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OBSTETRICS

Influence of preoperative anxiety on hypotension after spinal anaesthesia in women undergoing Caesarean delivery

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Editor's key points

- This study assessed the effect of preoperative anxiety on arterial pressure changes after spinal anaesthesia for Caesarean delivery.
- Increased preoperative anxiety was associated with a greater reduction in systolic arterial pressure after spinal anaesthesia.
- This finding might be induced by anxiety-mediated increase in baseline sympathetic activation.

Background. We designed a prospective observational study to assess the effect of preoperative anxiety on hypotension after spinal anaesthesia.

Methods. After IRB approval and signed informed consent, 100 healthy term parturients undergoing elective Caesarean delivery under spinal anaesthesia were enrolled. Direct psychological assessments of preoperative anxiety were verbal analogue scale (VAS) (0–10) anxiety score and State-Trait Anxiety Inventory questionnaire (STAI-s); salivary amylase was measured as an indirect physical assessment of anxiety. Direct and indirect anxiety data were transformed into ordinal groups for low, medium, and high anxiety (VAS: low 0–3, medium 4–6, high 7–10; STAI-s: low <40, medium 40–55, high >55; $\log_{10}$ salivary amylase: low <3, medium 3–4, high >4). Spinal anaesthesia was performed using hyperbaric bupivacaine 10 mg and fentanyl 20 μg. All patients received i.v. crystalloid 500 ml prehydration and 500 ml cohydration. Hypotension was treated by standardized protocol (fluid bolus and ephedrine or phenylephrine depending on maternal heart rate). Systolic arterial pressure (SAP) was measured at baseline and every minute after spinal anaesthesia. The effect of low, medium, and high anxiety groups on the maximum percentage change in SAP (%ΔSAP) was assessed (one-way analysis of variance, Tukey's honestly significant difference).

Results. Ninety-three patients were included in analysis. There was a significant effect of direct psychological measures of anxiety on %ΔSAP (VAS $P=0.004$; STAI-s $P=0.048$). There was a significant difference between low and high anxiety groups (VAS $P=0.003$; STAI-s $P=0.038$), but not between other anxiety groups. Salivary amylase did not correlate with %ΔSAP.

Conclusions. Preoperative anxiety assessed by VAS had a significant effect on hypotension after spinal anaesthesia.

Keywords: anaesthesia; anxiety; bupivacaine; Caesarean delivery; complications, hypotension; intrathecal; spinal

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Spinal anaesthesia is the most popular form of regional anaesthesia used for Caesarean delivery.[1] The most common side-effect of spinal anaesthesia is maternal hypotension,[2] occurring in up to 83% of cases,[3 4] although its incidence depends on how hypotension is defined.[5 6] Maternal hypotension after spinal anaesthesia depends on many factors, including dose of local anaesthetic, patient positioning, fluid preloading and co-loading, and the use of prophylactic or therapeutic vasopressors.[7] Neonates born by Caesarean delivery under spinal anaesthesia are more acidaemic when compared with those delivered after either epidural or general anaesthesia;[8 9] while this may be, in part, a direct consequence of maternal hypotension, current evidence suggests that this is largely a consequence of the vasopressors used to treat or prevent it.[8 9]

The principal mechanism by which spinal anaesthesia causes maternal hypotension is the blockade of sympathetic efferent neurones. Patients with higher baseline sympathetic

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activation have been shown to have more marked hypotension after spinal anaesthesia.[10 11] Anxiety causes generalized sympathetic activation.[12] Together, these findings provide a rational basis for the hypothesis that patients with higher preoperative anxiety would experience more marked hypotension after the induction of spinal anaesthesia. However, we were unable to find any published study that has assessed the effect of markers of preoperative anxiety on the development of hypotension after neuraxial anaesthesia. As such, we designed a prospective observational study to assess the effect of preoperative anxiety on arterial pressure changes after spinal anaesthesia for Caesarean delivery.

Methods

After Institutional Review Board approval and signed informed consent, healthy term parturients undergoing elective Caesarean delivery under spinal anaesthesia were enrolled. Exclusion criteria included active labour, chronic hypertension or preeclampsia, other active medical or psychiatric disorders requiring regular medication, any contraindication for spinal anaesthesia, and refusal of patient consent.

