Anti-Hypertensive Therapy and Risk Factors Associated with Hypotension during Colonoscopy under Conscious Sedation*

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Abstract

Background & Aims: Pre-operative use of select anti-hypertensive therapy has been associated with peri-operative hypotension in the surgical setting. Our aim was to determine the effect of anti-hypertensive medications on blood pressure (BP) and procedural outcomes in gastrointestinal endoscopy. **Methods**: Our study was a prospective, cross-sectional survey of outpatients undergoing colonoscopy with conscious sedation. We enrolled patients with hypertension that took anti-hypertensive medications within 24 hours of the procedure and patients without hypertension that were not on BP-lowering agents. We recorded mean BP prior to, during, and after the procedure. **Results**: 626 patients (338 males; mean age 56.0 ± 10.4 years) were enrolled, and 158 patients were on anti-hypertensive therapy. There were 57 patients who developed hypotension, defined as systolic BP <90 mmHg and/or diastolic BP <60 mmHg, during the colonoscopy. Taking a BP medication, regardless of class, was not associated with an increased risk of procedural hypotension (all p >0.05). Age, body mass index, gender, duration, fentanyl dose, midazolam dose, and co-morbidities (asthma, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease) were also not associated (all p >0.05). Instead, a lower pre-procedure systolic BP (OR=0.97, 95% CI=0.95-0.99; p=0.004) and diastolic BP (OR=0.95, 95% CI=0.92-0.97; p<0.001) were identified as the only risk factors. **Conclusion**: Patients should continue their anti-hypertensive therapy leading up to endoscopy. A lower pre-procedure BP is the main risk factor for procedural hypotension in patients undergoing colonoscopy with conscious sedation. Future studies should explore other factors, such as bowel preparation, that can affect pre-procedure BP.

Introduction

Patient sedation is standard practice for gastrointestinal endoscopy. In the United States, 98% of upper and lower endoscopic examinations are performed with sedative medications [1]. Three quarters of these procedures are done under conscious sedation, while the remaining are performed using deep sedation [1, 2]. The use of sedative agents is on the rise worldwide, although rates vary greatly across continents [3]. Sedation is generally safe, but associated cardiopulmonary events remain a leading cause of morbidity and mortality [4]. Cardiac and pulmonary complications related to sedation, such as hypotension and hypoxemia [5-8] have been reported with an overall frequency of 90 per 1,000 procedures [4].

There are currently no evidence-based guidelines in endoscopy regarding whether anti-hypertensive therapy should be continued prior to examination. The American College of Cardiology, American Heart Association, and the European Society of Cardiology advise caution in the continuation of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) in the morning of non-cardiac surgery under anesthesia [9, 10]. Other authors believe that diuretics should be held as well pre-operatively [11]. Patients on ACE inhibitors and ARBs appear to be at higher risk of intra-operative hypotension [12-15], while patients on diuretics can develop cardiac arrhythmias from electrolyte imbalances [11]. Recommendations that are endorsed for surgery have not been fully evaluated for gastrointestinal endoscopy.

Therefore, the goal of this prospective study is to determine the impact of anti-hypertensive medications on blood pressure and procedural outcomes.

Patients and methods

Overview

This study was a prospective, cross-sectional survey of outpatients undergoing colonoscopy for any indication at Temple University Hospital's Digestive Diseases Center (Fig. 1). We did not include inpatients or any patient felt by the investigators to have an urgent or emergent need for colonoscopy. We only studied examinations performed under the administration of conscious sedation with fentanyl and midazolam (Versed, Baxter, Deerfield, IL). Patients who had a history of hypertension or had taken an anti-hypertensive medication within 24 hours of the procedure were identified. Patients who were on anti-hypertensive medications, but were non-compliant or had not taken them within 24 hours of the colonoscopy, were considered to be off therapy and excluded. Patients undergoing multiple procedures (e.g. colonoscopy with upper endoscopy), receiving propofol or supplemental sedatives (e.g. diphenhydramine), or who had had an incomplete colonoscopy (e.g. aborted endoscopic exam due to poor bowel preparation) were excluded from analysis. Patients with current benzodiazepine or narcotic medication use, decompensated liver disease, diarrhea, inflammatory bowel disease, or end stage renal disease on dialysis were also excluded. All patients received a bowel preparation with polyethylene glycol solution (Golytely, Braintree Laboratories Inc., Braintree, MA) in the day prior to colonoscopy.

