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Main Article

A prospective comparative study to examine the effects of oral diazepam on blood pressure and anxiety levels in patients with acute epistaxis

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Abstract

Objective: To examine the effects of oral diazepam on blood pressure and anxiety in patients with acute epistaxis.

Study design and setting: A prospective comparative study in an otorhinolaryngology tertiary referral centre.

Participants: Patients with acute epistaxis requiring hospital admission.

Intervention: Oral diazepam.

Main outcome measures: Anxiety and blood pressure levels.

Results: 32 patients received diazepam and 45 did not (control). On average, patients were hypertensive on admission (mean [standard deviation (SD)] systolic blood pressure diazepam group = 157 mmHg [26], control = 152 mmHg [23]; diastolic blood pressure diazepam group = 87 mmHg [16], control = 87 mmHg [18]). Both groups showed significant blood pressure reduction on discharge ($p < 0.0001$) but the difference in mean blood pressure reduction between the two groups was insignificant (systolic blood pressure $p = 0.16$, 95% confidence interval [CI] = −5 to +19 mmHg; diastolic blood pressure $p = 0.43$, 95% CI = −8 to +10 mmHg). Anxiety was significantly lower on discharge ($p < 0.0001$) but the difference in mean fall in anxiety scores between the two groups was insignificant ($p = 0.08$, 95% CI = 0 to +2). There was no significant correlation between total diazepam and changes in blood pressure (systolic blood pressure $p = 0.32$; diastolic blood pressure $p = 0.65$) or anxiety ($p = 0.73$), nor between blood pressure and anxiety on admission (systolic blood pressure $p = 0.45$; diastolic blood pressure $p = 0.72$).

Conclusions: Elevated blood pressure and anxiety in acute epistaxis patients reduced on epistaxis resolution irrespective of oral diazepam use. The elevated blood pressure does not appear to be directly related to anxiety.

Key words: Epistaxis; Blood Pressure; Anxiety; Diazepam

Introduction

Epistaxis and hypertension are both common in the general population and an association between these two conditions is controversial.[1–7] Hypertension has been postulated as a general risk factor for acute epistaxis[1–4] and acute refractory epistaxis[5] but results from studies have been equivocal.[6,7] It has been observed that patients with acute epistaxis often have higher blood pressures on presentation.[3,4] The underlying mechanism is not fully understood. In addition, there are currently no guidelines on the management of acute hypertension in epistaxis patients during their active bleeding. In clinical practice, acute hypertension in these patients is often managed in a variety of ways including the use of oral anti-hypertensive medication such as beta-blockers or calcium channel blockers.[8] In some cases, the oral benzodiazepine diazepam has been suggested as an alternative due to its hypotensive side effects.[9]

Various studies have demonstrated that anxiety in general can increase blood pressure levels.[10,11] However, the role of anxiety in acute hypertensive epistaxis is uncertain. To date, there is no published study on whether patients with acute epistaxis have higher anxiety levels and whether there is an association between anxiety and hypertension during acute epistaxis. A recent telephone survey of the otorhinolaryngology departments of 10 major teaching hospitals within the United Kingdom

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showed that the prescription of oral diazepam, a long-acting benzodiazepine, is common practice in patients with acute epistaxis requiring hospital admission on the assumption that anxiety is a prominent feature (ie JF Thong and SLO, unpublished date). Diazepam is an anxiolytic agent and when administered intravenously, it has been shown to reduce blood pressure.[12,13] When administered orally, however, hypotension is an uncommon side effect.[9] No published study has yet determined if oral diazepam truly has a therapeutic role in acute epistaxis, especially where patients have elevated blood pressure levels during the active phase of their epistaxis.

The aims of this study were therefore to determine the levels of anxiety and blood pressure in patients with acute epistaxis; to examine the effects of oral diazepam on the levels of anxiety and blood pressure in these patients; and to determine if anxiety is associated with the higher blood pressure observed in patients during their acute epistaxis.

