Risk Factors Associated with Carotid Sinus Hypersensitivity

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A. Background

Syncope and falls are common in the elderly. Close to one-third of all those aged 65 and older living at home suffer a fall each year[1,2]. Incidence rates for falls increase with advancing age and frailty and falls represent the single most common cause of accidental mortality in people over 65 years of age, accounting for 70%.[3] Five to 30% of falls in the community result in injury. Most of the injuries are mild and superficial, but up to 5% result in fracture and 1% in hip fracture. About one in 40 of community dwelling elders who fall will be hospitalized. Only about half of the elderly patients hospitalized as a result of a fall will be alive one year later.

Carotid Sinus Hypersensitivity [CSH] has traditionally been considered a rare cause of syncope and almost never is invoked as the cause of falls. It is uncommon in the young, but the incidence of CSH increases with age, being detectable in a significant percentage of the general elderly population.[5] Recent epidemiological data suggests that the prevalence of CSH in elderly patients with unexplained falls may be considerably higher than in the general elderly population, approaching 25%.[6]

Carotid sinus hypersensitivity is associated in many cases with hypertension, cardiovascular, cardiac and peripheral vascular diseases[7] and seems to have a preponderance for the male sex. [8,9]

Carotid Sinus Massage (CSH) has been employed as a provocative maneuver to elicit carotid sinus hypersensitivity. It is performed by applying digital pressure at the bifurcation of the internal and external carotid arteries.[10,11], below the angle of the jaw [12] at the level of the cricothyroid cartilage, for no more than 5 seconds [13,14,15,16,17] on only one side 18 at a time. Carotid sinus massage is typically performed during continuous electrocardiographic and blood pressure monitoring. Initially, it should be performed in the supine position. However, performing CSM during erect posture enhances the sensitivity of carotid sinus massage in identifying subjects with CSH.[19,20]

The most commonly reported complications of carotid sinus massage are ventricular arrhythmias and neurologic sequela. It is reasonable to avoid CSM in patients with a history of a ventricular arrhythmia, and in those at increased risk for developing ventricular arrhythmias, such as in patients with a recent myocardial infarction, or patients on digoxin with abnormal potassium levels. Despite the twenty-three cases reported in the literature, the true incidence of neurologic complications after CSM is extremely low as reported by Lown and Levine [21], Sigler [22] and Munro et al.[23] Recent data from Davies[12] confirmed an extremely low incidence of neurologic complications [11 in 16,000; an incidence of < 0.1%], when appropriate screening criteria are utilized. Additionally, almost all of the neurologic events in this extremely large series were without long-term sequela.

CSH is classified according to its predominant hemodynamic manifestation: either prolonged sinus pauses [>3 seconds; cardio-inhibitory CSH] or marked falls in systolic blood pressure [>50 mm Hg, vasodepressor CSH] or both [mixed CSH][24] Initial series reported that the cardio-inhibitory type was responsible for 60-80% of all cases. Recent reports have demonstrated that the phenotype of CSH is vasodepressor or mixed in greater than 80% of cases.

Carotid sinus syndrome is only one of the many neurally mediated reflex disturbances of blood pressure. Its pathophysiology is not well understood. Two hypotheses have been proposed however: the denervation of the sternocleidomastoid hypothesis and the vascular hypothesis.

Tea et al evaluated 17 patients with carotid sinus syndrome (CSS) and age-matched controls with respect to their sternocleidomastoid electromyography and found significant difference between the two groups. The authors proposed that the sternocleidomastoid has proprioceptive sensitivity, which could modulate information coming from the stretch receptors inside the carotid sinus, thereby providing an inhibitory effect on the reflex arc. When the ste mocleido mastoid becomes denervated, the proprioceptive

sensory pathways cease to exert that inhibitory effect and the carotid sinus would lose this regulation.[25] Blanc et al[26] confirmed similar finding in a study of 30 patients.

