

IVIIG vs Corticosteroids in Idiopathic Thrombocytopenia Purpura

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Patient TG: Subjective

- CC: TG presented to the ER on 4/2/09 with a 2 week history of uterine bleeding and two syncopal episodes in the same day
- HPI:
 - Menarche began approximately 1 year ago
 - Periods had been irregular, heavy, and erratic
 - Had stabilized in the last 6 months but flow remained heavy and lasted 5-6 days on average
 - Saw PMD on 3/30/09
 - Syncopal episodes this morning while getting ready for school and then again at school
 - Went back to PMD who sent her to the ER

Subjective cont.

- Allergies: NKDA
- PMH:
 - Persistent prolonged epistaxis
 - Occasional bleeding from gums
 - ADHD x 2-3 years
- FH:
 - No bleeding history
 - Ovarian cancer in grandmother

Subjective cont.

- SH:
 - Parents divorced
 - No siblings
 - In 7th grade
- Immunizations: UTD
- Home medications:
 - Dexmethylphenidate 20 mg po qd
 - “Iron vitamin” po qd

TG: Objective

- Physical exam:
 - Negative except for pale appearance, fatigue, and previously mentioned pelvic abnormality
- Height: 5'2"
- Weight: 49 kg

Vitals

Date	T _{max}	Pulse	RR	BP	O ₂ Sat
4/2/09 (ER)	99.4	102-109	16-20	90/61	100% on RA
4/3/09	99	75-102	20-26	91-124/ 44-84	100% on RA
4/4/09	98.8	88-131	16-20	95-105/ 44-72	
4/5/09	100	81-100	20	88-106/ 47-50	92-99% on RA
4/6/09	99	76-92	18-24	98-100/ 49-56	
4/7/09	99.4	80-97	16-18	96/55	

Objective: Labs

■ 4/2 in ER

- BMP: WNL
- LFTs: WNL
- Coagulation:
 - PT: 14.6 sec (10.2-12)
 - INR: 1.1
 - PTT: 23.9 (26-37)
- ANA: negative
- Direct Coombs: negative

– CBC:

- WBC: 7.91
- Hemoglobin: 6.4 g/dL (14)
- Hematocrit: 18.9% (41)
- Platelets: 26K/ μ l (150-350K/ μ l)
- Reticulocyte count: 5.6% (0.5-1%)

Idiopathic Thrombocytopenia Purpura

- Also known as immune thrombocytopenia purpura¹
- Autoimmune disease characterized by increased peripheral platelet destruction
 - Results in thrombocytopenia and bleeding diathesis
 - Most commonly results in mucocutaneous bleeding, but intracranial hemorrhage is the most feared complication
 - Bleeding generally occurs when platelet counts drop below 20,000/ μ l

Idiopathic Thrombocytopenia Purpura

■ Diagnosis²:

- Isolated thrombocytopenia (all other blood counts normal and smear is normal)
- No clinically apparent associated conditions that may cause thrombocytopenia
- Typically presents in an otherwise healthy child with abrupt onset of bruising and/or bleeding

■ Prognosis:

- Self-limiting in most cases with a high rate of spontaneous resolution (~80% at 6 months)
- Different from Chronic Thrombocytopenia Purpura
 - Defined as platelets <150K/ μ l for longer than 6 months

Idiopathic Thrombocytopenia Purpura

- Management is controversial^{1,3}
 - “Watch and wait”
 - Most experts agree that treatment should begin if platelets reach $<10\text{K}/\mu\text{l}$ or are $<20\text{K}/\mu\text{l}$ with significant mucosal bleeding
- Treatment options:
 - IVIG
 - IV RhIG (IV anti-D rhesus 0 immunoglobulin)
 - Splenectomy
 - Immunosuppressive drugs
 - Corticosteroids
 - Azathioprine, vinca alkaloids, cyclophosphamide, and cyclosporine
 - Transfusions

Back to TG: Hospital Course

- Day 1 (ER)
 - Several labs drawn
 - PT, PTT, Hgb, Hct, Platelets, Retic abnormal
 - Pelvic ultrasound completed
 - 1 unit PRBCs transfused
- Day 2
 - 2nd unit PRBCs given
 - More labs ordered
 - Hematology/Oncology and OB/GYN consulted
 - IVIG given

Hospital Course

■ Day 3

- Still bleeding profusely (3-4 pads/day)
 - Estrogen therapy started by OB/GYN
- 2 more units PRBCs transfused
 - H&H significantly improved (6.2 & 19.3 to 10.7 % 32.2)
- Patient c/o headache and nausea after IVIG infusion
 - Ondansetron and morphine given

■ Day 4

- Patient looks and feels much improved
- Vaginal bleeding persists

Hospital Course

■ Day 5

- Still bleeding, but amount has decreased
 - Down to 2 soaked pads/day
- Taper for estrogen written