Pre-anaesthesia anxiety

The primary independent variable was preoperative anxiety. This was assessed in the preoperative ward on the day of surgery using two previously validated direct psychological measures of anxiety: verbal analogue scale (VAS) anxiety score[13 14] and State-Trait Anxiety Inventory questionnaire;[15] and one indirect physical measure that has been reported to be associated with anxiety: salivary amylase.[16] *VAS anxiety score:* parturients were asked to rank subjective anxiety on a VAS where 0 was no anxiety at all and 10 the worst anxiety imaginable. *State-Trait Anxiety Inventory questionnaire*: parturients were asked to fill out the State-Trait Anxiety Inventory questionnaire, a two-part questionnaire composed of self-reporting scales to measure situational anxiety (STAI-s). *Salivary amylase:* saliva was collected and analysed using a hand-held monitor (Cocorometer, Nipro, Osaka, Japan); salivary amylase level above 60 KU litre^{-1} ($\log_{10}$ value 4) has been reported to be associated with anxiety.[16] After examination for normal distribution, direct and indirect anxiety data (VAS, STAI-s, and $\log_{10}$ salivary amylase) were transformed into ordinal groups corresponding to high, medium, and low anxiety. For VAS anxiety: low 0–3, medium 4–6, high 7–10; for STAI-s: low <40, medium 40–55, high >55; for $\log_{10}$ salivary amylase: low <3, medium 3–4, high >4.

Hydration and spinal anaesthesia

An i.v. line was inserted and parturients received 500 ml of Ringer's lactate during the hour immediately before surgery. Patients were brought to the operating theatre and received a further bolus of 500 ml of Ringer's lactate over the next 30 min, during positioning and during and immediately after spinal anaesthesia administration. Spinal anaesthesia was performed in the sitting position at the L3–4 or L4–5 interspace using 10 mg hyperbaric bupivacaine with 20 μg fentanyl. Immediately after spinal anaesthesia, parturients were placed in the supine position with a wedge placed under the right hip. Supplemental oxygen was administered by a facemask. Surgery was allowed to begin when the sensory level was confirmed by pinprick to be at least T4 level bilaterally.

Maternal arterial pressure

Arterial pressure was measured in the operating theatre by oscillometry (Datex Ohmeda, AS3, GE Healthcare, Madison, WI, USA). All measurements were made in the supine position with left uterine displacement. Arterial pressure was measured at baseline, immediately before spinal anaesthesia, and every minute after spinal anaesthesia until delivery. Systolic arterial pressure (SAP) below 100 mm Hg was treated by a 250–500 ml fluid bolus; SAP below 90 mm Hg was treated by i.v. vasopressors depending on maternal heart rate (>80 beats min^{-1}, phenylephrine 100 μg repeated as needed; <80 beats min^{-1}, ephedrine 5 mg repeated as needed).

Statistical analysis

The primary independent variables were the direct psychological assessments of anxiety (VAS anxiety score and STAI-s); the indirect physical measure of anxiety (salivary amylase, $\log_{10}$ value) was a secondary independent variable. Data were transformed to ordinal groups corresponding to low, medium, and high anxiety as described above.

The primary dependent variable was the maximum percentage change in SAP (%ΔSAP) after spinal anaesthesia with respect to baseline. Secondary dependent variables were the maximal absolute change from baseline (ΔSAP) and the number of patients requiring vasopressors. Dependent variables were analysed as continuous data; low, medium, and high anxiety groups were compared using one-way analysis of variance (one-way ANOVA) and differences between the groups compared using Tukey's honestly significant difference *post hoc* test. Correlations, where appropriate, were performed using Pearson's correlation coefficient. Statistical significance was assumed if $P<0.05$; as there was a directional hypothesis (i.e. high measures of anxiety associated with high levels of spinal hypotension), one-tailed tests were used.

Sample size was calculated based on a pilot sample that had a mean (SD) 25% (15) reduction in SAP after spinal anaesthesia for Caesarean delivery. We calculated that 82 subjects would be required to identify a 10% difference between the groups for the change of SAP with respect to baseline, with a power of 86% and a *P*-value of 0.05.

