Evaluation of Efficacy and Complications of N-Acetylglucosamine for Hemostasis of Femoral Arterial Catheterization Wounds

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Abstract

Background- Reports to the FDA of local vascular complications associated with the use of hemostasis devices following cardiac catheterizations and resulting in serious injuries have raised concerns about the safety of these devices. A review of the medical literature also has posed cause for concern. We performed this study to assess the efficacy and risks of local adverse events in hemostasis following cardiac catheterization with N-Acetylglucosamine-facilitated manual compression versus manual compression alone.

Methods- N-Acetylglucosamine was used for hemostasis in 205 patients who underwent diagnostic cardiac catheterization performed via femoral access at a single site. Another 205 patients underwent diagnostic cardiac catheterization and received routine manual compression and served as the control group. Ambulation was permitted 12 hours after manual compression and 6 hours after using N-Acetylglucosamine. Poisson regression analysis using four different outcomes was used to assess the risk associated with the type of hemostasis, while controlling for confounding variables.

Results- Overall, the unadjusted incidence of any vascular complication was 4.8% for the manual compression and 5.4% for the N-Acetylglucosamine group. No serious adverse events were seen in this study.

Conclusions- N-Acetylglucosamine does not appear to pose a greater risk for local vascular complications following cardiac catheterization than the manual compression method. This method permitted early ambulation and was as safe as manual compression. ***(Iranian Heart Journal 2010; 11 (1):17-23).***

Key words: N-Acetylglucosamine ■ hemostasis■ catheterization

Crdiac catheterizations are usually performed by percutaneous access using the femoral artery. Following the completion of the procedure, hemostasis is traditionally performed by manual compression, followed by 6 hours of bed rest.[1] Hemostatic patches have been used as an adjunct to manual compression for the management of femoral access site sheath removal.

The use of such patches has been shown in small studies to reduce the time for hemostasis and ambulation compared to manual compression after procedures via femoral artery access.[2, 3, 4]

Reports to the Center for Devices and Radiological Health (CDRH) of the FDA regarding serious injuries and deaths associated with the use of vascular hemostasis devices[5] provided the impetus for this study.

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These devices are used primarily to stop bleeding from the femoral artery catheterization site following diagnostic or interventional procedures.[6]

Studies that have assessed the risks of vascular hemostasis device use compared to no device use (i.e. use of manual compression to stop bleeding) have produced mixed results with regard to the relative risks of adverse events (such as hemorrhage).

Some have demonstrated no difference between device use vs. manual compression controls,[7-9] whereas others have shown a greater risk[10-13] or a lesser risk[14, 15] associated with device use.

Despite the issuance of a public health notification by the FDA in 1999,[16] reports of serious injuries and deaths associated with the use of these devices continued to occur without a decrease in frequency.

Accordingly, we compared vascular complications in a group of patients with femoral artery access managed by routine manual compression to a group of patients managed with N-Acetylglucosamine-facilitated manual compression.

Methods

In a period of about 6 months, 410 patients scheduled for diagnostic cardiac catheterization via femoral access site in our institution were randomized with block randomization into two groups of 205 patients each. Patients receiving anticoagulation or undergoing percutaneous interventions using an 8Fr size sheath or larger were excluded before entrance to this study. Catheterization procedures were performed according to standard techniques. Arterial access management after sheath removal following catheterization was done by the cardiologist using standard manual compression for about 10-20 minutes and using a 1-kilogram sandbag over the wound thereafter in the control group. Ambulation was permitted after about 12 hours in this group.

On the other hand, arterial access management in the intervention group was performed using about 300 milligrams of N-Acetylglucosamine over the catheterization wound associated with manual compression for about 5 minutes. A sand bag was not used in this group and ambulation was permitted after a total period of about 6 hours.

This study was performed by cardiologists, who were blind at the level of data collection. Examination of each patient in both control and study groups was performed after ambulation. Pseudoaneurysms and arteriovenous fistulae were ruled out by a Doppler ultrasound study of the catheterization site after detecting a bruit or hematoma on physical examination.

All the patients stayed in the hospital for at least 24 hours after cardiac catheterization for probable late onset complications and were examined again later.

