NAME OF PROJECT:
Immune Thrombocytopenia and Obstetric Neuraxial Anesthesia at Low Platelet Counts – An International Registry

Subcommittees
Women’s Health Issues in Thrombosis & Hemostasis SCC
Platelet Physiology SSC
Platelet Immunology SSC

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Description Abstract
State the application’s broad, long-term objectives and specific aims, making reference to the health relatedness of the project. Suggested length is 2-3 paragraphs.

Primary immune thrombocytopenia is defined by a platelet count below 100x10^9/L, following exclusion of competing etiologies. It affects around 1-2/1,000 pregnancies and may present prior to conception or during the antenatal period. Peripartum, the presence of ITP often proves particularly challenging, especially as it affects pain management for labour and delivery.

Contemporary obstetric analgesia largely relies on neuraxial techniques including epidural, spinal, and combined-spinal epidural (CSE), to provide a superior level of pain control. Yet fearing neuraxial hematoma, with its potential for irreversible neurologic injury, many anesthetists are hesitant to perform obstetric neuraxial anesthesia (OBNA) at platelet counts below 70-80x10^9/L.

It is important to recognize that, in contrast to other thrombocytopenic conditions (e.g. HELLP syndrome), that are characterized by platelet dysfunction, in ITP (despite accelerated platelet destruction), the function of the remaining platelets typically remains intact, modulating bleeding risk. Furthermore, the literature suggests that the risk of neuraxial hematoma in the context of OBNA is lower than in the non-obstetric population, quoted in one study as 1:200,000 vs. 1:29,000 following epidural placement or 1:50,000 vs. 1:22,000 following spinal placement.

Yet, owing to the rarity of the condition, and lack of clear determination of the specific platelet count predictive of complications related to neuraxial anesthesia, countless pregnant women with ITP and intermediately low platelet counts (50-80x10^9/L) are denied access to OBNA, resulting in suboptimal pain control, a situation typically unacceptable in other areas of medicine.

Our recent systematic review of patient-level data (in press Canadian Journal of Anesthesia), summarizing the entirety of the literature to date, demonstrated that of 291 pregnant women with ITP and platelet counts below 100x10^9/L, 166 received OBNA, with only 61 of these women receiving OBNA at platelet counts below 80x10^9/L. While no neuraxial hematomas were reported, given the small sample size and the rarity of neuraxial hematoma, particularly in the obstetric population, our review could not conclusively determine the safety of OBNA in ITP.
patients with platelet counts below 80x10⁹/L. The study further highlighted the continued reluctance to offer OBNA below the commonly quoted platelet count of 80x10⁹/L, based largely on consensus and theoretical presumption of risk, further negatively influencing the accrual of large-scale data that would enable evidence-based decisions in this regard.

Hence the objective of the proposed study is to set up an international registry to prospectively record outcomes of neuraxial anesthesia in women with ITP and platelet counts below 100x10⁹/L. The overarching aim of this registry would be to gather robust evidence to ascertain the safety of neuraxial anesthesia in this context, affording pregnant women with ITP at intermediate to low platelet counts the opportunity to receive neuraxial anesthesia peripartum, to more optimally manage the pain of childbirth.

**Design and methodology** (Data expected to collect, sample size and statistical analysis):

Describe concisely the research design and methods for achieving these goals. Suggested length 2-3 paragraphs

A prospective, international registry providing a platform for obstetric practitioners (Anesthesiologists, Hematologists, Obstetricians, Maternal-Fetal Medicine Physicians, Obstetric Medicine Physicians and others) to document details and outcomes of cases involving OBNA provided during the peripartum period to women with ITP and low platelet counts (below 100x10⁹/L).

Housing the registry in REDCap, with the support of the ISTH, would allow participation of practitioners world-wide, contributing to accrual of data for this relatively rare condition.

**Study population** (Inclusion, exclusion, eligibility) (patient population; recruitment of participating institutions/physicians and subjects; minimum number needed; expected number):

Suggested length 2-3 paragraphs

The study population would include pregnant women with ITP and peripartum platelet counts below 100x10⁹/L who received neuraxial anesthesia in the form of epidural, spinal or combined spinal-epidural. Acknowledging that the lowest platelet count accepted even by advocates of OBNA at lower platelet counts in this population is 50x10⁹/L, occasional reports of OBNA at even lower platelet counts are available, and all such reports will add valuable data; hence no lower range restriction for platelet count would be placed with respect to inclusion in the registry.

Pregnant women with thrombocytopenia other than ITP would be excluded.

Recruitment via advertisement of the registry at various national and international sub-specialty meetings of Anesthesiology, Obstetrics, Maternal-Fetal Medicine, Obstetric Medicine, and Hematology would be valuable in raising its profile and increasing data input. Recruitment via commentaries introducing the registry in target journals would also be submitted.

Given the rarity of the outcome and the relative rarity of the condition in question, an international registry is the only possible means by which adequate data will be accrued.
SSC Subcommittee Project/Collaborative Project

According to a calculation by Beilin (1997), if the risk of neuraxial hematoma in individuals with platelet counts above 100 x 10(9)/L is assumed to be 1:10,000, then detection of twice that incidence in patients with platelet counts below 100 x 10(9)/L would require over 200,000 patients. ITP complicates 1/1,000 (0.001) pregnancies. Conservatively, moderate-severe thrombocytopenia is encountered in approximately a quarter (0.00025) of these pregnancies. Globally, there are approximately 160 million pregnancies every year, with a conservative estimate of 50% of which (80,000,000) obtain OBNA. Thus, OBNA in pregnancies with moderate to severe thrombocytopenia could theoretically be provided in 20,000 pregnancies per year. With these numbers, it would take 10 years to accrue the necessary data.

However, even shy of these ambitious targets, the data gathered are expected to far exceed numbers generated by isolated institutions and will provide invaluable insight with respect to the safety of OBNA for pregnant women with ITP at intermediately low platelet counts, with the anticipation that the added data will result in eligibility of more women to benefit from OBNA.

Expected timeline:

- **Project stage/set up:** 3 months from approval
- **Launch:** Once set up is complete; likely Dec 2019
- **Duration:** 10 years
- **Finalization/analysis:** 6 months
- **Reporting:** 3 months

Expected outcomes (ie. publications):

SSC communication, original publication, potential change to existing guidance documents.

Description of project set/up and management, needed infrastructure and resources (summary):

The collaborative network provided by the ISTH would provide an invaluable platform through which to reach relevant clinicians. Likewise, access to REDCap provided by the ISTH would allow the input of data from international collaborators. If approval is granted, we would work with the relevant SSCs to create the REDCap registry and with relevant collaborators to input data over time.

Each individual wishing to add data into the registry would be responsible for obtaining consent from the patient. Data could be entered directly, or via an electronic data form provided to the clinician, which would then be e-mailed to the principal investigator and subsequently entered into REDCap.
Possible references:


