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Review

# Overview of the management of postural tachycardia syndrome in pregnant patients

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A B S T R A C T

Postural tachycardia syndrome (POTS) is a chronic condition characterized by symptoms of orthostatic intolerance.

Pregnancy can cause different physiological changes in cardiovascular parameters, that could have greater impact on POTS patients.

In this review, we discuss the management of POTS in the pregnant and obstetric settings.

## 1. Introduction

Postural tachycardia syndrome (POTS) is a chronic condition characterized by symptoms of orthostatic intolerance such as lightheadedness, palpitations, fatigue, trouble concentrating, exercise intolerance, and in severe cases, it can result in syncope. In addition to symptoms, in adults, diagnosis requires increase in heart rate (HR) ≥ 30 beat per minute (bpm) within 10 min of standing or upright tilt-table test, in the absence of orthostatic hypotension (a decrease in systolic blood pressure > 20 mm Hg). Diagnosis requires exclusion of other causes of orthostatic intolerance like prolonged bedrest, medications, severe anemia or dehydration (Grubb, 2008; Raj, 2013). POTS is more predominant in females of child-bearing age.

In this article, we review the available literature regarding POTS in pregnancy. A computerized search in the PubMed, Medline and Embase database was performed to retrieve the related studies between years 1970 and 2017. Subsequently, a manual search of the reference lists from the retrieved articles was done to identify additional articles.

## 2. Postural tachycardia syndrome and pregnancy

### 2.1. Normal physiology in pregnancy

Pregnancy is associated with various physiological changes in cardiovascular parameters. Increase in blood volume (both plasma volume as well as red blood cell mass), usually starts early in the first trimester of pregnancy and continues until third trimester (Pritchard and Jack, 1965). Blood volume increases by up to 50% and is important to supply the great vascular system of the uterus, protect against reduced venous return in supine position, and finally protect against the effects of blood and volume loss during delivery and early postpartum period.

Cardiac output increases during the first and second trimesters, varies during third trimester and falls postpartum. The increase in cardiac output occurs due to an increase in heart rate and stroke volume (van Oppen et al., 1996). The latter results from an increase in blood volume as described above. During the late stages of pregnancy, cardiac output is somewhat position dependent, as the gravid uterus can compress the inferior vena cava and reduce venous return while supine (Kerr, 1965).

Despite the increase blood volume and cardiac output, there is a normal decline in blood pressure during pregnancy which results from peripheral vasodilatation. This is mediated by decreased sensitivity to vasoconstrictors such as angiotensin and norepinephrine and an increased production of vasodilators like nitric oxide and prostacyclin (Goodman et al., 1982; Gant et al., 1980).

### 2.2. Review of prior literature on pregnancy in POTS

The degree of cardiovascular adaption during pregnancy, discussed above, is variable among patients. As such the course of POTS in pregnancy is quite variable. Generally, two thirds of patients experience symptomatic improvement in the second and third trimester that reverses rapidly after delivery, and about one third experience worsening symptoms (Kanjwal et al., 2009).

The first report of POTS in pregnancy was in 2005 by Glatter et al. (2005), who reported two cases of full-term pregnancy with patients with POTS. Both patients reported improvement in their symptoms up to six months of pregnancy with worsening symptoms after. Both

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patients delivered healthy babies by cesarean delivery and had improvement in symptoms postpartum. The only reported complication during pregnancy for both patients, was hyperemesis gravidarum which was successfully treated with ondansetron. In a series of 22 patients by Kanjwal et al. (2009), 55% of patients reported improvement in symptoms, 13% unchanged symptoms and 31% had worsening symptoms. Another report of nine pregnancies in seven patients with POTS reported variable change in symptoms during pregnancy and no increase in pregnancy related complications (Powless et al., 2010). In a study of 116 pregnancies, Kimpinski et al. (2010) compared POTS between parous and nulliparous and found no significant difference except for disease duration which was longer in parous women. Peggs et al. evaluated 29 POTS patients who became pregnant and compared them with 23 controls, they found no statistical difference in symptoms during pregnancy nor statistical difference of pregnancy related complications (Peggs et al., 2010). Blitshteyn et al studied 17 pregnancies in 10 patients with POTS and found no significant change in maternal or fetal related complications (except for high rates or vomiting and hyperemesis gravidarum in the first trimester), 60% of patients remained stable or improved during pregnancy (Blitshteyn et al., 2012).

### 2.3. Management of POTS during pregnancy

So far, no reports have associated adverse maternal or fetal outcomes related to POTS. However, patients with debilitating POTS symptoms may want to consult with a high-risk obstetrician, and any obstetrician working with a POTS patient should take time to learn about the condition, and be familiar with the medications used to treat it.

