressure, it has been reported that the effect may be apparent for more than 4 hours after intake.³ However, longer periods may be required to fully eliminate the blood pressure effect from caffeine use.⁴

Magnitude of Blood Pressure Change

A review that included 20 studies assessing the acute impact of caffeine on normotensive patients reported systolic blood pressure increases that ranged from 3 to 14 mm Hg and diastolic increases that ranged between 4 and 13 mm Hg.³ Similarly, a review of 24 articles reported acute increases in systolic blood pressure between 5 and 15 mm Hg and diastolic increases of 5 to 10 mm Hg.⁴ Variables that have been identified and account for such broad

ranges include dose,¹⁶ hypertensive status (greater increase in hypertensive patients),^{3,4,17-19} age (greater elevation with advanced age³ and in younger patients^{16,20}), physical or psychological stress,^{3,4} past caffeine use,³ tolerance,^{7,12} source of caffeine (less elevation with dietary versus tablet source), and coffee-making method (eg, boiled, filtered, instant, in descending order of effect).²¹

Two meta-analyses reviewed the effect of chronic caffeine consumption on blood pressure. Noordzij et al.²¹ defined chronic caffeine consumption as regular intake for 7 or more days, while Jee et al.¹⁶ required a study duration of 24 hours or more. In these meta-analyses, the blood pressure changes found in individual studies ranged from -2.1 to 12 mm Hg systolic and from -2.4 to 5.0 mm Hg diastolic.^{16,21} The pooled results varied from a change in systolic pressure of 2.04-2.4 mm Hg and in diastolic pressure of 0.73-1.2 mm Hg.

Dose has an important effect on blood pressure changes and must be considered. Jee et al.¹⁶ reported that each cup of coffee led to an incremental elevation in blood pressure (0.8 mm Hg systolic and 0.5 mm Hg diastolic per cup). In addition, pooled results showed that for studies ($n = 4$) in which participants consumed 1-4½ cups of coffee a day, systolic blood pressure was increased 0.1 mm Hg (95% CI -2.1 to 2.3) and diastolic blood pressure was increased 1.0 mm Hg (95% CI -1.1 to 3.0). However, for studies ($n = 7$) in which participants consumed 5 or more cups of coffee a day, the systolic increase was 3.2 mm Hg (95% CI 1.8 to 4.6) and diastolic increase was 1.4 mm Hg (95% CI 0.5 to 2.3).

Tolerance

The effect of chronic caffeine consumption is relevant to the discussion of caffeine and blood pressure timing because the acute effects often occur in patients who are chronically consuming caffeine; therefore, tolerance must be considered. Tolerance has been examined in studies that sampled 85 ambulatory¹² and 97 laboratory⁷ based normotensive adults. The studies measured acute blood pressure changes induced by a caffeine challenge (3 doses of 250 mg in one day) following 5 days of placebo or caffeine 300 or 600 mg/day.^{7,12} Caffeine and placebo were provided in gelatin capsules. The low tolerance group was identified as the portion of the subjects whose blood pressure elevation from the caffeine challenge following 5 days of caffeine 600 mg/day was above the median. The remaining half (high tolerance group) had a diminished blood pressure response to the caffeine challenge. In the ambulatory study, the blood pressures of the low tolerance group while awake demonstrated caffeine-induced elevation of 4.6 mm Hg systolic and 5.2 mm Hg diastolic following 5 days of placebo versus 2.8 mm Hg systolic and 2.2 mm Hg diastolic after 5 days of caffeine 300 mg/day.¹² The high tolerance group had a blood pressure elevation of

3.7 mm Hg systolic and 4.4 mm Hg diastolic after 5 days of placebo versus no significant elevation after 5 days of caffeine intake. Neither group had a statistically significant elevation after 5 days of caffeine 600 mg/day. Based on these results, patients who consume caffeine regularly for a short period of time will vary as to the degree of blood pressure tolerance that develops.