Methods

A prospective comparative non-randomised study was carried out in an otorhinolaryngology tertiary referral centre in London on patients admitted with acute epistaxis between July 2004 and May 2005. Those with a known psychiatric history, history of uncontrolled hypertension, on long-term benzodiazepine medication, or who were started on anti-hypertensive medication during the epistaxis admission for persistently elevated blood pressure were excluded.

The patients were divided into two groups. The diazepam group, which consisted of patients who were prescribed regular oral diazepam (2 mg oral three times a day (tds)) throughout their period of hospitalisation, and the control group, who did not receive oral diazepam during any stage of their hospital admission. The decision to commence diazepam in the patients was made by the admitting physician. It is normal practice in our department for the admitting physician to commence diazepam in patients with acute epistaxis if it was felt the patient was anxious. This arises from the common belief that anxiety causes an elevation in blood pressure which in turn exacerbates epistaxis. Standard treatment for epistaxis in our department is nasal cautery followed by an algorithm of anterior nasal packing, posterior nasal packing and eventually theatre for examination under general anaesthesia with or without sphenopalatine artery ligation, if there is no resolution of epistaxis.

Anxiety levels on admission and upon discharge were measured using a validated questionnaire based on the Clinical Anxiety Scale of Snaith *et al.*[14] The questionnaire consisted of seven questions, three of which measured the anxiety state of the patient and four of which measured the anxiety trait. Each question had a score from 0 to 4, with the total score ranging from 0 to 28.

The patient's blood pressure on admission and on discharge was measured, with the assessor blinded as to whether the patient had received oral diazepam. In the current study, hypertension was defined, in accordance with the British Hypertension Society, as a blood pressure above 140/90 mmHg.[8]

Following descriptive analysis, statistical analysis was conducted in a hospital computer using the Statistical Package for the Social Sciences (SPSS). Paired and unpaired Student's *t*-test and regression analysis were used. A p value of less than 0.05 was considered to be statistically significant.

Results

Seventy-seven patients were included in the study (32 diazepam group, 45 control group). The mean (SD) age of patients in the diazepam group was 64 years (18) (range 21–91) and in the control group, 71 years (18) (range 13–94).

Epistaxis control interventions

In the diazepam group, 30 (94 per cent) patients required nasal packing, of which four required examination under general anaesthesia with or without sphenopalatine artery ligation. In the control group, 41 (91 per cent) required nasal packing and none required theatre. The mean (SD) duration of nasal packing was two (one) days (range one to five) in the diazepam group and similarly, two (one) days (range one to four) in the control group.

Length of stay

The mean (SD) length of stay in the diazepam group was three (two) days (range one to seven) and similarly, three (two) days in the control group (range one to 11).

History of hypertension

There was a mixture of patients with and without a previous history of controlled hypertension in each group (see Tables I and II). Seventeen patients out of 32 (53 per cent) in the diazepam group had a past history of controlled hypertension compared to 22 patients out of 45 (49 per cent) in the control group. Statistical analysis to compare patients with a history of controlled hypertension to those without a history of hypertension, did not reveal any significant differences in terms of their mean blood pressures on admission in the diazepam group or in the control group. On discharge, there were also no significant differences in mean blood pressures between patients with or without a past history of hypertension in the diazepam group. No statistically significant differences were found between the mean length of stay of patients with and without a history of hypertension in the diazepam group (mean [SD] history of hypertension = three [two] days, no history = three [two] days; $p = 0.35$) or control group (mean [SD] history of hypertension = three [one] days, no history = two [one] days; $p = 0.11$).