The vascular hypothesis regarding the pathophysiology of CSH relies on the clinical observations that CSH is associated with atherosclerotic diseases[9,10,11,27,28] and increases in frequency with age. Since the carotid baroreceptor reflex is initiated by stretch receptors located in the walls of the carotid artery, decreases in arterial distensibility with age and with arteriosclerosis may impair the transduction process and reduce neural activity of the afferent limb of the reflex loop. As a result of impaired afferent baroreflex input, the expected compensatory effect is baroreflex efferent hypersensitivity.[29]

Patients with CSH and symptoms [so called carotid sinus syndrome] are usually treated according to the frequency and severity of their symptoms. The recently revised Joint Task Force of the American Heart Association and the American College of Cardiology on guidelines for implantation of pacemakers[30] recommends permanent pacing only for those subjects with recurrent syncope and a cardio-inhibitory response to CSM. In contrast, others have recommended treatment for patients with even single syncopal episodes[31] or for falls.[6] For patients who have controversial indications for treatment, an individualized approach is probably best, where each case is assessed with special attention to the severity of the attack [i.e. injury versus no injury], circumstances before the attack [i.e. a clear trigger mechanism which can be avoided], the presence or absence of a significant prodrome and the patient's occupation and needs. In general, treatment options include pacemakers, pharmacologic therapy and surgical denervation, which are aimed at targeting the cardio-inhibitory or vasodepressor component or both.

Cardiac pacing is the most effective form of therapy for patients with cardio-inhibitory or mixed CSH,[32,33] with recurrence rates for syncope of 57% and 47% of the non-pacing group and in 0% and 9% of the pacing group. Pacing, however, has been ineffective in treating subjects with pure vasodepressor responses or mixed responses with a significant vasodepressor component.[30] Newer pacing algorithms show promise for helping alleviate some of he vasodepressor induced hypotension. The role of pacing among elderly patients with recurrent unexplained falls and CSH is being evaluated in an ongoing prospective randomized trial - SAFE-PACE.

Although we are not able to help everyone with CSH, we can make a difference in the lives of a substantial number of them. Unfortunately, we often see these people after they have had an event and have already suffered significant damage as a result of falls and/or syncope. Therefore, identification of risk factors that could potentially predict the coexistence of CSH is valuable, as it may lower the threshold for suspecting the disease and pursue its diagnosis before irreparable harm has been done.

B. Study Goals

This study is intended to look at gender and a history of stroke and/or TIAs as risk factors for CSH, the former because it has been suggested in the literature, the latter because it has been reported as a sequelae of CSM (used to elicit CSH).

C. Study Design and Statistical Analysis

This is a cross-sectional study. Odds ratio, relative risk and a logistic regression model will be used to analyze the data.

D. Study Procedure

1. Carotid Sinus Massage (CSM) will be used to try to identify people with carotid sinus hypersensitivity. Once subjects have been selected and consented, they will be taken to the tilt-table lab. There, they will be attached to electrographic (EKG, to monitor the heart rate) and blood pressure (noninvasive devices that utilizes plethysmography or applanation tonometry to record beat-to-beat arterial wave forms) monitors. Their

carotid sinus will be massaged, using the current accepted method of CSM, as described in the literature and as reported in the background (see above). First, the procedure will be performed in the supine position and if it yieds a positive result, we will stop there. In the event of a negative result, the massage will be repeated in the upright position.

2. Subjects who test positive for CSH will be placed in a group labeled "A" and those who test negative in another labeled "B".
3. Groups A and B will then be compared with respect to various characteristics, specifically gender and a history of stroke and/or TIA. Other factors that will be looked at are: age, hypertension, history of coronary artery disease
4. Lastly, a third group labeled "C", made up of people without a history of syncope and/or falls, matched by age and gender with the subjects in group "A" will serve as the control group.

E. Sample Size

In order to get enough power, with a 20% difference between the groups considered significant, we will need a total of 198 subjects.

F. Subject Selection

a. Group "A" and "B".