Blood pressure medications

Upon arrival at the pre-procedure area, all patients were evaluated by a registered nurse and physician to clarify past medical history and to reconcile current medications. Co-morbidities, which included asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure, and coronary artery disease, were documented. For patients taking anti-hypertensive medications, further details (name, dose, last time medication taken) were gathered. If a patient did not recall the name or dose of an anti-hypertensive drug, review of electronic medical records and a call to the patient's pharmacy were performed. We restricted our inclusion criteria to patients taking anti-hypertensive therapy to the following classes: ACE inhibitor, ARB, beta blocker (BB), calcium channel blocker (CCB), and diuretic. Drugs from other classes were rarely used in our patients, and we anticipated too few patients for a meaningful analysis.

Pre-procedure

Patients were affixed with a Masimo SET pulse oximeter (Masimo Corporation, Irvine, CA), cardiac leads for continuous electrocardiographic monitoring, and an automated blood pressure cuff. These were connected to a Datascope Passport 2 monitor (Datascope Corporation, Fairfield, NJ) throughout the patient's stay. Vital signs (blood pressure, heart rate, respiratory rate, oxygen saturation) were charted automatically in Provation MD software (Provation Medical, Minneapolis, MN) every four minutes. Pre-procedure vital signs were defined as all readings from the time the patient was connected to the Datascope Passport 2 monitor in the pre-procedure area until the commencement of sedation in the endoscopy room.
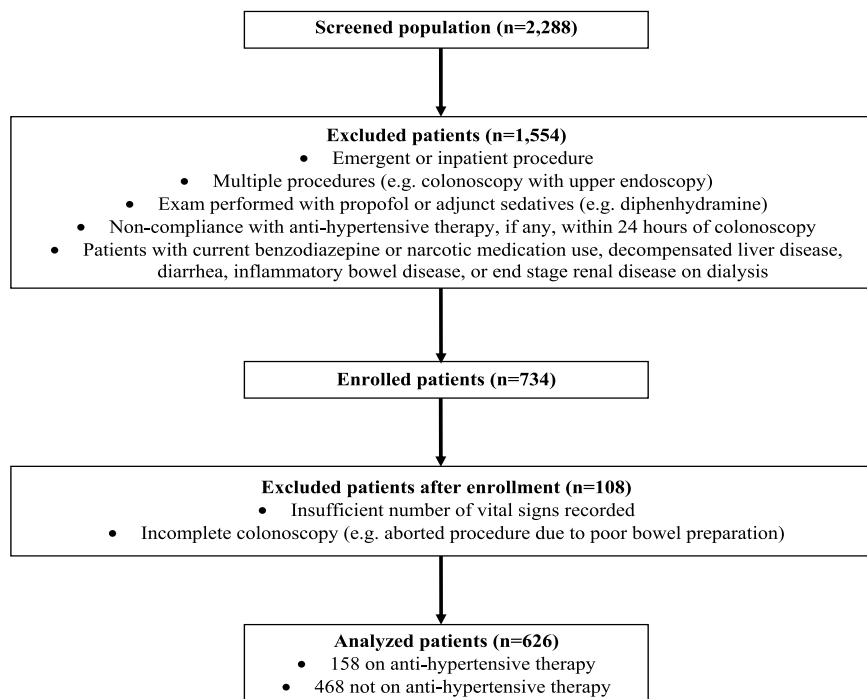

Fig 1. Patient enrollment into the study over 8 months.

Procedure & post-procedure

During colonoscopy, total doses of fentanyl and midazolam were documented. Intravenous normal saline was co-administered with sedation and subsequently run at a rate of 150 mL per hour throughout the examination. Procedure vital signs were all readings between the beginning of sedation and the "scope out" time documented by the nurse. Post-procedure vital signs were all readings after the colonoscope had been withdrawn until the patient was discharged from the recovery area.

Hypotension & adverse events

The mean of the vital sign readings for the pre-, peri-, and post-procedure periods were used for analysis. Hypotension was defined as a systolic blood pressure <90 mmHg and/or a diastolic blood pressure <60 mmHg. These parameters were selected because other authors have used these in the past when studying physiologic changes during colonoscopy with conscious sedation [16, 17]. There is otherwise no standard definition for intraoperative hypotension [18]. Adverse cardiopulmonary events were instances in which either the patient became symptomatic (e.g. chest pain, palpitations, shortness of breath) or required medical intervention (e.g. early termination of the procedure, pharmacotherapy) in the judgment of the attending physician.

