Polycythemia Vera

Polycythemia Vera Cancer Cluster Investigation in Northeastern Pennsylvania

Updated and expanded study of polycythemia vera and other myeloproliferative neoplasms in the tri-county area

Study Purpose

The purpose of this study was to examine PV reporting to the Pennsylvania Cancer Registry (PCR) following the original Agency for Toxic Substances and Disease Registry (ATSDR) polycythemia vera (PV) investigation; to determine whether other myeloproliferative neoplasms (MPNs) were similarly underreported or falsely reported; and to determine whether a cancer cluster persisted in the follow-up period. The original ATSDR PV cancer cluster investigation was conducted in a tri-county area in northeast Pennsylvania in 2006. This study was initiated to update and expand the original investigation.

Background

MPNs are a group of blood cancers characterized by overproduction of blood cells and include PV, essential thrombocytopenia (ET), primary myelofibrosis (PMF), and chronic myelogenous leukemia (CML). In 2005, several groups of researchers identified a mutation, *JAK2V617F*, that was present in a large percentage of PV patients (97%) and approximately half of ET and PMF patients. In 2008, the World Health Organization (WHO) included *JAK2V617F* mutation testing as part of the major criteria for diagnosing PV, ET, and PMF.

In 2005, using state cancer registry records, the Pennsylvania Department of Health (PADOH) determined that there was a significantly higher incidence of PV in Luzerne and Schuylkill counties compared to the rest of Pennsylvania. In 2006, PADOH asked ATSDR to help study PV patterns among residents in this area of northeast Pennsylvania. ATSDR reviewed medical records and conducted genetic testing for the *JAK2V617F* mutation. ATSDR confirmed the presence of a cluster of PV at the center of three counties (Carbon, Luzerne, and Schuylkill) in northeast Pennsylvania. The study also found that greater than 50% of PV cases that were reported to the cancer registry did not have PV or there was not enough information to confirm the diagnosis. Underreporting to the cancer registry occurred with 15 of the 33 confirmed cases not being reported.

What was studied

In this component of the overall PV cluster investigation, ATSDR asked PADOH to update and expand the original PV cluster investigations. PADOH awarded a subcontract to the University of Pittsburgh's Department of Biostatistics which conducted the study. The main goals of the study were to examine reporting of PV to the Pennsylvania Cancer Registry (PCR) for the years immediately following the original PV investigation, to determine if other MPNs had similar rates of underreporting and false reporting, and to determine if the original cancer cluster persisted in the follow-up study period.

Gathering and Analyzing the Data

Cases living in the tri-county area at the time of diagnosis were identified. PCR staff identified cases by searching PCR case reports and by visiting hematologist/oncologists offices to ascertain cases that should have been reported to the PCR. Additionally, cases could self-identify to study investigators.

The following cases by diagnosis and year of diagnosis were included in the analysis:

- PV, 2006-2009
- ET, 2001-2009
- PMF, 2001-2009
- CML, 2001-2009

Cases of acute panmyelosis with myelofibrosis, MPN not otherwise specified, and myeloid leukemia were also reviewed.

Persons identified as having these diseases were asked to complete a telephone survey, to release medical records relating to their MPN diagnosis, and to have a *JAK2V617F* mutation test if one had not previously been performed. Each case was reviewed and classified by three expert panel members to form a consensus opinion of each case as "definitely" or "probably" a case (true cases), "possibly" a case (indeterminate), or "definitely not" or "probably not" a case (false cases).

The researchers determined the completeness of the PCR for PV, ET, PMF, and CML. The accuracy of cases reported to the PCR was calculated, and the "true" incidence of the different MPNs was estimated. The researchers used software, SaTScan, which analyzes spatial and temporal data to determine if there were any geographic clusters of PV, ET, PMF, or CML.

Conclusion and Key Results

The researchers found that most cases had been reported to the PCR but only about half were true cases.

- Of the 56 cases reviewed by the expert panel, 88% of them were from the original PCR dataset.
- The expert panel's review of the 56 cases determined that 31 were true MPN cases, and 15 were false cases. There was not enough information to decide for 10 cases.
- Almost all CML cases were determined to be true cases (92%), while 69% of ET cases, 33% of PMF cases, and 30% of PV cases were determined to be true cases.
- The review of the subset of cases in this study that were originally reported to the PCR indicated that 47% were true cases. This means that many false cases of PV are reported to the PCR.
- All PV and CML cases determined to be true cases were included in the PCR dataset; however, only 78% of the ET cases were included in the PCR dataset. This means that approximately 20% of true ET cases are not reported to the PCR.

SaTScan analysis was performed for disease with five or more true cases (PV, CML and ET).

- Using the seven true PV cases, no statistically significant clusters were identified in space or in space-time.
- Using the eleven true CML cases, no statistically significant clusters were identified in space or in space-time.
- Using nine true ET cases, a statistically significant cluster was identified at the zip-code level when evaluated in space, but not in space-time.

The estimated incidence rates for most MPNs are lower than the rates calculated from the original PCR database.

- The estimated PV incidence rate was 2.5 (0.8-5.1) per 100,000, 64% lower than the original rate based on PCR reports after correcting for completeness and accuracy.
- The estimated ET incidence rate was 2.3 (0.6-3.8) per 100,000, slightly higher than the original rate based on PCR reports after correcting for completeness and accuracy.
- However, the wide range of values for estimated incidence rates reflects the variability associated with the findings based on the low response rate. The response rate for this study was 26%. This means that approximately ¼ of the identified cases agreed to participate in this study.

For More Information

When the results from all of the ongoing research projects for ATSDR's PV investigation are publicly available, ATSDR will plan a public forum to share and discuss the results with interested stakeholders.

Visit ATSDR's Web page on PV: http://www.atsdr.cdc.gov/sites/polycythemia_vera/index.html

Call ATSDR's toll-free PV information line (866-448-0242) or email jcx0@cdc.gov, which will connect you to Dr. Elizabeth Irvin-Barnwell, ATSDR Division of Toxicology and Human Health Sciences.

Contact Lora Siegmann Werner, ATSDR Region 3, by phone at 215-814-3141 or by email at lkw9@cdc.gov.