Results

One hundred women were enrolled in this study. Seven subjects were subsequently excluded for the following reasons: in one case, the operation was cancelled because of

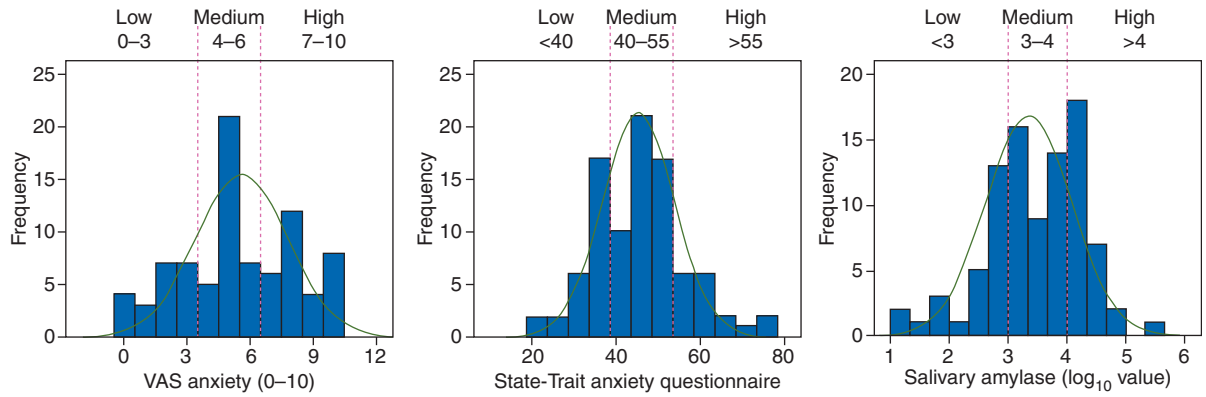

Fig 1 Primary and secondary independent variables were normally distributed. Subjects were divided into low, medium, and high anxiety groups. The primary independent variable was subjective anxiety rated using VAS (0–10), where low anxiety=0–3, medium anxiety=4–6, and high anxiety=7–10. Secondary independent variables were STAI-s (see text) where low anxiety <40, medium anxiety 40–55, and high anxiety <55; and salivary amylase (log_{10}) where low anxiety <3, medium anxiety 3–4, and high anxiety <4.

successful external cephalic version; in two cases, surgery was postponed to a later date when research personnel were not available; in three cases, there was failure of spinal anaesthesia and in one case, there was inadequate data collection. Ninety-three women were included in the final analysis.

The baseline data that correlate with anxiety (VAS, STAIs, and log_{10} salivary amylase) are presented in Figure 1. All data were normally distributed. Patient characteristic data are presented in Table 1 based on the three groups of low, medium, and high anxiety using VAS anxiety (0–10). There were no statistically significant differences between the groups except for gestational age which was significantly higher in the medium anxiety group than in the low or high anxiety group.

The effect of low, medium, and high baseline anxiety on baseline SAP, lowest SAP, maximal %ΔSAP, and maximal absolute ΔSAP are represented in Figures 2 (VAS) and 3 (STAI-s). When comparing low, medium, and high anxiety based upon the VAS score, there was a significant effect on the %ΔSAP after spinal anaesthesia (one-way ANOVA, $P=0.004$). There was a significant difference between low and high anxiety groups [$P=0.003$; mean difference −13%; 95% confidence interval (CI) −21 to −5], but the differences between low and medium anxiety ($P=0.07$) and the medium and high anxiety groups ($P=0.61$) were not significant. When comparing low, medium, and high anxiety based upon the STAI-s, there was a significant effect on the %ΔSAP after spinal anaesthesia (one-way ANOVA, $P=0.048$). There was a significant difference between low and high anxiety groups ($P=0.038$; mean difference −11%; 95% CI −18 to −4), but the differences between low and medium anxiety ($P=0.39$) and the medium and high anxiety groups ($P=0.23$) were not significant.

The absolute ΔSAP after spinal anaesthesia was significantly affected by anxiety assessed by VAS (one-way ANOVA, $P=0.007$). There was a significant difference between low and high anxiety groups ($P=0.006$; mean difference −19 mm Hg, 95% CI −30 to −7), but the differences between low and medium anxiety ($P=0.057$) and the medium and high anxiety groups ($P=1.0$) were not significant. The absolute ΔSAP after spinal anaesthesia was not significantly affected by anxiety assessed by STAI-s (one-way ANOVA, $P=0.065$).

