

Exploring the Link Between Down Syndrome and Hypercoagulability with a Focus on the Use of Oral Contraceptives and the Development of Acute Thrombosis



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BACKGROUND

Adults with Down syndrome (DS) have additional risk factors for hypercoagulability compared to the general population.¹ Non-modifiable risk factors include congenital heart disease, hematologic malignancies and Moyamoya disease, while modifiable risk factors include obesity, a sedentary lifestyle and smoking status.^{1, 2} Accordingly, there are anecdotal clinical patterns suggesting an increased occurrence of deep vein thrombosis (DVT) and acute thrombotic events in adults with DS who are on an oral contraceptive pill (OCP). These findings highlight the need for careful monitoring and consideration of hypercoagulable states in people with DS, particularly those on OCPs, to manage their heightened risk effectively.

OBJECTIVES

1. Identify modifiable and non-modifiable risk factors contributing to hypercoagulability in adults with DS.
2. Evaluate the patterns of the existing anecdotal evidence of acute thrombus development in patients with DS on an OCP.
3. Begin to formulate practical guidelines to support best medical practices for managing patients with DS on an OCP or considering alternative agents for contraception and menstrual management.

METHODS

Using a PubMed search from 1960 to Present, we performed a literature inquiry seeking information on health guidelines pertaining to an increased risk of venous thrombosis and hypercoagulability in patients with DS. Critical key questions were formulated *a priori* to inform the search strategy. The MeSH terms [Down syndrome] and [thrombosis] were used for the first search. Additional searches were conducted with the terms [hypercoagulability], [thromboembolism], [thrombus], and [clot].

Consensus Questions:

- 1) What are the risk factors for thrombosis in adults with DS?
- 2) What are the risk factors for thrombosis in typical adults who take OCPs?
- 3) What are the standard risk factors for thrombosis in typical adults?
- 4) Do the risk factors differ for adults with DS?
- 5) What is the prevalence of thrombosis in this population?
- 6) How do the risk factors impact the morbidity and mortality in people with DS?
- 7) Do OCPs increase the risk of thrombosis in adults with DS at a higher rate than adults without DS?

RESULTS

The search strategy produced no results, however there have been three cases that generated our interest on this topic:

Criteria	Case 1	Case 2	Case 3
Demographics and Medical History	39-year-old female with DS, hypothyroidism, and gastroesophageal reflux disease BMI > 30 kg/m ²	19-year-old female with DS; otherwise healthy BMI > 30 kg/m ²	26-year-old female with DS, Moyamoya disease, juvenile idiopathic arthritis, bronchiectasis, anxiety, and depression BMI > 30 kg/m ²
Current Medications	OCP Levothyroxine Omeprazole	OCP	Infliximab Methotrexate Citalopram Albuterol inhaler OCP
Presenting Complaint	Acute right-sided weakness	Refusal to walk/ bear weight on leg with unilateral swelling	Dizziness, vertigo, left-sided headache
Diagnostic Workup	CT Head MRI Head Hypercoagulability panel	Doppler US	CT Head CTA Head
Outcome	Thalamic stroke confirmed Cardiac and hypercoagulability workup unremarkable	Acute DVT diagnosed No further workup pursued	Bilateral MCA stroke repaired with bypass

Table 1: Case presentation of three patients with DS diagnosed with acute thrombus.

REFERENCES



The authors have no disclosures.



DISCUSSION

- Virchow's triad describes categories of factors that contribute to thrombosis including blood hypercoagulability, hemodynamic changes, and endothelial injury.
- Patients with DS are predisposed to congenital heart disease, hematologic malignancies, blood vessel structural abnormalities, and sedentary lifestyles.³ Therefore, at baseline, they compromise elements of Virchow's triad and therefore are at increased risk of acute thrombosis.
- Additionally, Moyamoya disease, a direct contraindication for OCP use, is three times more common in patients with DS than in the general population.^{4,5} A sequelae of this illness is vascular proliferation around the stenosed vessels forming collaterals that are delicate and prone to injury and thrombus formation.
- Experts suggest that Moyamoya disease is typically diagnosed before the need for OCPs in adults with DS who menstruate. Due to the natural history of the disease, many patients come to care before menarche.^{6,7} However, there is a dual peak in incidence, and as Case 3 in **Table 1** demonstrates, some diagnoses occur later in life.⁶ This is problematic because combination of Moyamoya and OCPs can lead to thrombosis.⁵
- OCPs create a hypercoagulable state. When started in a patient with DS, there must be careful evaluation of underlying risk factors. However, these risk factors may not be initially apparent or even discoverable on routine exam.
- A retrospective analysis at Children's Medical Center Dallas (2000 - 2005) found that children with DS were significantly more likely to develop thrombosis, with notable cases of DVT and arterial ischemic stroke.⁸ These results suggest that DS may be an independent risk factor for thrombotic complications in childhood. Unfortunately, we were unable to find research to support these findings in adults with DS who menstruate.
- This lack of direct evidence complicates and increases the potential risks of prescribing OCPs to adults with DS, despite their higher likelihood of having risk factors for thrombosis.

CONCLUSIONS

The lack of current peer-reviewed information exploring the relationships between adults with DS and hypercoagulability creates challenges formulating guidelines for OCP use in adults with DS who menstruate. Upon OCP prescription, patient counseling should emphasize the initial signs and symptoms of an acute thrombus to seek emergency medical attention without delay. We encourage providers to assess the modifiable and non-modifiable risk factors for acute thrombosis in adults with DS who menstruate and use shared decision making to discuss treatment options to minimize the risk of thrombotic events.