■ Day 6

- Bleeding subsided (no pads)
- Discharged home to parents' care
- Will f/u with OB/GYN in 1 week and her PMD in 2 weeks

Clinical Question

- **Is IVIG superior to corticosteroids in the management of idiopathic thrombocytopenia purpura?**

Blanchette, et al.⁴

- Objective
- Methods
 - Prospective, randomized trial in 5 centers in Canada
- Inclusion criteria
 - Age >6 months and <18 years
 - Platelet count $\leq 20 \times 10^9/L$
 - Bone-marrow aspirate that showed normal or increased numbers of megakaryocytes
- Exclusion criteria
 - If other labs were inconsistent with ITP
 - If an alternative cause of the thrombocytopenia was found
 - Evidence of Chronic ITP

Blanchette, et al.

- Study protocol
 - IVIG vs prednisone vs no therapy
- Primary outcomes
 - Number of days the children continued to have platelet counts less than $20 \times 10^9/L$
 - Number of days required to reach platelet counts greater than $50 \times 10^9/L$
- Secondary outcome
 - Any adverse effect of therapy

Blanchette, et al.

■ Results

- Prednisone and IVIG significantly better than no therapy in both outcomes
- IVIG significantly better than prednisone in time to reach platelet count of 50K/ μ l

■ Adverse effects

- IVIG: n/v (63%), headache (56%), fever (19%)
 - Most common 24-72 hours after infusion
- Prednisone: weight gain (average gain of 3.6% of weight before therapy)

■ Authors' conclusions

■ Strengths and Weaknesses

Ancona, et al.⁵

- Objective
- Methods
 - Prospective, randomized trial of 77 patients at a single center
- Inclusion criteria
 - Platelet count $<20 \times 10^9/L$ with associated findings suggestive of ITP
 - Peripheral smear consistent with ITP
- Exclusion criteria
 - None identified

Ancona, et al.

- Protocol
 - IVIG vs methylprednisolone
- Results
 - Both treatments statistically significantly increased platelet counts from baseline from 24 hours to 4 weeks
 - IVIG was statistically significantly better in the first week
- Authors' conclusions
- Strengths and weaknesses

Beck, et al.⁶

- Objective
- Study design
 - Systematic review and meta-analysis
- Primary outcome
 - Number of patients with a platelet count $>20,000/\text{mm}^3$ at 48 hours after the initiation of treatment
- Secondary outcomes
 - Number of patients with a platelet count $>20,000/\text{mm}^3$ at both 24 and 72 hours
 - Number of patients who developed chronic ITP
 - Presence of ICH
 - Mortality

Beck, et al.

- Inclusion criteria

- Must be RCT
- Patients 3 months to 18 years presenting for the first time with ITP
- Minimum of 2 arms in the study
- Reporting of platelet counts

- Exclusion criteria

- Studies of children with an underlying disorder
- Children previously treated for ITP
- Patients with chronic ITP

Beck, et al.

- Results
 - Primary endpoint
 - RR of achieving platelet count $>20,000/\text{mm}^3$ at 48 hours was 0.74 (95% CI:0.65,0.85)
 - NNT= 4.55
 - Explanation
 - Secondary endpoints
 - RR of achieving at 24 hours was 0.63 (95% CI: 0.48,0.83)
 - NNT= 5.88
 - RR of achieving at 72 hours was 0.83 (95% CI: 0.76,0.91)
 - NNT= 6.25
 - 21% of patients developed chronic ITP
 - 25% in steroid group vs 18% in IVIG group (p=0.04)
- Authors' conclusions
- Strengths and weaknesses

My Conclusion

- Use of IVIG at a dose of 1 gm/kg for 1 or 2 days results in a more rapid increase in platelet count when compared to corticosteroids.
- In the case where the platelet count is less than 20,000/mm³ and there is evidence of bleeding, IVIG should be the treatment of choice to prevent potential intracranial hemorrhage and stop current bleeding.

Back to TG: Assessment

■ Assessment

- TG presented with a platelet count of 19,000/mm³ on the morning after admission along with heavy vaginal bleeding and decreased H & H
- Rapid recovery of the platelets is desirable to reduce current bleeding and reduce the risk of ICH
- Hematology and OB/GYN consults both appropriate
- IVIG is an appropriate choice in this circumstance
- Estrogen is also appropriate to help stop the bleeding in this case

Back to TG: Plan

■ Plan

- As was done in TG, IVIG at a dose of 1 gm/kg should raise the platelet count to a more reasonable level
 - Monitor for adverse effects such as headache, fever, and nausea
 - Treat these adverse effects as needed (also done in this case)
- Continue estrogen therapy to prevent further bleeding
 - Monitor for adverse effects such as headache, abdominal cramping, and nausea
 - Treat adverse events as needed
- Follow-up with OB/GYN in one week, PMD in 2 weeks

References

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