When comparing low, medium, and high anxiety based upon the log_{10} amylase measurement, there were no significant effects on the %ΔSAP after spinal anaesthesia (one-way ANOVA, $P=0.090$) or absolute ΔSAP ($P=0.074$). There were no significant differences between the groups in these secondary comparisons. There was a significant correlation

Table 1 Maternal patient characteristic data for low, medium, and high anxiety groups, based on VAS anxiety (low anxiety 0–3, medium anxiety 4–6, high anxiety 7–10). Data are mean (range) for age, or mean (SD). *$P<0.05$ between high and medium groups

	Low anxiety	Medium anxiety	High anxiety
Age (yr)	32.3 (27–35)	33.7 (23–50)	31.8 (20–41)
Weight (kg)	82.5 (12.8)	80.1 (15.5)	77.1 (16.8)
Height (cm)	163.7 (6.7)	164.8 (5.8)	164.3 (8.7)
Gestational age (weeks+day)	38 (6)	39 (6)*	38 (6)*
Gravida	2.8 (1.5)	3.2 (1.2)	2.9 (1.7)
Parity	1.3 (1.1)	1.8 (1.0)	1.3 (0.9)
Baseline systolic arterial pressure (mm Hg)	126.9 (12.1)	134.3 (20.8)	132.9 (14.1)
Baseline pulse pressure (mm Hg)	52.4 (10.8)	53.3 (15.1)	50.7 (8.6)
Baseline haematocrit	34.5 (2.2)	34.3 (2.8)*	35.9 (2.9)*