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TABLE I

COMPARISONS OF MEAN (SD) BLOOD PRESSURES IN MMHG (ON ADMISSION AND ON DISCHARGE) BETWEEN PATIENTS WITH AND WITHOUT A HISTORY OF CONTROLLED HYPERTENSION IN THE DIAZEPAM GROUP

	History of hypertension Mean (SD)	No history of hypertension Mean (SD)	*p* value
Systolic BP on admission	154 (30)	162 (19)	0.20
Diastolic BP on admission	85 (17)	91 (16)	0.16
Systolic BP on discharge	130 (24)	128 (20)	0.26
Diastolic BP on discharge	74 (10)	72 (11)	0.27

BP = blood pressure; SD = standard deviation

TABLE II

COMPARISONS OF MEAN (SD) BLOOD PRESSURES IN MMHG (ON ADMISSION AND ON DISCHARGE) BETWEEN PATIENTS WITH AND WITHOUT A HISTORY OF CONTROLLED HYPERTENSION IN THE CONTROL GROUP

	History of hypertension Mean (SD)	No history of hypertension Mean (SD)	*p* value
Systolic BP on admission	155 (22)	152 (24)	0.32
Diastolic BP on admission	85 (20)	88 (16)	0.26
Systolic BP on discharge	131 (26)	133 (21)	0.43
Diastolic BP on discharge	69 (16)	74 (15)	0.13

BP = blood pressure; SD = standard deviation

Comparison of blood pressure between diazepam and control groups

Hypertension was defined as blood pressure above 140/90 mmHg in the current study. Patients were on average hypertensive on admission in both the diazepam and control groups. There was no statistically significant difference between the mean admission blood pressures in both groups (systolic blood pressure $p = 0.26$, diastolic blood pressure $p = 0.42$).

On discharge, blood pressures were significantly lower in both the diazepam and control group. However, the difference in mean fall in blood pressure on discharge between both groups was not significant. Twelve (27 per cent) patients out of 45 in the control group had a blood pressure of >140/90 mmHg on discharge and this was similar in the diazepam group where nine (28 per cent) out of 32 patients had a blood pressure of >140/90 on discharge.

There was no correlation between changes to blood pressure on discharge and the total dose of oral diazepam received during hospital admission (systolic blood pressure $r = 0.21$, $p = 0.32$; diastolic blood pressure $r = 0.10$, $p = 0.65$) (see Figure 1). There was also no correlation between initial blood pressure and total dose of diazepam received (systolic blood pressure $r = 0.11$, $p = 0.60$; diastolic blood pressure $r = 0.04$, $p = 0.84$). See Tables III and IV.

Comparison of anxiety levels between diazepam and control groups

On admission, the mean anxiety score of patients in the diazepam group was similar to that of patients in the control group ($p = 0.35$) (Table V). There was a significant reduction in anxiety levels on discharge in both groups ($p < 0.0001$ in both groups), but the difference between the two groups was not significant (mean difference in reduction of anxiety levels [95% CI] = 1 [0 to 2], $p = 0.08$). No correlation was found between changes to anxiety scores and total dose of diazepam received during hospital admission ($r = 0.07$, $p = 0.73$) (see Figure 2). No correlation was found between initial anxiety scores on admission and total dose of diazepam received ($r = 0.05$, $p = 0.82$).

Patients with acute hypertensive epistaxis

Fifty-seven patients in total were hypertensive on admission (mean [SD] systolic blood pressure 165 mmHg [17], range 143–208 mmHg), of whom 31 had a diastolic blood pressure of more than or equal to 90 mmHg (mean [SD] diastolic blood pressure 104 mmHg [8], range 90–123 mmHg). This group of patients were examined separately to determine if the hypertension on admission was an acute event or whether patients had undiagnosed chronic hypertension. The effects of diazepam on the blood pressure and anxiety levels in these patients were also examined.

