PREAMBLE

For several years there has been concern among anesthesiologists that there is an increased risk of clinically significant intra-operative bleeding in patients on longstanding Valproic acid therapy. There have been several cases where it is possible that valproic acid may have played a role in significant hemorrhage. However, the majority of our patients on longstanding valproic acid therapy require this treatment for prevention of seizures as they have failed other therapies. It can be very difficult to wean these patients off of valproic acid and onto another anticonvulsant therapy.

Upon review of available evidence the following guideline was developed that balances the risk of intra-operative bleeding and the risk and difficulty in stopping the valproic acid.

Evidence

The findings of an extensive review of the evidence were ambivalent. There is no definitive answer in the literature to the question “does longstanding valproic acid therapy (greater than 6 months) increase the risk of surgical bleeding?” There are several published case reports (1, 2) of patients on valproic acid experiencing hemorrhage but there is not clear evidence that valproic acid causes clinically significant surgical bleeding.
There are studies that found evidence of abnormal coagulation apparent on coagulation tests (prolonged aPTT, reduced vWF, decrease in Factor XIII), however, it is not clear that these findings have clinically significant effect on bleeding (3, 4, 5).

**POLICY**

The following protocol must be followed for any patient receiving valproic acid therapy have a minor or major surgical procedure.

**PROTOCOL**

Given the inconclusiveness of the evidence and the difficulty in switching patients off valproic acid following plan for patients coming for elective surgery is recommended:

a) **Patients on valproic acid having minor procedures OR procedures where blood loss is unlikely. Examples:** g-button changes, hernia repairs, BMT

- DO NOT STOP valproic acid.
- NO BLOOD WORK required.
- Proceed with surgery.

b) **Patients on valproic acid having major procedures or procedures where blood loss is a known risk/significant concern (e.g. scoliosis repair, T&A, major abdominal surgery):**

- DO NOT STOP valproic acid.
- At least 2 months prior to surgery: order lab tests as recommended by Hematology (see Appendix B). These tests MUST be ordered at least 8 weeks prior to surgery as some specimens must be sent out to specialist coagulation laboratories.
- IF any abnormal results, a consult to Hematology MUST be sent 1 month prior to surgery date. This is to allow our Hematology colleagues enough time to see the patients and make any necessary plans with blood bank.
- If required, the Hematologist will make suggestions and preparations for how to appropriately manage excessive bleeding if it occurs.
- Hematologist will liaise with Blood Bank to ensure that the appropriate products are available on the day of the case.
- The hematologist will be available by telephone on the day of the case for advice and questions should excessive bleeding occur.
- **NOTE:** if this timeline is not respected (8 weeks prior for blood work and 4 weeks prior for consult), the case will be postponed until this procedure is followed.
In the event of emergent surgery and there is a concern for bleeding intra-operatively, suggest using platelets and then plasma (in that order) to obtain hemostasis. Tranexamic acid (10mg/kg intravenously) may also be used if not contra-indicated (eg contra-indicated in bleeding of upper urinary tract.)

this is the safest possible approach to these patients based on evidence currently available. It allows the patient to remain on their necessary medication while appropriately planning for possible excessive bleeding. This plan will require careful planning by surgeons to ensure that any necessary bloodwork and consultation requests are put in in a timely fashion.

REFERENCES


5. Effects of chronic administration of valproic acid to epileptic patients on coagulation tests and primary hemostasis Epilepsia March 2015, e49-e52.

Appendices

Appendix A - Valproic Acid Algorithm

Appendix B - Pre-Surgical Screening for Patients on Valproic Acid
Appendix A

Valproic Acid Algorithm

Patient is on Valproic Acid

- **YES**
  - Minor Procedure: OR Procedure with Minimal chance of Blood Loss
    - DO NOT STOP valproic acid. PROCEED WITH SURGERY
  - Major Procedure: OR Procedure where risk of blood loss is significant or a known risk
    - DO NOT STOP Valproic acid
    - 2 MONTHS prior to surgery: Blood work as recommended by Hematology - See Appendix B

- **NO**
  - Abnormal Results?
    - **YES**
      - Do NOT stop valproic acid
      - CONSULT Hematology for recommendations at least 1 MONTH prior to surgery
    - **NO**

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APPENDIX B

Pre-Surgical Screening for Patients on Valproic Acid

- DO NOT STOP valproic acid.
- This is the suggested panel of investigations for patients undergoing surgery that is deemed at higher risk for bleeding (see Appendix A).
- This needs to be requested at least 8 weeks prior to surgery date and interpreted before the day of surgery.
- In the event of emergent surgery/cases where this has not been requested, and there is a concern for bleeding intra-operatively, suggest using platelets and then plasma (in that order) to obtain hemostasis. Tranexamic acid (10mg/kg intravenously) may also be used if not contraindicated (eg contraindicated in bleeding of upper urinary tract.)

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IWK Policies Being Replaced

(new)

***

Version History

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