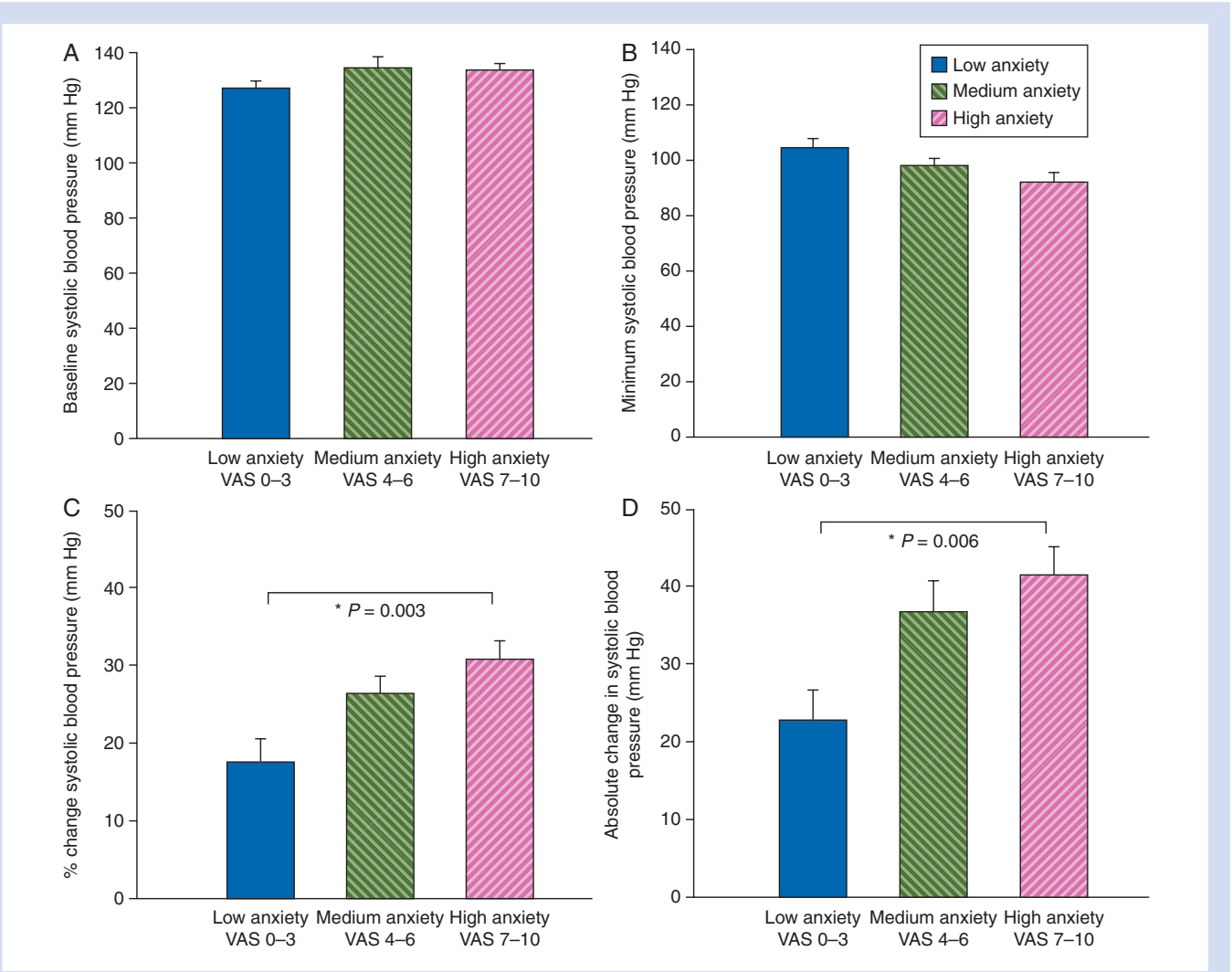

Fig 2 The effect of subjective anxiety (VAS 0–10) in the preoperative ward on SAP at (A) baseline and (B–D) after spinal anaesthesia. (B) The lowest recorded SAP, (C) the maximal % change in SAP and (D) the maximal absolute change in SAP. *(*P*-value) Statistical significance; error bars represent the standard error of the mean.

between the VAS anxiety as a continuous variable with both the %ΔSAP ($P<0.0001$; Pearson's correlation 0.376) and the absolute ΔSAP ($P=0.002$; Pearson's correlation 0.335). STAI-s did not correlate with either %ΔSAP or absolute ΔSAP (%ΔSAP $P=0.128$, Pearson's correlation 0.162; absolute ΔSAP $P=0.259$, Pearson's correlation −0.120). The $\log_{10}$ amylase weakly correlated with the %ΔSAP ($P=0.042$, Pearson's correlation −0.215) and with the absolute ΔSAP ($P=0.058$, Pearson's correlation 0.201).

VAS anxiety strongly correlated with STAI-s ($P<0.001$, Pearson's correlation=0.629). There was no correlation between VAS anxiety and $\log_{10}$ amylase ($P=0.931$, Pearson's correlation=−0.01). The use of vasopressors (either ephedrine or phenylephrine) in low, medium, and high anxiety groups is represented in Figure 4. Although there appeared to be a trend to increased vasopressor use with increasing anxiety, this was not significant in this sample (χ^2 test $P=0.24$; for ordinal series Spearman's correlation $P=0.093$).

Neonatal data are presented in Table 2. There are no differences in neonatal outcomes except for Apgar score at 1 min which was lower in the medium anxiety *vs* high anxiety group.

Discussion

In this study, we demonstrated that increased preoperative anxiety was associated with a greater reduction in SAP after spinal anaesthesia for Caesarean delivery. This change in SAP was not due to a return to normal values of preoperative hypertension associated with preoperative stress, as the preoperative arterial pressures were not different in the low, medium, and high anxiety patients. This difference was clinically relevant and statistically significant for both relative and absolute change from baseline. The greater hypotension seen in the high anxiety group was observed, despite a tendency to increased use of vasopressors in those patients. The difference was not explicable by differences in preoperative