Treatment for POTS symptoms in pregnancy should be individualized. So far, there is no single agent found to be universally effective in treating POTS patients, nor there are FDA approved medications for POTS. We recommend using the general guidelines when treating POTS patients in pregnancy (Sheldon et al., 2015).

Exercises with a goal of 25–30 min three times a week are encouraged. Generally, exercising while avoiding upright posture (such as recumbent bike or swimming) is better tolerated. Oral hydration (about 2 l a day) and salt intake (3–5 g of salts per day) are used as a first line non-pharmacological therapy (Grubb, 2008), but should be used in caution since hypertensive disorders of pregnancy are of special concern and are associated with increased mortality and morbidity for both the mother and the fetus. Elastic medical compression stockings can be helpful in some patients, and such stockings are often covered by insurance as a durable medical good with a prescription. Compression stockings designed to be worn during pregnancy are available. Lying on the patients left side while recumbent can minimize vena caval compression.

Non-pharmacological interventions are often adequate in the vast majority of patients, and whenever possible we try to wean patients off of medications prior to pregnancy. However, there are patients with more severe and disabling symptoms (in particular those with recurrent syncope) who may sometimes require pharmacotherapy. Table 1 shows the common medications used to treat POTS patients and their pregnancy classification. As illustrated, most medications commonly used for POTS patients are classified as pregnancy class C, except for desmopressin, octreotide, pyridostigmine (class B), and ivabradine (class D). Class C medications should be used with caution, due to weak evidence showing safety in humans. Furthermore, some showed harm in animal studies. For example, in animal studies, Midodrine was associated with increased rate of embryo resorption and reduced fetal body weight (*Product Information. ProAmatine (midodrine)*, n.d.); beta-blockers were linked to placental hypo-perfusion leading to intrauterine growth retardation (Meidahl Petersen et al., 2012), fetal and neonatal bradycardia, and hypoglycemia; and fludrocortisone was associated with teratogenicity (*Product Information. Florinef Acetate (Fludrocortisone)*, n.d.).

When medications are necessary, the α1-receptor agonist; midodrine (pregnancy category C) can be beneficial. Midodrine was trialed in pregnant patients with POTS with no adverse maternal or fetal outcome (Kanjwal et al., 2009; Glatter et al., 2005). Midodrine increases systemic vascular resistance, counteracting normal vasodilatory response in pregnancy. It can be started at a dose of 5 mg 3–4 times a day and then titrated up to 10 mg four times a day if necessary. It should be given every 4–6 h with avoidance of a bedtime dose.

Alternatively, beta-blockers (e.g. propranolol) were found to be effective (Raj et al., 2009). Beta-blockers decrease plasma norepinephrine levels in a hyperadrenergic state, and improve symptoms in patients where tachycardia is the chief complain. However, their use should be avoided in cases where tachycardia is thought to be a compensatory mechanism to hypotension or low output state.

In pregnancy, beta-blockers were successfully used with no adverse outcomes (Kanjwal et al., 2009; Powless et al., 2010; Lide and Haeri, 2015). Atenolol is another beta-blocker that can be used to treat POTS patients. However, it's classified as pregnancy category D and should be avoided in pregnancy if possible.

To augment intravascular volume after oral salt and fluid intake has been maximized, fludrocortisone (pregnancy category C) at 0.1 to 0.2 mg per day or desmopressin (pregnancy category B) at 0.1 mg to 0.2 mg at bedtime, are often used. Fludrocortisone was used by Kanjwal et al. (2009) in pregnant patients with POTS with no significant adverse effects. While fludrocortisone is used for its mineralocorticoid properties in POTS, it does have some glucocorticoid properties and glucocorticoids are generally used in pregnancy with caution.

In patients who are not responsive to or intolerant of the abovementioned therapies, duloxetine (pregnancy category C) and venlafaxine (pregnancy category C) may be added, which seem to be of particular benefit for patients with predominant symptoms of fatigue and anxiety.

Pyridostigmine (pregnancy category B) is an acetylcholinesterase inhibitor that improves tachycardia and symptoms in patients with POTS (Raj et al., 2005; Kanjwal et al., 2011). Pyridostigmine also increases bowel motility and many patients will not tolerate it due to multiple GI side effects (Kanjwal et al., 2011).

In patients with severe and disabling symptoms and in whom lifestyle modifications and prior therapy have failed, a trial of intermittent intra-venous hydration with normal saline for intravascular volume expansion was shown to be effective in reducing symptoms and improving quality of life (Ruzieh et al., 2017). Although this strategy has not been well evaluated in pregnant patients, infusing 1 L of normal saline over 1–2 h every week can be helpful in refractory cases. Hydration therapy can then be titrated up or down as needed. If the decision is made to start intravenous hydration, it should be considered on outpatient basis without the need for hospitalization. To minimize the risk of infections and thrombosis, the use of central lines and infusion ports is not recommended.