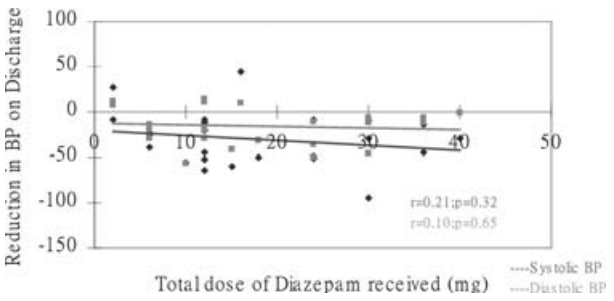

FIG. 1

Scatter chart with regression lines showing no statistically significant correlation between changes to blood pressure on discharge and the total dose of oral diazepam received during hospital admission (systolic BP $r = 0.21$, $p = 0.32$, diastolic BP $r = 0.10$, $p = 0.65$). BP = blood pressure

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TABLE III

MEAN (SD) SYSTOLIC BLOOD PRESSURE MEASUREMENTS (IN MMHG) ON ADMISSION AND ON DISCHARGE IN BOTH THE DIAZEPAM AND CONTROL GROUPS

	Systolic BP on admission Mean (SD)	Systolic BP on discharge Mean (SD)	Difference in Systolic BP (OD–OA) (95% CI)	*p* value
Diazepam	157 (26)	129 (22)	28 (18–38)	<0.0001
Control	152 (23)	132 (23)	22 (15–28)	<0.0001
p value	0.26	0.33	0.16	

OA = on admission; OD = on discharge; SD = standard deviation; BP = blood pressure

TABLE IV

MEAN (SD) DIASTOLIC BLOOD PRESSURE MEASUREMENTS (IN MMHG) ON ADMISSION AND ON DISCHARGE IN BOTH THE DIAZEPAM AND CONTROL GROUPS

	Diastolic BP on admission Mean (SD)	Diastolic BP on discharge Mean (SD)	Difference in Diastolic BP (OD–OA) (95% CI)	*p* value
Diazepam	87 (16)	73 (10)	14 (7–21)	<0.0001
Control	87 (18)	72 (15)	15 (9–20)	<0.0001
p value	0.42	0.30	0.43	

OA = on admission; OD = on discharge; SD = standard deviation; BP = blood pressure

On discharge, there was a mean reduction in blood pressure in these patients in both the diazepam (mean reduction in systolic blood pressure = 35 mmHg, diastolic blood pressure = 17 mmHg) and control groups (mean reduction in systolic blood pressure = 26 mmHg, diastolic blood pressure = 16 mmHg). However, there was no statistically significant difference between the two groups (mean difference in reduction of systolic blood pressure [95% CI] = 9 [−4 to 21] mmHg, $p = 0.07$; diastolic blood pressure [95% CI] = 1 [−9 to 11] mmHg, $p = 0.40$).

Anxiety scores on admission were similar in the diazepam (mean [SD] = 9 [6]) and control groups (mean [SD] = 8 [5]) and significantly lower on discharge in both groups (mean [SD] diazepam group = 5 [4], control group = 6 [4]). The degree of reduction in mean anxiety scores between the two groups was similar (mean difference in anxiety reduction [95% CI] = 2 [0 to 4], $p = 0.08$).

Association between blood pressure and anxiety scores

No correlation could be found between blood pressure and anxiety scores on admission (systolic $r = 0.09$, $p = 0.45$; diastolic $r = 0.04$ $p = 0.72$) (see Figure 3).

Discussion

As far as we are aware, this is the first study to examine the effects of oral diazepam on blood pressure and anxiety levels in patients with acute epistaxis. There have also not been any previous studies examining the levels of anxiety in these patients nor its correlation with blood pressure levels.

In the current study there was a mixture of patients with and without a past history of hypertension. Patients with a history of controlled hypertension were included as previous studies by Fuchs *et al.* and Fasce *et al.* failed to find any association between the occurrence of epistaxis and a history of hypertension.[6,7] To further support their findings, results from our study showed that admission and discharge blood pressure levels between epistaxis patients without a past history of hypertension were similar to those with a past history of controlled hypertension. Patients with and without a history of hypertension were therefore analysed as a whole in both the diazepam and control groups.

