Choosing a vasopressor for the pregnant patient
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Sometimes it is necessary to administer a vasopressor to the obstetrical patient. However, increasing the mother's blood pressure does not necessarily increase placental perfusion. In this article, the authors review the vasopressor choices available to the anesthetist.

In addition to the possible need for analgesia and anesthesia for childbirth, the pregnant patient may present with additional anesthetic needs unrelated to the pregnancy. Emergency non-obstetrical surgery may be necessary for a variety of reasons including infection, visceral obstruction, neoplasm, and trauma.

It should also be noted that more parents are desiring to become active participants in the birth experience. Mothers want to be awake; therefore, regional anesthesia is playing an increasingly important role in obstetrics.

Although hypotension is considered the most common complication of regional anesthesia, it can also be encountered with general anesthesia, especially in the emergency patient. The mechanisms of hypotension are primarily due to:

1. Aorto-caval compression secondary to the pregnant uterus;
2. The sympathectomy created by the regional anesthesia; and
3. Hypovolemia.

Hypotension is enhanced in the pregnant patient because of the pressure created by the gravid uterus on the vena cava which further decreases venous return when the patient is in the supine position. Prophylactic measures which can be taken to avoid hypotension include: (1) preloading the circulatory volume with IV fluids; (2) utilizing a left or right lateral tilt to displace the uterus off the vena cava; and (3) using two-thirds of the recommended dose of the local anesthetic. This latter measure is suggested because of the diminished size of the epidural and subarachnoid space secondary to the congestion of the internal venous plexus.

Despite these prophylactic measures, hypotension still occurs, and it may become necessary to administer a vasopressor. The improper selection of a vasopressor for the correction of hypotension in the pregnant patient may cause complications for both mother and child. The question now arises as to which vasopressor should be used.

To correct hypotension following regional anesthesia, one must remember that after a sympathectomy, further uterine artery vasodilatation does not occur. Therefore, one does not want to administer a vasopressor which produces uterine vasoconstriction. Simplistically, the well being of the fetus is largely dependent upon uterine blood flow (UBF).

\[ UBF = \frac{\text{perfusion pressure}}{\text{vascular resistance}} \]
It has been observed that fetal bradycardia develops when maternal systolic blood pressure falls below 80 torr, however, 100 torr is the current guideline.8

With decreased blood pressure, there can be decreased uterine blood flow and an associated decreased placental perfusion and oxygenation. Hypotension must be corrected in the pregnant patient without further decreasing uterine blood flow. It then becomes necessary to review the pressor drugs and their effects on the uterine vascular bed in relationship to the pregnant patient before one can select the vasopressor of choice.

Choosing the pressor drug

A pressor drug can be defined as a drug which increases blood pressure above the existing level.4 Unfortunately, the manometer reading rather than the patient is often treated. Elevating the blood pressure does not necessarily improve tissue perfusion, especially uterine blood flow. Most pressure drugs are sympathomimetic amines and can be classified by the three methods which elevate the blood pressure:

1. Target organs stimulated, that is, (a) the heart, and (b) the periphery.

2. Type of action, that is, (a) Direct—action on the receptor site which produces a response similar to norepinephrine and is not altered by a depletion of norepinephrine, and (b) Indirect—dependent upon the release of norepinephrine and an intact nerve.

3. The third method suggested by Alquist in 1948 is perhaps the simplest for selecting a vasopressor and involves the adrenergic receptors stimulated being either: (a) alpha, or (b) beta.

The following outline is effective

Figure 1.
Changes in maternal and fetal arterial pH following maternal spinal hypotension and subsequent correction with methoxamine.

<table>
<thead>
<tr>
<th>CONTROL</th>
<th>HYPOTENSION</th>
<th>METHOXAMINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.00</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(MATERNAL --- --- --- --- --- ---)
(FETAL --- --- --- --- --- ---)
(MEAN ± S.E. --- --- --- --- --- ---)

in predicting the response of the receptor site to sympathomimetic drugs.²

<table>
<thead>
<tr>
<th>Alpha receptors</th>
<th>Beta</th>
</tr>
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<tbody>
<tr>
<td>Blood vessels</td>
<td></td>
</tr>
<tr>
<td>Vasodilatation</td>
<td></td>
</tr>
<tr>
<td>Uterine vessels</td>
<td></td>
</tr>
<tr>
<td>Uterine muscle</td>
<td></td>
</tr>
</tbody>
</table>

Using the most common vasopressors, one can classify and predict the response of vasopressors accordingly.⁵

<table>
<thead>
<tr>
<th>Vasopressor</th>
<th>Direct / Indirect</th>
<th>Alpha</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenaline</td>
<td>Direct</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>Both</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Metaraminol (Aramine®)</td>
<td>Both</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Mephentermine (Wyamine®)</td>
<td>Both</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Isopropenol (Isuprel®)</td>
<td>Direct</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>Phenylephrine (Neosynephrine®)</td>
<td>Direct</td>
<td>++++</td>
<td>-</td>
</tr>
<tr>
<td>Methoxamine (Vasoxyl®)</td>
<td>Mainly direct</td>
<td>+++</td>
<td>-</td>
</tr>
</tbody>
</table>

Looking at the classification according to the adrenergic receptor being stimulated, one would assume methoxamine produces intense vasoconstriction. In a survey conducted in Ohio (1973) given to anesthesiologists, obstetricians, and CRNA's, more than 50% of the individuals responding chose methoxamine as a first choice to treat hypotension.⁶ Along with the intense peripheral vasoconstriction produced by methoxamine, there is uterine vascular bed constriction; therefore, placental blood flow is decreased with the potential for fetal hypoxia, hypercarbia, and metabolic acidosis as demonstrated by Shnider, et al.⁸ (Figure 1.)