Tolerance to caffeine brings into question the impact on blood pressure levels of discontinuing chronic caffeine use. James⁴ stated that discontinuing caffeine for 10-12 hours may avoid the pressor effect and blood pressure values may actually fall 12-24 hours after cessation. However, the latter has not been consistently demonstrated.³ Nurminen et al.³ identified 4 studies showing that blood pressure dropped 2-5 mm Hg after caffeine cessation, while 5 other investigations did not find any significant alteration in blood pressure following discontinuation. It has been suggested that "more than a day" is required to totally remove the effect of chronic caffeine use.⁴

Hypertensive Status

When evaluating caffeine's impact on blood pressure elevation, it is important to consider the individual's blood pressure status. Three studies examined patients with elevated blood pressure compared with a normotensive control group and found that patients with higher baseline blood pressures had a greater acute increase in blood pressure¹⁷ (diastolic only^{18,19}) associated with caffeine use.

Hartley et al.¹⁷ examined 182 men who were placed into the following categories based on their initial blood pressure screening status: optimal (<120/80 mm Hg), normal (120-129/80-84), high-normal (130-139/85-89), stage 1 hypertension (140-159/90-99), and previously diagnosed hypertension. Subjects abstained from caffeine for at least 12 hours and had their blood pressure checked at baseline and 45-60 minutes after caffeine ingestion (anhydrous caffeine 3.3 mg/kg added to grapefruit juice). While systolic and diastolic blood pressures were elevated in every group, the magnitude of elevation was dependent on pre-existing blood pressure status. In fact, there was more than a 1.5-fold greater increase in blood pressure values from caffeine in patients diagnosed with hypertension versus in those with an optimal blood pressure. The key finding here is that even small changes in baseline blood pressure may cause a patient to be more sensitive to the effects of caffeine.

Two additional studies by Sung et al.¹⁹ and Pincomb et al.¹⁸ compared hypertensive (mild and borderline) and normotensive men. Both studies required a 12 hour period of abstinence and a caffeine dose of 3.3 mg/kg mixed with grapefruit juice. These studies found a larger increase in diastolic pressure for hypertensive patients versus controls (a two- to threefold greater increase according to Pincomb et al.¹⁸), but this was not true for systolic blood pressure.^{18,19} In

addition, Pincomb et al.¹⁸ found that one-third of the borderline hypertensive patients had hypertensive readings (140–160/>90 mm Hg) 40 minutes after caffeine ingestion; this was true for both the systolic and diastolic readings.

Literature Limitations

While caffeine's acute and chronic effects on blood pressure have been studied for decades, there are significant limitations to the research. First, many of these studies involved very small samples. For example, of the 19 studies included in the 2 meta-analyses examining chronic caffeine consumption on blood pressure, only 3 exceeded 100 patients and 4 studies included fewer than 20 patients.^{16,21} Second, the dosage of caffeine differed greatly among the trials, as did the units of measurement (eg, mg/kg doses, fixed mg doses regardless of weight, specific number of cups of coffee).³ These variations in dosage would be expected to produce differences in the magnitude of blood pressure changes. Third, many studies looked at the impact of an additional variable (eg, stress, age) combined with caffeine consumption, which complicates the analysis of caffeine's effect on blood pressure but highlights actual scenarios that occur with caffeine use.^{3,4} Fourth, studies are not consistent in their requirements for patients to abstain from factors that also may affect blood pressure, such as the use of alcohol or cigarettes.^{18,19} Fifth, some studies were carried out in a laboratory setting while others used ambulatory blood pressure monitoring outside of a laboratory.^{7,12,15,17-20} Although variables are more easily controlled in the former, the latter setting is more consistent with actual blood pressure in a patient's daily routine. Sixth, study designs have varied greatly and may influence the potential to extrapolate the results beyond the sample. For example, in the 19 investigations examined in the meta-analyses on chronic caffeine intake, only 7 had a double-blind crossover design.^{16,21} Seventh, the impact of tolerance was studied by administering caffeine after only 5 days of caffeine consumption, which may not be consistent with the impact of acute ingestion following longer periods of caffeine intake.^{7,12} These limitations complicate analysis and must be considered in examining the research, but they do not negate the consistent findings related to blood pressure elevation following acute ingestion of caffeine.