Subjects will be selected from the emergency room of the New-York Presbyterian Hospital, Columbia campus. They will be people who present with the chief complaints of syncope and/or falls and who subsequently got admitted for work-up, since no apparent cause could be identified. Shortly after admission (that afternoon or the next day), patients will be interviewed and examined by a member of the research team (an MD). Once they have been determined eligible, the study will be explained to them with its risks and benefits (see below) and informed consent will be obtained, should they decide to participate Additional patients will be recruited from the Allen Pavilion emergency room if necessary to complete the 198 people needed.

b. Group "C"

Those subjects will be randomly chosen from Admission Data Base and matched accordingly.

c. Inclusion Criteria

Age ≥ 50 years, 3 unexpained falls in previous year, ± syncope, normal gait and balance, normal vision, sinus rhythm, no carotid bruits, 3 seconds asystole or 50 mmHg decrease in systolic blood pressure on one occasion (supine or upright).

d. Exclusion Criteria

Age < 50, abnormal gait or balance, hearing or vision impairment, sensory deficits, peripheral vascular disease, physical disabiltities such as rheumatoid arthritis or degenerative joint disease, use of a cane or walker or wheelchair, history of arrhythmias of any kind, history of myocardial infarction or stroke within 3 months, presence of a carotid bruit, sustained orthostatic hypotension, neoplasm, chronic renal or liver failure, class III or IV heart failure, medications which enhance vagal activity.

G. Risks and Benefits

The risks are ventricular arrhythmias and neurologic sequela, both of which occur vey rarely. There are 5 cases of sustained ventricular tachycardia/ventricular fibrillation documented in the literature and all of those patients either had a serious underlying cardiac or non-cardiac disease, were on digoxin, or had abnormal potassium levels. Although there are 23 cases of neurologic complications in the literature, the incidence is very low. A very

recent study of 16,000 patients found an incidence of <0. 1 %.[12] Moreover, none of the neurological events had long-term sequela

The benefits include the option of intervening before a potentially deadly or morbid event occur, such as syncope and/or fall.

H. Compensations

Participation is on a voluntary basis. The results of the test will be made available to the patients and the treating team who will, together, decide on how to proceed.

I. Consent

Please see back.

J. Citations

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Consent Form

Greetings:

You are invited to participate in a study in which we are trying to identify people with a disease called "Carotid Sinus Hypersensitivity". This disease puts people at risk of "passing out" or falling, potentially causing them serious damages, including broken arms or hips and bleeding in the head.

You are invited to participate, because you came to the emergency room after having either "passed out", fallen, or both.

If you agree to participate, you will have to let us interview you (to get your medical, surgical and social history) and examine you. Once we have all the data, we will determine whether you are eligible to participate in the study.

If you are found eligible, you will be asked to sign the bottom of this sheet, saying that you have read it, that you understand the study and its purpose, and that you understand the risks involved.

Once you sign the sheet, we will then take you (not necessarily the same day) to another room where we conduct the study. There, you will be placed on a table that can tilt. We will place monitors on you to follow your heart rate and your blood pressure. We will then rub on the side of your neck, one at a time for about 5 seconds each. We will do this, first with you lying flat. Depending on the result we get, we may or may not tilt the table to repeat the same procedure.

After you are done you will be taken back to your room. There, we will tell you the results of your test. In case of a positive test, we will provide you and your doctors with information about treatment and you will make the final decision.

Your participation in the study will not in any way prevent you from getting the care that you would get, had you not been a part of it. The results will only provide you with additional and better intervention in case the study is positive. **The information we get from you will be kept anonymous in our study.**

The risks of the study are very few. They include the possibility of having abnormal rhythms of the heart and neurological symptoms (like you are having a stroke). However, these occur very rarely and the study is done is a wellmonitored room where you will be watched by medical doctors the whole time.

I have read the above information which was also explained to me. I understand the purpose of the study as well as the potential risks of the procedure. All my questions have been answered. I agree to participate.

Name: _____ Signature: _____ Date: _____