Fall and syncope precautions should be employed in all patients. In those with recurrent syncope or falls, partial bedrest is recommended to avoid traumatic injury to the mother or fetus.

Patients with Ehlers-Danlos syndrome (EDS) represent a considerable portion of POTS patients. This subgroup of POTS population is at higher risk for maternal and fetal complications as well prolonged bleeding and wound healing, and thus requires more monitoring and closer follow up (Jones and Ng, 2008; Sorokin et al., 1994).

### 2.4. Intrapartum management

In pregnant women with POTS, vaginal delivery and cesarean section surgery can both be carried out successfully without complications (Glatter et al., 2005; Powless et al., 2010; Blitshteyn et al., 2012; Lide and Haeri, 2015), and the choice for mode of delivery should be based solely on obstetrical considerations. Similarly, no evidence was found favoring one type of anesthesia, general vs. regional vs no anesthesia,

**Table 1**
Common medications used to treat POTS with their pregnancy category safety and breast milk secretion.

| Medication | Pregnancy category | Excreted in milk | Main side effects |
|---|---|---|---|
| Bisoprolol | C | Unknown | Dizziness, bradyarrhythmias, insomnia |
| Bupropion | C | Yes | Dry mouth, weight loss, insomnia, agitation |
| Clonidine HCL | C | Yes | Dry mouth, fatigue, dizziness |
| Desmopressin acetate | B | Yes | Headache, hyponatremia |
| Droxidopa | C | Unknown | Headache, dizziness, hypertension |
| Duloxetine HCL | C | Yes | Nausea, dry mouth, sleep disturbances |
| Erythropoietin | C | Unknown | Fever, nausea, hypertension |
| Escitalopram oxalate | C | Yes | Headache, nausea, sexual problems, insomnia |
| Fludrocortisone acetate | C | Unknown | Hypokalemia, glucose intolerance, adrenal suppression |
| Ivabradine | D | Unknown | Bradycardia, atrial fibrillation, visual brightness |
| Methylphenidate | C | Unknown | Insomnia, headache, hypertension, dependency |
| Metoprolol | C | Yes | Fatigue, headache, bradycardia |
| Midodrine | C | Unknown | Paresthesia, itching, hypertension |
| Octreotide acetate | B | Unknown | Gallbladder problems, hypothyroid, bradycardia |
| Propranolol | C | Yes | Bradycardia, hypotension, depression |
| Pyridostigmine bromide | B | Yes | Nausea, diarrhea, urinary frequency |
| Venlafaxine HCI | C | Yes | Headache, nausea, insomnia |

and the decision should not be influenced by the diagnosis of POTS, but rather should be left to the discretion of the treating obstetrician and anesthesiologist. In one report, epidural anesthesia was found to be safe, and didn't results in provoking POTS symptoms (Corbett et al., 2006).

During delivery, the second stage usually produces the maximum degree of strenuous Valsalva maneuver pressure which may produce a drop in blood pressure. In addition, pain and fluid loss may cause worsening hypotension and tachycardia, therefore hemodynamic parameters should be monitored frequently during this phase. Furthermore, vasodilation resulting from anesthesia can worsen hemodynamics. For those who experience hypotension, volume expansion with intravenous fluids and the use of vasopressors can be used as needed, detailed in part 2 below.

Tachycardia during delivery is most likely secondary to labor stress and pain, and should not be routinely attributed to POTS. Other causes of tachycardia such as hypovolemia, anemia, hyperthermia, anxiety, or pulmonary embolism should be considered and treated in the appropriate clinical settings.

### *2.5. Post-partum management*

After delivery, patients may experience either improvement or worsening symptoms of POTS (Kanjwal et al., 2009; Glatter et al., 2005). However, the majority remain stable (Kanjwal et al., 2009). Physical reconditioning after delivery helps symptoms, however, the decreased plasma volume caused by excessive postpartum diuresis can worsen symptoms in some patients. Breastfeeding should be encouraged when possible, as it stimulates the secretion of oxytocin, with its antidiuretic effect (Bernal et al., 2016), it counteracts excessive diuresis after delivery.

The use of medication during breastfeeding should be cautious as most commonly used medications for POTS may potentially enter breast milk. See Table 1.

## 3. Conclusion

There is a lack of data regarding the management and outcome of POTS patients in the pregnant and obstetric settings, and further research is warranted.

Management is individualized and should follow the general guidelines (Sheldon et al., 2015). The decision regarding the mode of delivery and need for anesthesia must be based on obstetrical and surgical considerations only and not influenced by the pre-existing diagnosis of POTS.

## Conflicts of interest

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