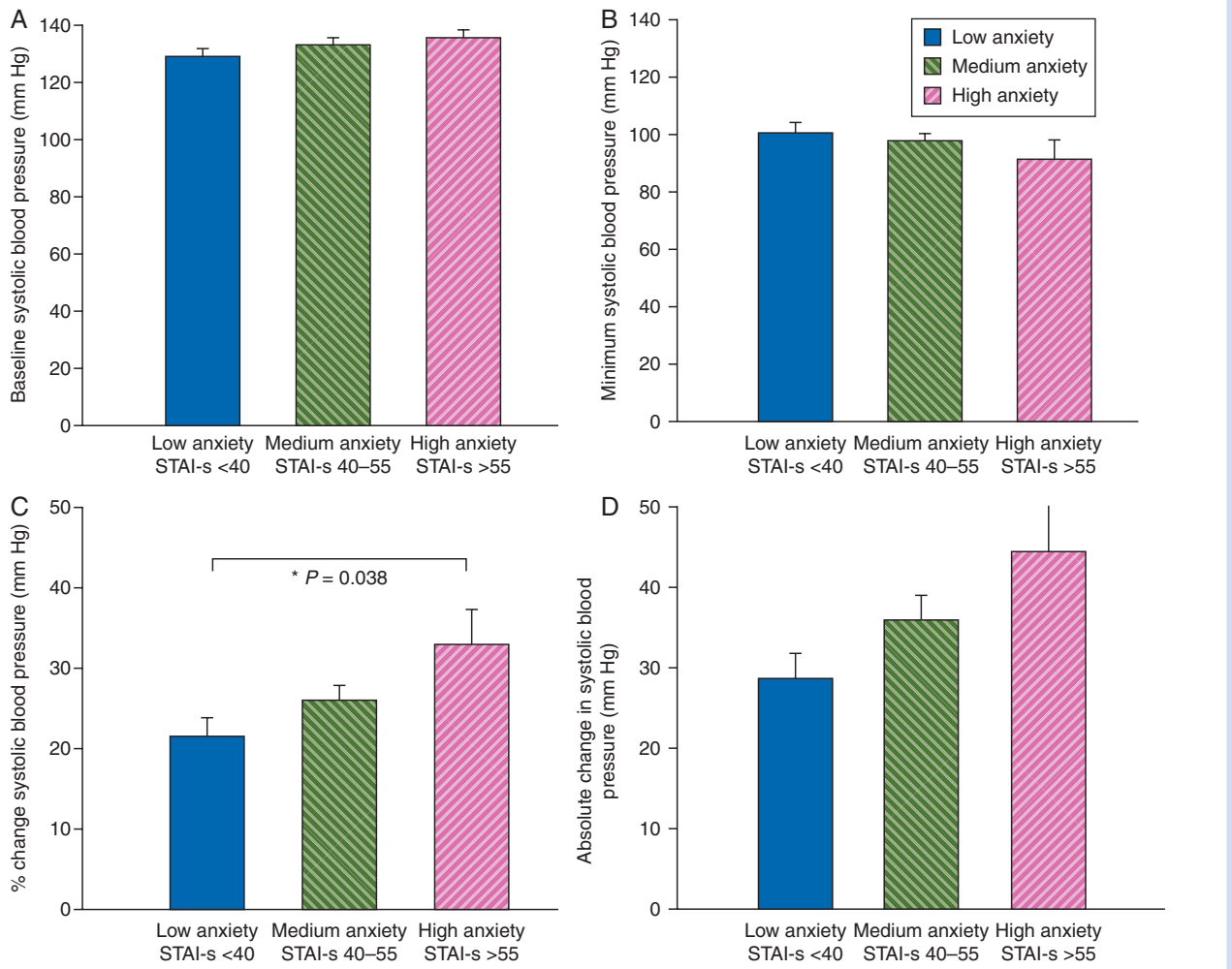

Fig 3 The effect of subjective anxiety (STAI-s) in the preoperative ward on SAP at (A) baseline and (B–D) after spinal anaesthesia. (B) The lowest recorded SAP, (C) the maximal % change in SAP, and (D) the maximal absolute change in SAP. *(*P*-value) Statistical significance; error bars represent the standard error of the mean.

hydration status; baseline heart rate and pulse pressure and the baseline haematocrit were not significantly different between high and low anxiety groups and all patients received the same fluid management protocol.

Our results suggest that a simple subjective preoperative anxiety score may predict hypotension after spinal anaesthesia. We speculate that this is associated with an anxiety-mediated increase in baseline sympathetic activation. As hypotension induced by spinal anaesthesia is mediated by sympatholysis, it seems plausible that the higher the baseline sympathetic activation, the more dramatic will be the haemodynamic effect of spinal anaesthesia. This has been demonstrated in a variety of studies using different endpoints measures as surrogate indicators of sympathetic activation, including maternal baseline heart rate,[17] maternal heart rate variability,[10 11] entropy of the maternal R–R interval,[18] skin conductance,[19] and maternal postural arterial pressure changes.[20] Anxiety has been objectively shown to increase sympathetic activation in studies of heart variability[20–23] and postural arterial pressure changes[24] and also to reduce vagal control.[25] Although seemingly self-evident, the connection between objective measures of preoperative anxiety and hypotension after spinal anaesthesia has not been demonstrated in previous studies.

Although we assessed two direct psychological measures of anxiety in this study (VAS and STAI-s), the latter is considered the more widely accepted measure. Although increases in both measures were significantly associated with greater hypotension after spinal anaesthesia, the results for VAS were slightly stronger. However, the difference between the effects of stress on VAS and on STAI-s was not significant.