Statistical analysis

Univariate comparisons of categorical and continuous predictor variables were accomplished using the chi-square test or independent samples t-test respectively. We performed binary logistic regression analyses to look for variables associated with the presence or absence of procedural hypotension. To create the model, we used sequential forward conditional analysis by entering predictor variables from the univariate analysis with a p-value <0.05. From this analysis, the odds ratios and 95% confidence intervals of the odds ratios were determined. Data was recorded in Microsoft Excel (Microsoft Corporation, Redmond, WA), and SPSS version 19 (IBM, Armonk, NY) was used for data analysis. All p-values were from 2-tailed calculations.

Results

Overall study population

During the consecutive 8 month period, 626 outpatients (mean age 56.0 ± 10.4 years) were prospectively enrolled into the study (Table I). The majority of our study population was male (54.0%), black (59.6%), and had an American Society of Anesthesiologists (ASA) class II physical status (83.9%). Overall, mean pre-procedure systolic blood pressure (135.0 ± 16.7 mmHg), diastolic blood pressure (79.3 ± 12.0 mmHg), heart rate (73.6 ± 11.6 beats per minute), respiratory rate (15.7 ± 3.1 breaths per minute), and oxygen saturation (98.7 ± 1.6%) were within normal range.

There were 158 patients who had a known diagnosis of hypertension and had taken an anti-hypertensive medication within 24 hours of the colonoscopy. Fifty nine of these patients (37.3%) had taken their medications within 6 hours

Table 1. Characteristics of 626 study patients.

Demographics / Pre-Procedure Variables	
Age (mean years ± SD)	56.0 ± 10.4
Body Mass Index (kg/m^2 ± SD)	28.9 ± 5.3
n (%)	
Males	338 (54.0)
Ethnicity	
White	114 (18.2)
Black	373 (59.6)
Hispanic	110 (17.6)
Asian	21 (3.4)
Other	8 (1.3)
ASA Physical Status Class	
I	84 (13.4)
II	525 (83.9)
III	12 (1.9)
IV	0 (0.0)
Blood Pressure Medication Class	
≥1 Medication	158 (25.2)
Multiple (≥2 Medications)	133 (21.2)
ACE inhibitor	78 (12.5)
CCB	69 (11.0)
Diuretic	69 (11.0)
BB	47 (7.5)
ARB	28 (4.5)
Co-Morbidities	
Asthma / COPD	45 (7.2)
Coronary Artery Disease	12 (1.9)
Congestive Heart Failure	6 (1.0)

ACE – angiotensin converting enzyme; ARB – angiotensin receptor blocker; ASA - American Society of Anesthesiologists; BB – beta blocker; CCB – calcium channel blocker; COPD – chronic obstructive pulmonary disease; SD – standard deviation

of the procedure. There were 133 patients (84.1%) on two or more agents for blood pressure control. The three most common anti-hypertensive medications were ACE inhibitors (12.5%), calcium channel blockers (11.0%), and diuretics (11.0%).

There were 468 individuals who did not have a known diagnosis of hypertension and were not on any medications that could potentially lower their blood pressure. In this group, one procedural complication was documented – a 57 year old male developed bradycardia during the colonoscopy that responded to atropine. His pre-, procedure, and post-procedure blood pressures ranged from 118-140 mmHg over 64-90 mmHg. His respiratory rate and oxygen saturation were within normal limits. The patient otherwise completed the endoscopic examination.

The comparison of cardiopulmonary status and procedural variables in patients with and without hypertension yielded two statistically significant differences (Table II). The 158 patients with hypertension had a higher pre-procedure systolic blood pressure (p<0.001) and required less fentanyl during the colonoscopy (p=0.02) than the 468 patients without hypertension. There were otherwise no differences in other pre-procedure vital signs and procedural variables.

Anti-hypertensive therapy in procedural hypotension

Of the overall population of 626 patients, there were 57 patients (40 females; mean age 54.5 ± 11.9 years) who

Table II. Cardiopulmonary status and procedural variables of 626 study patients.

