Title: Comparison of quality of bone marrow biopsy and patient convenience and pain control by a battery powered drill versus conventional methods in patients with plasma cell disorders

PRINCIPAL INVESTIGATOR:

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AIMS

1. Primary endpoint - Assessing the quality and quantity of bone marrow core biopsies.
2. Secondary endpoint –
   (a) Assessing the nature of pain by established VAS questionnaires.
   (b) Timing of the actual procedure

BACKGROUND:

Since the introduction of Jamshidi needle in 1971, we have not seen any advances in bone marrow sampling technology (Jamshidi & Swaim, 1971). In 2007, a new battery-powered bone marrow biopsy system was developed by OnControl Vidacare Corporation, Shavano Park, Texas, USA. This technology using a battery-powered drill to operate the needle to gain access to the posterior iliac bone was approved by the United States Food and Drug Administration (FDA) and currently commercially available.

The traditional method for gaining bone marrow involves grinding a needle by hand through a patient's skin and bone.

The oncontrol bone marrow biopsy device consists of a powered driver and biopsy needle set. The lithium battery-powered driver resembles a small hand-held drill and drives a needle into medullary cavity of the top ridge of your rear hip bone (iliac crest) to obtain the soft tissue located in the marrow space . The

needle set consists of two parts: an outer cannula, 11 gauge × 4 inches (102 mm) long; and a bevel-tip inner stylet, used to penetrate the cortex of the bone.

This method is most commonly carried out on the top ridge of the rear hip bone with a patient in the right or left lateral position. Procedure performed under anesthesia (medication that causes numbness), local anesthesia is provided via infiltrating an adequate area of the periosteum. Commonly a skin insertion is made (with a lancet) and the needle is inserted through the skin, once the needle touches the bone the drill is started. During the procedure, you will hear a sound and feel the vibration of the needle. After the powered drill advances the needle into the marrow cavity the inner stylet is removed and the threaded cannula grabs the marrow.

Marrow has both solid and liquid parts. Aspiration is the procedure used to collect the liquid part of the marrow. If the solid portion of the bone is sampled, this is called a biopsy.

In the aspiration, an incision will be made and a needle inserted through the skin. Once the needle touches the bone, the power driver will be started and you may feel some vibration. Within a few seconds, your doctor will stop and take a sample of liquid marrow with a syringe.

For the biopsy, after the aspirate has been collected, the power driver is restarted and, in a matter of seconds, your doctor will capture a sample of the solid marrow

Few randomized controlled trials (RCTs) compared the use of the battery powered bone marrow biopsy system to the traditional manual methods however they have certain limitations. Though the use of a powered drill is justified in selected patients, the results are not uniform. Swords et al reported that powered drill significantly reduces needle insertion pain and procedural time when compared to a manual technique (Swords et al., 2011)delivering similar quality of specimens by both method (Swords et al., 2010). In another RCT by Read et al evaluating hematologists-in-training, they were significantly faster and sampling was superior in quality when performed with the power drill (Reed et al., 2011). In the most recent RCT by Bucher et al, both methods produces similar results. In the absence of using conscious sedation, reported pain during the procedure is lower with the powered drill (Bucher et al., 2013). The limitations with these RCTs included relatively small number of patients, significant heterogeneity in patient population, and inclusion of patients with all indications. At our institution we have adapted to the power drill system and majority of the patients receive conscious sedation (by personal communication). We are proposing to conduct a RCT to identify the optimal procedure in patients with plasma cell disorders undergoing bone marrow biopsy due to technical challenges with concomitant osteoporosis/ osteopenia and ongoing bone loss in this particular set of patients.

PATIENTS AND METHODS:

Design

Prospective randomized control trial in multiple myeloma patients.

Outcomes:

- Bone marrow core biopsy length (in mm) and artifacts assessed by the pathologist blinded for the sample.
- Intensity of Pain as measured via VAS (visual analogue scale) for pain, a 10 point scale.
- Time taken by the procedure measured in seconds.