Patients with acute epistaxis were found, on average, to be hypertensive on admission. Three quarters of the patients admitted with acute epistaxis had blood pressure levels of more than or equal to 140/90 mmHg. This finding concurs with observations made by Herkner *et al.* who reported that patients with acute epistaxis had higher blood pressures compared with controls without active bleeding and that active epistaxis was associated with arterial hypertension.[3,4] In both our diazepam and control groups, blood pressure levels on discharge were significantly lower than on admission.

TABLE V

MEAN (SD) ANXIETY LEVELS ON ADMISSION AND ON DISCHARGE IN BOTH THE DIAZEPAM AND CONTROL GROUPS

	Anxiety on admission Mean (SD)	Anxiety on discharge Mean (SD)	Difference in Anxiety (OD–OA) (95% CI)	*p* value
Diazepam	9 (5)	5 (4)	4 (3–5)	<0.0001
Control	8 (5)	5 (4)	3 (2–4)	<0.0001
p value	0.36	0.82	0.08	

OA = on admission; OD = on discharge; SD = standard deviation

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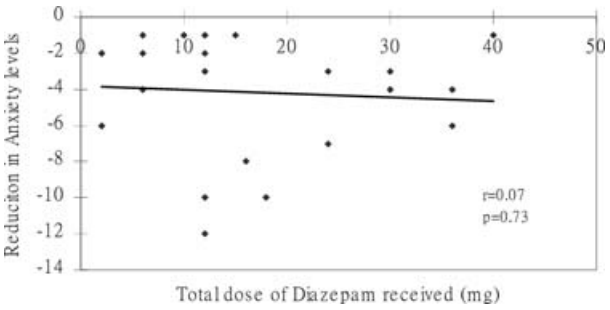

FIG. 2

Scatter chart with regression line showing absence of correlation between changes to anxiety scores and total dose of diazepam received during hospital admission ($r = 0.07$, $p = 0.73$).

However, the degree of reduction in blood pressure was similar whether the patient received diazepam or not and this was irrespective of the total dose of diazepam received by the patient during hospitalisation. This suggests that oral diazepam has little, if any, extra effect on blood pressure by the time of patient discharge.

What is not known, however, is whether oral diazepam reduces blood pressure earlier than in the control group as the daily blood pressure trends of patients were not recorded. Although this is of significance as hypertension has been shown to be a major factor in the refractoriness of acute epistaxis,[2] comparing daily blood pressure and anxiety level measurements would be inaccurate because of the large variations of interventions received by patients during their admission (e.g. nasal packing, surgery, blood transfusion). Hence, we only measured blood pressure and anxiety levels on admission and at discharge. For the same reasons the duration of hospitalisation has not been used as an outcome measure in this study.

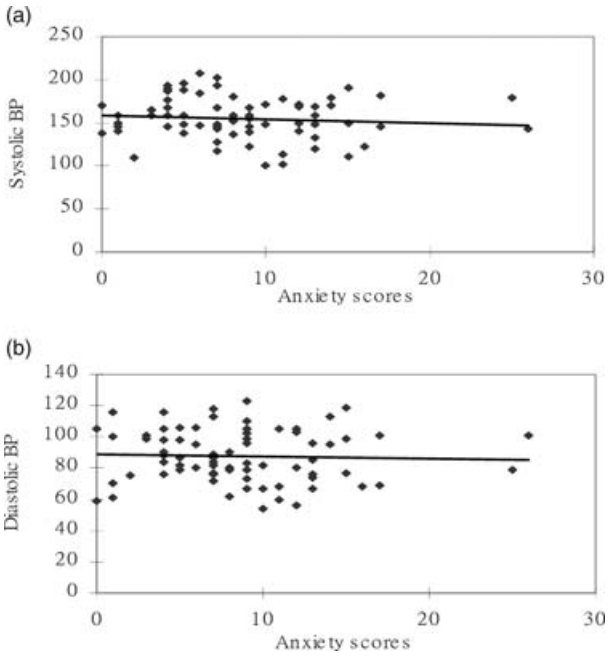

FIG. 3

(a) and (b) Scatter chart with regression lines showing no correlation between blood pressure and anxiety scores on admission (systolic $r = 0.09$, $p = 0.45$; diastolic $r = 0.04$, $p = 0.72$).