Discussion

The literature indicates that there is an elevation in blood pressure following the acute consumption of caffeine,^{3,4} which is consistent with caffeine's pharmacologic and pharmacokinetic profile.³ The current recommendation is that caffeine be avoided for 30 minutes prior to a blood pressure measurement.^{1,8,9} This practice does not appear sufficient to avoid caffeine's effect because patients who have consumed caffeine in the previous 30–120 min-

utes typically experience an elevation and peak change in blood pressure during this time frame.³ If the intention is to minimize the impact of caffeine, then a much longer period must be allowed after caffeine is consumed. Hartley et al.¹⁷ noted a similar concern; their data indicated that interference would last at least 60 minutes after caffeine consumption. However, 60 minutes also appears too short, because this would coincide with the time frame in which the peak blood pressure effect is usually observed.³

One must keep in mind that individuals vary greatly in the magnitude of their blood pressure response to caffeine; this is dependent on factors such as hypertensive status, age, stressors, and tolerance.^{3,7,12} For example, patients with elevated blood pressures typically experience a greater effect from caffeine¹⁷⁻¹⁹ and patients who develop tolerance may see minimal to no change in blood pressure with caffeine.^{7,12}

The requirement for a set time frame between caffeine consumption and blood pressure measurement may needlessly delay measurement and may result in patients foregoing the procedure altogether. Interestingly, recommendations from the American Heart Association's Council on High Blood Pressure Research do not even mention caffeine as a factor to consider when performing blood pressure monitoring.² A better approach may be to simply question the patient as to his/her daily caffeine intake and determine when the patient consumed caffeine last. This knowledge will help to more appropriately interpret blood pressure values.

Summary

Caffeine ingestion has been found to elevate blood pressure acutely (3–15 mm Hg systolic and 4–13 mm Hg diastolic), with values peaking in 30–120 minutes and persisting for hours.^{3,4} Therefore, abstaining from caffeine for 30 minutes prior to blood pressure monitoring is not adequate to avoid caffeine's acute blood pressure elevation. A preferred approach would be to ask the patient about recent caffeine consumption and interpret the blood pressure reading based on this information.

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El Tiempo de la Medida de Presión Sanguínea Relacionado al Consumo de Caféina

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EXTRACTO

OBJETIVO: Determinar si los pacientes deben esperar 30 minutos luego del consumo de cafeína para tomarse la medida de presión sanguínea.

FUENTES DE INFORMACIÓN: Se realizó una búsqueda de la literatura en el sistema MEDLINE (1980–septiembre 2007), *Abstractos Farmacéuticos*

Internacionales (1980–septiembre 2007), y en la base de datos Cochrane de Revisiones Sistemáticas (1994–septiembre 2007). La búsqueda de términos incluyó cafeína y presión sanguínea. La literatura también fue obtenida de citas en artículos relevantes.

SELECCIÓN DE FUENTES DE INFORMACIÓN Y MÉTODOS DE EXTRACCIÓN DE INFORMACIÓN: Se revisaron artículos que examinaron el efecto agudo de la cafeína en la presión sanguínea, con un enfoque adicional en la tolerancia a cafeína y el estado hipertensivo.