Our study demonstrated a poor correlation between the direct psychological assessments of anxiety (VAS and STAI-s) and salivary amylase; not surprisingly, the salivary amylase also correlated weakly with hypotension after spinal anaesthesia. In previous studies, salivary amylase

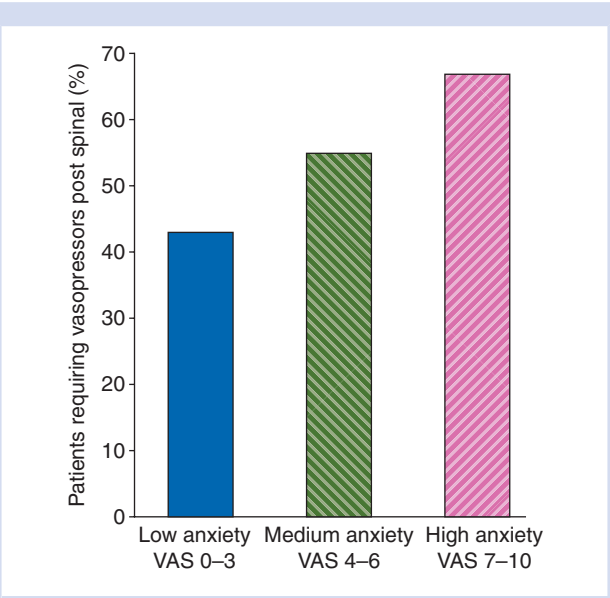

Fig 4 The use of vasopressors (either ephedrine or phenylephrine) in low, medium, and high anxiety groups (based on VAS), after the administration of spinal anaesthesia. See text for protocol for vasopressor use. Although there appeared to be a trend to increased vasopressor use with increasing anxiety, this was not significant (χ^2 test $P=0.24$; for ordinal series Spearman's correlation $P=0.093$).

Table 2 Neonatal patient characteristic and outcome data for low, medium, and high maternal anxiety groups, based on VAS anxiety (low anxiety 0–3, medium anxiety 4–6, high anxiety 7–10). *$P<0.05$ between high and medium groups

	Low anxiety	Medium anxiety	High anxiety
Weight (kg)	3.1 (0.5)	3.2 (0.4)	3.1 (0.4)
Apgar (1 min)	9.0 (0.0)	8.7 (0.9)*	9.0 (0.0)*
Apgar (5 min)	9.9 (0.3)	9.8 (0.5)	9.9 (0.2)
pH	7.3 (0.03)	7.3 (0.05)	7.3 (0.05)

has been found to be an accurate marker of sympathetic activation.[16 26–29] Salivary amylase has been found to increase in a wide range of stressful activities,[16] cold pressure test,[27] mental arithmetic tasks,[16] and during examination stress.[28] Likewise, salivary amylase has been found to be strongly correlated with STAI-s scores in patients exposed to similar stressful situations.[16] A recent study found that salivary amylase increased in pregnant women waiting for Caesarean delivery.[29] A possible explanation for the poor correlation found in our study is the reported attenuation of the salivary amylase response to psychosocial stresses in pregnant women.[30] However, it is more likely that this indirect physical measure of stress was not associated with spinal hypotension because of its questionable validity as a measure indexing psychological anxiety. In contrast, the two direct psychological measures used in this study, STAI-s and VAS, capture the essence of the subjective experience. Participants are questioned about their feelings regarding a stressful situation and their responses (reported on a numeric scale) are combined to create a measure of anxiety. As the questions directly address subjective feelings, they usually provide a good estimate of how anxious participants truly are. By comparison, salivary amylase is, at best, only indirectly related to anxiety. Even in stereotypically stressful situations, it is impossible to predict the individual level of salivary amylase, which is affected by a range of physical and psychological factors.

We were concerned that dehydration could be a potentially confounding factor, since preoperative dehydration may increase anxiety and other stress-related symptoms and might also precipitate more marked hypotension after spinal anaesthesia. However, the baseline heart rate and pulse pressure and the baseline haematocrit were only marginally different between the groups and there was no difference in pulse pressures or fluid loading, so preoperative dehydration is unlikely as an alternative explanation for our findings.

In conclusion, preoperative anxiety, assessed by a simple subjective VAS score, had a significant effect on the reduction in SAP after the onset of spinal anaesthesia for Caesarean delivery. These data should remind anaesthetists of the importance of alleviating anxiety in our patients before operation. Although it may be speculated that prophylactic phenylephrine infusions might confer additional benefit in highly anxious patients, this hypothesis should be assessed by a future prospective study.

Declaration of interest

None declared.

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