	Patients with Hypertension (n = 158)	Patients without Hypertension (n = 468)	P Value
Pre-Procedure Vital Signs (mean ± SD)			
Systolic Blood Pressure (mmHg)	143.6 ± 16.8	132.1 ± 15.7	**<0.001**
Diastolic Blood Pressure (mmHg)	80.8 ± 12.2	78.8 ± 12.0	0.08
Heart Rate (beats per minute)	75.0 ± 11.8	73.1 ± 11.5	0.07
Respiratory Rate (breaths per minute)	15.7 ± 3.2	15.7 ± 3.1	0.91
Oxygen Saturation (%)	98.6 ± 1.5	98.7 ± 1.6	0.34
Procedure Variables (mean ± SD)			
Duration (minutes)	23.3 ± 9.0	23.0 ± 9.4	0.73
Fentanyl Dose (mcg)	100.5 ± 30.5	107.3 ± 32.3	**0.02**
Intravenous Fluids (mL)	353.3 ± 207.4	347.7 ± 185.0	0.75
Midazolam Dose (mg)	5.4 ± 1.9	5.7 ± 2.1	0.17

SD – standard deviation

developed hypotension, which was defined as systolic blood pressure <90 mmHg and/or diastolic blood pressure <60 mmHg, during the colonoscopy (Table III). There were no differences (all p >0.05) in the use of anti-hypertensive therapy among the five medication classes between the two groups. Of the 57 patients who developed procedural hypotension, 12 patients (21%) were on blood pressure-lowering medications. Seven patients were on a single anti-hypertensive agent, and each of the medication classes was represented. Four patients were on either a two or three drug combination therapy, while one patient was on a regimen that included medications from all five anti-hypertensive classes.

Univariate factors in procedural hypotension

Univariate analysis (Table III) revealed an association between the female gender and procedural hypotension (p=0.01). In addition, patients who developed procedural hypotension had a lower systolic blood pressure (123.2 ± 15.8 vs. 136.2 ± 16.3 mmHg; p<0.001) and lower diastolic blood pressure (68.9 ± 11.0 vs. 80.4 ± 11.7 mmHg; p<0.001) prior to colonoscopy than those who did not develop procedural hypotension. There were no differences (all p>0.05) in the remaining demographics (age, body mass index), duration of colonoscopy, fentanyl dose, midazolam dose, or the prevalence of co-morbidities (asthma, COPD,

Table III: Variables associated with procedural hypotension.

Mean ± SD	Univariate			Multivariate*			
	Procedural hypotension (n=57)	No procedural hypotension (n=569)	P Value	Slope	Odds Ratio	95% CI	P Value
Age (years)	54.5 ± 11.9	56.2 ± 10.2	0.23				
Body Mass Index (kg/m^2)	27.7 ± 5.1	29.0 ± 5.3	0.08				
Female Gender (%)	70.2	52.4	0.01	0.58	0.56	0.30-1.05	0.07
Procedure (mean ± SD)							
Duration (minutes)	23.4 ± 8.4	23.1 ± 9.4	0.89				
Fentanyl dose (mcg)	106.1 ± 33.5	105.5 ± 31.9	0.73				
Midazolam dose (mg)	5.7 ± 2.3	5.6 ± 2.0	0.78				
Pre-procedure SBP (mmHg)	123.2 ± 15.8	136.2 ± 16.3	<0.001	-0.03	0.97	0.95-0.99	0.004
Pre-procedure DBP (mmHg)	68.9 ± 11.0	80.4 ± 11.7	<0.001	-0.06	0.95	0.92-0.97	<0.001
Medications (%)							
ACE inhibitor	10.5	12.7	0.64				
ARB	5.3	4.4	0.76				
BB	8.8	7.4	0.70				
CCB	7.0	11.4	0.31				
Diuretic	5.3	11.6	0.15				
Co-morbidities (%)							
Asthma / COPD	10.5	6.9	0.31				
Congestive heart failure	1.8	0.9	0.52				
Coronary artery disease	1.8	1.9	0.93				

* Logistic regression analysis using backward elimination to derive odds ratios and 95% CI. All odds ratios are adjusted for the other variables entered into the model, including fentanyl dose, gender, midazolam dose, pre-procedure DBP, and pre-procedure SBP.
ACE – angiotensin converting enzyme; ARB – angiotensin receptor blocker; BB – beta blocker; CCB – calcium channel blocker; CI – confidence interval; COPD – chronic obstructive pulmonary disease; DBP – diastolic blood pressure; SD – standard deviation; SBP – systolic blood pressure

congestive heart failure, coronary artery disease) between the two groups.

Multivariate factors in procedural hypotension

When controlling for other model variables and factors using multivariate logistic analysis (Table III), only pre-procedural systolic blood pressure (OR=0.97, 95% CI=0.95-0.99; p=0.004) and diastolic blood pressure (OR=0.95, 95% CI=0.92-0.97; p<0.001) were inversely associated with the development of procedural hypotension. After controlling for other model variables, gender was not associated with hypotensive episodes (OR=0.56, 95% CI=0.30-1.05; p=0.07).