SÍNTESIS: La cafeína aparenta afectar la presión sanguínea a través de la inhibición de los receptores de adenosina y el aumento en la liberación de varios neurotransmisores. Los niveles de cafeína llegan a su pico en 30–120 minutos luego del consumo oral y la vida media de la cafeína es de 3–6 horas. El efecto de la cafeína en la presión sanguínea se ha examinado por décadas con resultados variables dependiendo de factores como, la población examinada (por ejemplo, estado hipertensivo, estresores físicos, edad) y el diseño de los estudios (por ejemplo, efectos agudos, ingesta crónica o revisión epidemiológica retrospectiva). La tolerancia a la cafeína disminuye el efecto agudo de la cafeína en la presión sanguínea, e individuos hipertensos son más susceptibles a cambios en presión sanguínea. Revisiones del efecto agudo de la cafeína en la presión sanguínea indican cambios de 3–15 mm Hg en sístole y de 4–13 mm Hg en diástole. Cambios en la presión sanguínea ocurren típicamente dentro de 30 minutos, llega a su pico en 1–2 horas y puede persistir por más de 4 horas.

CONCLUSIONES: El abstenerse del consumo de cafeína 30 minutos antes del monitoreo de la presión sanguínea no es adecuado para evitar los potenciales efectos de la cafeína. Un acercamiento que sirve como alternativa en el monitoreo de la presión sanguínea sería el preguntarle al paciente sobre el consumo reciente de cafeína e interpretar la lectura de la presión sanguínea basado en esta información. En adición, los profesionales de la salud deben proveer educación considerando los efectos de la cafeína.

Traducido por Jennifer Guzmán

Le Temps de Prise de la Tension Artérielle en Lien avec la Consommation de Caféine

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RÉSUMÉ

OBJECTIF: Préciser s'il est suffisant, pour les patients qui ont consommé de la caféine, d'attendre 30 minutes avant qu'une mesure de la tension artérielle ne soit faite, afin que celle-ci soit la plus précise possible.

REVUE DE LITTÉRATURE: Une recherche de la littérature médicale a été faite dans les banques de données informatisées MEDLINE (1980–septembre 2007), *International Pharmaceutique Résumé* (1980–septembre 2007), ainsi que dans la base de données Cochrane portant sur les revues systématiques de sujets particuliers (1994–septembre 2007). Les mots-clé utilisés étaient caféine et tension artérielle. Les articles cités en référence dans les articles identifiés par cette recherche ont aussi été retenus.

SÉLECTION DES ÉTUDES ET DE L'INFORMATION: Les articles traitant des effets immédiats de la caféine sur la tension artérielle ont été revus, tout en portant une attention particulière sur la tolérance à la caféine et le degré d'hypertension.

RÉSUMÉ: La caféine semble influencer la tension artérielle par inhibition des récepteurs de l'adénosine et par augmentation de la libération de certains neurotransmetteurs comme la noradrénaline, la dopamine, l'acétylcholine glutamate et l'acide γ -aminobutyrique. Les niveaux sériques de caféine plafonnent de 30–120 minutes après la prise orale et la demi-vie plasmatique de la caféine est de 3–6 heures. L'effet de la caféine sur la tension artérielle a été évalué pendant plusieurs décennies et les résultats sont variables, en raison des divers facteurs populationnels qui ont été pris en considération (statut hypertensif, stressseurs physiques, âge) et en raison du devis des études (effets immédiats, ingestion chronique ou étude épidémiologique rétrospective). Faits intéressants à noter, la tolérance à la caféine amoindrit les effets immédiats sur la tension

artérielle et les individus hypertendus sont plus sensibles à des variations de la tension artérielle. La revue de toutes les données montre des variations de 3–15 mm Hg de la tension systolique et de 4–13 mm Hg de la tension diastolique. Habituellement, les variations de la tension artérielle surviennent dans les 30 minutes suivant la prise de caféine, sont à leur maxima en 1–2 heures et peuvent persister plus de 4 heures.

CONCLUSIONS: S'abstenir de prendre de la caféine 30 minutes avant la prise de la tension artérielle n'est pas adéquat pour éliminer les variations causées par la caféine. Une approche possible de suivi de la tension artérielle serait de demander au patient sa consommation récente de caféine et d'interpréter les mesures de la tension artérielle en tenant compte de cette information. De plus, les professionnels de la santé devraient éduquer les patients sur les effets de la caféine sur la tension artérielle.

Traduit par Denyse Demers

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