No significant differences in admission anxiety levels were found between the diazepam and control groups suggesting that the admitting physician's subjective evaluation of anxiety levels in these patients may not be reflective of the actual anxiety experienced. Patients were found to be significantly more anxious on admission than on discharge. The explanation for this may be that brisk epistaxis, especially that severe enough to require hospital admission, can be a terrifying experience and hence result in the higher anxiety levels. Following treatment and resolution of the epistaxis, anxiety levels returned to normal. Oral diazepam did not seem to reduce anxiety levels any more than in the control group, irrespective of the total dose of diazepam received by the patient during the period of hospitalisation. The criticism may be made that only a very small dose of oral diazepam was prescribed to patients in this study which may not be sufficient to have a significant effect on blood pressure and anxiety levels. However, the British National Formulary recommends that the initial regimen of oral diazepam prescription for the short-term management of anxiety to be 2 mg tds.[9]

With advancing age, there is a reduction in drug metabolism and renal clearance, resulting in markedly increased tissue concentrations of drugs. Elderly people are hence more prone to the side effects of drugs.[15] The main side effects of diazepam are drowsiness and confusion. This is of particular relevance to patients with acute epistaxis because they tend to be of an older age group as demonstrated in our study where the mean age of patients was 68 years. Sedation in these patients would lead to the risk of unnoticed posterior epistaxis and aspiration. In addition, because both blood pressure and anxiety levels returned to within normal limits regardless of whether diazepam was used, higher doses of diazepam were unlikely to yield any further benefit to the patient.

- **Patients with acute epistaxis may have higher blood pressures on presentation**
- **Diazepam is a benzodiazepine indicated for short-term relief of anxiety and intravenously, also has hypotensive effects**
- **Acute epistaxis is associated with higher anxiety as well as higher blood pressure levels**
- **The higher blood pressure found in patients with acute epistaxis does not seem to be related to anxiety levels**
- **Oral diazepam does not reduce anxiety or blood pressure levels more than in control patients, irrespective of the total dose received and hence, it does not appear to have a therapeutic benefit in patients with acute epistaxis**

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We hypothesised that anxiety caused the hypertension observed in patients with acute epistaxis, irrespective of any history of controlled hypertension. Curiously, the blood pressure did not seem to correlate with the anxiety levels on admission. This suggests that the higher blood pressure observed in patients with acute epistaxis was not directly associated with anxiety, nor that anxiety played a significant role in causing the higher blood pressure observed in these patients. The higher blood pressure and higher anxiety levels observed during the acute phase of epistaxis appear to be independent entities. A possible hypothesis then to explain the higher blood pressure observed in patients with acute epistaxis is that these patients have a more volatile blood pressure and that the higher blood pressure was triggered by another event and subsequently resulted in or contributed to the start of epistaxis. Alternatively, a bleeding lesion in the nasal cavity, a region of rich autonomous innervation, could have caused an arousal reaction manifested as elevated blood pressure.[4] Thus, the return of blood pressure to normal on discharge may have occurred naturally or may have been as a result of resolution of the epistaxis. It may have been interesting to note the fall in haemoglobin levels in these patients as well as any blood transfusions received, to examine the effects of blood loss on the final blood pressure level on discharge.

Conclusion

Patients with acute epistaxis were found to have elevated blood pressures and anxiety levels, and both reduced significantly when the epistaxis resolved irrespective of whether oral diazepam had been used. Hypertension and anxiety observed in these patients seemed to be independent of each other. Incidentally, physicians were found to be poor at judging anxiety levels in patients with acute epistaxis. In conclusion, the results of the current study do not show any evidence to support the use of oral diazepam in patients with acute epistaxis and we recommend that its use in current clinical practice be carefully reviewed.

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