Intravenous fluid administration

The 57 patients who developed hypotension during the endoscopic examination received a greater volume of intravenous normal saline than the remaining 569 patients (383.3 ± 182.8 vs. 345.7 ± 191.3 mL; p=0.16). The difference was not statistically significant.

Discussion

Our study of a large sample of outpatients undergoing colonoscopy with conscious sedation found that taking an anti-hypertensive medication prior to examination was not associated with procedural hypotension. Moreover, age, body mass index, gender, duration, fentanyl dose, midazolam dose, and the presence of co-morbidities (asthma, COPD, congestive heart failure, coronary artery disease) were also not significant predictors. Instead, lower pre-procedure systolic and diastolic blood pressures were the principal contributing variables. Our findings add to the literature available on the effect of anti-hypertensive therapy on blood pressure, in addition to the identification of risk factors for hypotension, during gastrointestinal endoscopy.

Blood pressure-lowering medications seem to play less of a role in procedural hypotension. In fact, the majority of our patients who experienced a hypotensive episode were not on anti-hypertensive agents. Findings from our study suggest that taking anti-hypertensive therapy prior to the examination, regardless of medication class, did not increase the risk of developing hypotension during the colonoscopy. However, the use of anti-hypertensive medications, particularly ACE inhibitors and ARBs, in the pre-operative setting has been shown to increase the incidence of intra-operative hypotension in a variety of surgeries under anesthesia [12-15]. These particular agents, in addition to the blood pressure-lowering effect of sedation, antagonize the renin-angiotensin system (RAS) that is vital in maintaining intra-operative arterial pressure [19, 20].

One prospective study of 308 patients showed that patients who took an ACE inhibitor or ARB within 10 hours of non-cardiac surgery developed more frequent hypotension during the first 30 minutes of anesthetic induction [13]. These medication classes were found to be more responsible for the fall in blood pressure in a subsequent study, when the hypotension responded to a vasopressin system agonist rather than a conventional pressor [12]. The contrast in our results from the surgical literature is likely due to differences in class of sedative agents and duration of the procedure. The longer duration of the procedure and the use of general anesthesia for surgical cases are likely to intensify the suppression of the RAS, and therefore, disrupt the body's ability to maintain a stable blood pressure.

Results from our study demonstrate that doses of fentanyl and midazolam are not significant contributors of hypotension. Midazolam can have greater effects on the cardiovascular system than fentanyl [6, 21] and has been linked to a decline in blood pressure during colonoscopy [7, 17, 22]. The difference in these results may be attributed to the use of another adjunct sedative or dissimilarities in the monitoring of cardiopulmonary status. Our findings further identify that having a lower initial blood pressure prior to endoscopy potentially increases the risk of procedural hypotension. Since this association appears less related to anti-hypertensive medications, one likely explanation is that a lower pre-procedure blood pressure could be a consequence of the colonoscopy bowel preparation [23]. Fluid deficits that lead to dehydration and hypotension are an increasingly prevalent complication among bowel purgatives [24]. A future study could explore this possibility.

Our study has several limitations. Our results apply to patients receiving conscious sedation with fentanyl and midazolam, but we did not include patients who received deep sedation with propofol. Nonetheless, we excluded these cases, because propofol is usually reserved for patients with substantial cardiovascular or pulmonary disorders. For similar reasons, we excluded inpatient procedures. Secondly, there is a potential for recall bias concerning medication history, although this should be non-differential. Another limitation is the administration of intravenous fluids at a standard rate in all patients without respect to blood pressure. Fluid resuscitation is performed with the goals of hydration and maintenance of blood pressure, but it has been shown in a previous study to not prevent hypotension in patients undergoing colonoscopy [25].

Conclusion

Our data suggest that patients should continue their blood pressure medications, including ACE inhibitors and ARBs, in the morning leading up to endoscopy. We found that anti-hypertensive therapy taken prior to examination was not associated with procedural hypotension, even after controlling for factors such as sedative dose. Instead, a lower pre-procedure blood pressure is the primary risk factor for the development of hypotension during colonoscopy under conscious sedation. Future studies should focus on other groups of endoscopic patients, such as inpatients, those undergoing complex lengthy procedures, and those with severe co-morbidities. Another potential area of interest is the relationship between bowel purgatives and their effect on BP before colonoscopy.

Conflicts of interests

None to declare.

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