ELIGIBILITY CRITERIA

All patients with existing plasma cell disorders and no history of psychiatric disorders and can receive conscious sedation are eligible to participate in the trial.

EXCLUSION CRITERIA

Pregnant women are excluded from participating in this study due to the uncertainty in the positioning of pregnant patients for the procedure.

METHODOLOGY

PATIENT IDENTIFICATION:
The patients with plasma cell disorders undergoing bone marrow biopsy procedure at the procedure bay in Winship Cancer Institute will be identified weekly. The list of prospective patients will be shared among the clinical and research team.

SEDATION/ANALGESIA:

The eligible patients would be assessed whether they can receive consciuso sedation. Any contraindication to receive conscious sedation will exclude the patients from the study. Standard agents for conscious sedation as approved by the Emory University will be used. Standard personnel who can administer the conscious sedation will be able to perform the sedation and bone marrow biopsy.

APPROACH:

The eligible patients on the day of the procedure will be approached and the study strategy and the procedures are explained to the patients. Informed consent is given to the patients and adequate time is given for the patient and family members to review and make a decision regarding participating in the study. Voluntary patients interested in participating in this non-therapeutic study after signing consents will be randomized to the power drill arm or the traditional (Jamshidi) bone marrow biopsy arm.

RANDOMIZATION:

All the study participants are randomized by using a shuffling card method. 100 cards with predestinated procedure name (50 with traditional and 50 with powered biopsy) printed on them are shuffled and patient is asked to pick one card from the deck and he/she will be placed in the respective group. Every time the card is picked it is not replaced into the deck. This helps us to approximately achieve a balance in number of patients in each of the study groups.

QUESTIONNAIRES:

Patients are asked to fill out the VAS pain questionnaire before the start of the procedure and 30 minutes after the procedure, day 1, day 3, and day 7. Subject will be given a VAS pain scale to score the intensity of the pain. Majority of the patients will return to Winship Cancer Institute in a few weeks to discuss the results of the bone marrow biopsy. Questionnaires will be collected during this visit. In the event that the patient is not returning to Winship, patients will use the return stamped envelope provided on the day of the procedure to return the questionnaires. Patients will be contacted over the phone as a reminder to return the completed the VAS questionnaire if not received during the follow-up clinic visit. For the secondary endpoint of time taken for the procedure, we will use a stopwatch from the beginning to the completion of the procedure (skin to skin)

Variables to be considered during analysis: Sample size, length of procedure, pain intensity before procedure and at different time points after procedure, age, gender and BMI. [i]

Statistical methods: Analyzed using a SAS 9.1 version. Continuous variables like, the bone marrow biopsy length, and time taken for procedure are studied with mean, median, range and standard deviation and compared by two-sample t-test. While the categorical variables, pain is studied with X^2 or Mann Whitney U test or Fisher's exact test.

DATA SAFETY MONITORING PLAN

The bone marrow drill procedure is done as a SOC at our institution, and we have established the safety of the procedure without any untoward events over the last 3-4 years. We have not proposed an interim analysis for futility or efficacy, taking into consideration that the final results of the study if fully

conducted will not harm a patient. Dr. Nooka will be the primary responsibility for overseeing the data and the interim analysis.

DATA STORAGE AND PROTECTION

All data will be maintained on the REDCap database supported by the Research and Woodruff Health Sciences IT (RWIT) Division at Emory University.. Access to the server is protected by (firewalls, encryption etc) and all accounts will be password protected.

Confidentiality

Your name, telephone number, social security number, residential and mailing addresses will be collected from your medical record for study related contact. Laboratory results, billing, clinical, radiology, physician, and hospital records will also be collected from your medical record.

The samples and medical information we collect will have a code number and will not include your name, social security number, or other information that could identify you.
For example:

Mary Jones becomes 31098756

We will use this code to keep track of your samples and information.

TIMELINE FOR COMPLETION: 04/01/2014-03/31/2015

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