

The UTHSCSA Bartter GCRC EBP and TQM Collaborative AE Monitoring Program
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Problem: The Frederick C. Bartter GCRC Data and Safety Monitoring program is mandated by NIH-NCRR and VA Office of Research Oversight (ORO). The program is managed by the Research Subject Advocate (RSA) in collaboration with GCRC VA Nursing staff. Nursing support is provided as part of a sharing agreement with UTHSCSA and the STVHCS. Part of the Data and Safety Monitoring Program is the tracking of adverse events, with the responsibility being given to the RSA. The problem is the number of studies being conducted at the GCRC (110) and the inability of the RSA to oversee every study at a given point. The GCRC VA Nursing staff play a key role in assisting the RSA with adverse event identification and follow-up, especially if the investigator and/or nursing staff are unaware of the AE or reporting requirements.

Strategy: Key elements of the Data and Safety Monitoring Program include documentation quality control (QC), informed consent quality assurance (QA), adverse event reporting / tracking (CQI), protocol compliance (QA), and subject safety (QC). The program is designed as an evidenced-based practice (EBP) and total quality management (TQM) subject monitoring collaboration between the RSA and the GCRC VA nursing staff. The Evidence-Based Practice (EBP) and Total Quality Management (TQM) approach reviews scientific and objective data in the execution of the nursing process - specific to the intervention, evaluation, and reporting of subject safety and protocol compliance elements. The intervention, evaluation and reporting activities are performed in collaboration with the GCRC RSA. Feedback is given to nursing by the RSA regarding the AE tracking report on a quarterly basis. In-services are conducted for Nursing Staff in response to AEs and specific to informed consent, protocol changes, and data and safety monitoring programming.

Practice Change: Rather than utilizing the EBP-TQM for every study, which is not efficient use of resources, the collaborative program focuses on high risk studies. From October 2004 to June 2005, GCRC high risk studies included: the anthrax vaccine clinical trial, the Disulfiram, cocaine, ethanol clinical trial, and the insulin clamp clinical trials, and insulin clamps with muscle biopsies trials. The insulin clamp studies became a concern after the risk of hypoglycemic reactions were reported by nursing and dietician after the insulin clamp procedure.

Evaluation and Results: Concerning the *anthrax vaccine study*, nursing reported to the RSA AES related to abnormal lab results of an increased CPKs, ALTs; decreased WBCs and K+. The investigator and study coordinator were alerted of this finding. Root cause analysis included a VA lab QC investigation, researching the type of subjects involved, and reviewing the protocol abnormal lab parameters. It was found that 1) the VA lab calibration techniques and frequency were appropriate; 2) The protocol lab parameters too restrictive for these tests; and the investigator was reporting non-high risk AEs. As a corrective plan, 1) the IRB recommended changing reporting requirement to Grades 3 and 4 only; 2) the consent revised to include possible abnormal lab findings, and the RSA provided consultation to the study coordinator on appropriate AE grading. Subsequently, from January to March 2005, no AEs were reported as probably or possibly related. From April to June 2005, no AEs were reported as probably or possibly related. Since then, no safety or risk issues have been identified.

In the *Disulfiram, cocaine, ethanol clinical trial*, two AEs reported by nursing staff to the RSA regarding hypotension. These cases occurred in May and June 2005. The RSA conferred with principal investigator about the subject safety monitoring and protocol modification. The study's DSMB recommended protocol modification and the IRB approved the changes to the infusion rates. No other AEs have been reported since June 2005. In the *insulin clamp clinical trials*, a hypoglycemia protocol / standing order was developed by the RSA and Nurse Manager and instituted on the GCRC. A two month prospective monitoring of reactions by nursing following hypoglycemia protocol implementation demonstrated one reaction following insulin clamp. This was reported by nursing and appropriate nursing and medical intervention occurred. Because of the large population with diabetes, many studies are being conducted on the GCRC with this chronic disease problem. As part of the studies, *insulin clamps with muscle biopsies* are done. Three AEs were reported by nursing staff to the RSA regarding subjects experiencing tingling, pain, and numbness at the muscle biopsy site. The issue

was brought to the attention of the principal investigator by the RSA. The issue was also communicated to the GCRC Advisory Committee. Recommendations were made to the P.I. to revise the informed consent and they were approved by the IRB.

Recommendations: These four cases demonstrate the importance of nursing assisting the RSA in the identification and reporting of potentially serious subject safety issues. Nursing uses the evidenced based practice (EBP) model in assessing the potential problem. EBP is supported through reviewing the protocol, informed consent and other nursing research strategies. The nurse's team collaboration contributes to the degree of subject safety on the GCRC.