Having already demonstrated the definite hazard in the use of methoxamine in correcting maternal hypotension, it is important to note those pressor agents which produce the least vasoconstriction as illustrated.⁷

From the graph in Figure 2, one can conclude that ephedrine and mephentermine produce the least uterine artery constriction. It has been suggested that ephedrine increases blood pressure by increasing cardiac output, and therefore the flow of the vascular beds is increased.

Pregnant ewes have been used to further evaluate uterine blood flow due to obvious potential hazards to the human fetus.⁹ In a study conducted by the Department of Anesthesia at the University of California Medical Center with the use of pregnant ewes, maternal and cardiovascular and acid-base changes following hypotension and the administration of ephedrine demonstrated that, in addition to correcting

Figure 2.
A comparison of the dose-response curves of isolated human uterine arteries to norepinephrine, phenylephrine, metaraminol, dopamine, mephentermine, and ephedrine. All tissues were first maximally contracted to norepinephrine (NE) before the responsiveness of the tissue to the biogenic amines was studied.
maternal hypotension, fetal deterioration was also arrested as illustrated.\textsuperscript{8} (Figure 3.)

In a similar study using pregnant ewes, mean changes in uterine blood flow at equal elevations of mean arterial blood pressure with vasopressor administration (as demonstrated by Ralston's work) showed that metaraminol and methoxamine decrease uterine blood flow at all levels.\textsuperscript{9} (Figure 4.) In addition to decreasing the uterine blood flow, methoxamine decreased cardiac output significantly. Ephedrine had no detrimental effect on uterine blood flow even in doses that increased maternal blood pressure as much as 50%. Also, one should note that although mephenetermine does decrease uterine blood flow, it is not as significant as metaraminol and methoxamine.

Therefore, one must conclude from the result of these studies that ephedrine and mephenetermine are vasopressors of choice in correcting maternal hypotension. Of these two, ephedrine offers the least impairment to uterine blood flow, and therefore is considered the better.

The usual initial dose of ephedrine in correcting maternal hypotension is 12.5-25.0 mg IV depending on the severity of the hypotension. If after one circulation time there is no response, the dose may be repeated or increased. Tachyphylaxis can be seen with ephedrine, and it may be necessary to change to mephenetermine 15-30 mg IV.

\textbf{Vasopressor-oxytocin synergism}

It would be an omission to discuss the use of vasopressors in obstetrics

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Changes in fetal arterial oxygen tension in Experiment 3 following maternal spinal hypotension, maternal hypoxia oxygen, and then ephedrine administration to the mother.}
\end{figure}
without exploring the vasopressor-oxytocin synergism. Cases of persistent postpartum hypertension and even cardiovascular accidents have been reported after the administration of an oxytocin and a vasopressor. Ergot preparations, methylergonovine (Methergine®) or Ergonovine (Ergotrate®) are potent vasconstrictors. Oxytocic drugs are routinely given post-delivery and cause the uterus to contract, thus increasing cardiac output and blood pressure. Vasopressors may sensitize the vessels to the effect of the ergot preparations.

After the removal of the placenta, a large arteriovenous shunt is removed. With regional anesthesia, these events seem to occur as the sympathetic blockade wears off and sympathetic tone returns. Ergot derivatives should be avoided in the patient who has received a vasopressor in the previous 3-4 hours. Hypertension has not been observed in the use of a synthetic oxytocic as syntocinon (Pitocin®). However, hypotension has been observed with an IV bolus injection of this synthetic oxytocin.10

**Conclusion**

The conclusions that are to be drawn from this article, although obvious, should be reiterated:

1. Maternal hypotension, a frequent complication of regional anesthesia, is accentuated by the aortocaval compression of pregnancy.

2. Vasopressors which primarily stimulate the alpha adrenergic receptors

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**Figure 4.**

Mean changes in uterine blood flow at equal elevations of mean arterial blood pressure after vasopressor administration.

markedly decrease uterine blood flow, and therefore should not be used in correcting maternal hypotension.

3. Ephedrine with more cardiac than peripheral effects appears to be the vasopressor of choice. Mephenetermine is the second choice.

4. Avoid the use of methergine or ergot preparations in the patient who has received a vasopressor within 3-4 hours. If necessary, use ergot preparations with careful monitoring of maternal blood pressure.

REFERENCES
(6) Survey, Dr. Thomas H. Joyce III, personal communication.

AUTHORS
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