Outcomes and definitions: The specific complications and one aggregate category related to the femoral artery catheterization site were assessed:

Bleeding*:* Blood loss at the site of arterial access or due to the perforation of a traversed artery or vein requiring transfusion or prolonging bed rest or causing a drop in hemoglobin >1g/dL. Bleeding attributable to the vascular access site could be retroperitoneal, a local hematoma, or external (entry site bleeding).

Loss of distal pulse: Loss of distal pulse requiring therapy.

Pseudoaneurysm: The occurrence of a disruption and dilation of the arterial wall without identification of the arterial wall layers at the site of the catheter entry demonstrated by ultrasound.

Arteriovenous fistula: A connection between the access artery and the accompanying vein demonstrated by ultrasound.

Statistical analysis

Analysis of potential confounding variables such as left ventricular ejection fraction, body mass index (BMI), systolic and diastolic blood pressure, gender, and age in both control and study groups revealed a comparable distribution.

The collected data were primarily compared using the T-test and chi-square test for the confounding variables, and then a multivariate analysis was done using the Poisson regression for the dependent variables.

We performed the step-wise backwards Poisson regression using each of the outcome variables individually as the dependent variables. The analysis was performed separately for each outcome. It was also performed separately for the two methods of hemostasis (manual compression versus N-Acetylglucosamine - facilitated manual compression). These analyses assessed the role of each method of hemostasis separately using manual compression as the control.

Results

Demographic data: Tables I-III demonstrate the basic demographic data and the distributions of the potential confounding variables in both control and intervention groups.

Distribution of the potential confounding variables as well as the demographic data was comparable in both groups. It is noticeable that there is higher than normal mean BMI (26/6) (assuming normal BMI 20-25) among the total study population.

Table I. Distribution of confounding variables

Group		Weight	BMI	DBP	SBP	EF
Control	Mean	72.05	26.7065	73.59	115.50	45.22
	SD	35.762	11.2742	10.969	16.346	10.445
	Median	70.00	26.0600	70.00	115.00	50.00
Study	Mean	72.49	26.6070	75.15	130.42	47.49
	SD	13.135	4.54820	11.263	23.915	9.274
	Median	72.00	26.3830	70.00	130.00	50.00
Total	Mean	72.27	26.6572	74.36	122.87	46.34
	SD	26.982	8.61612	11.129	21.736	9.936
	Median	70.00	26.1719	70.00	120.00	50.00

Table II. Distribution of gender

			Sex		Total
			Male	Female	
Group	Control	Count	114	94	208
		% within group	54.8%	45.2%	100%
	Study	Count	127	78	205
		% within group	62.0%	38.0%	100%
Total		Count	241	172	413
		% within group	58.4	41.6%	100%

Table III. Distribution of age

Group	N	Mean age	SD	Std. Error Mean
Control	208	54.30	13.856	.961
Study	205	55.49	11.996	.838

The T-test and chi-square test revealed no significant relationship between the confounding variables and vascular complications. The distribution of total vascular access site complications is shown in Table IV.

Table IV. Incidence of total vascular complications in both groups

			Complications		Total
			No	Yes	
Group	Control	Count	198	10	208
		% within group	95.2%	4.8%	100%
	Study	Count	194	11	205
		% within group	94.6%	5.4%	100%
Total		Count	392	21	413
		% within group	94.9%	5.1%	100%

The overall incidence of vascular complications was 5.1%. These occurred in 4.8% of the control group and 5.4% of the study group. Statistically, there was no significant difference between the control and study groups regarding total vascular complications (P=0.79).

Arteriovenous fistula occurred in 1.5% of the total study population, specifically in 1.9% and 1% of the control and study groups, respectively, with the difference not reaching statistical significance (P= 0.68, Table V).

Table V. Incidence of arteriovenous fistula

			AV Fistula		Total
			No	Yes	
Group	Control	Count	204	4	208
		% within group	98.1%	1.9%	100%
	Intervention	Count	203	2	205
		% within group	99%	1%	100%

Total	Count	407	6	413
	% within group	98/5%	1.5%	100%

Pseudoaneurysm, as another vascular complication, occurred in 1.2% of the total population studied: 1.9% and 0.5% in the control and study groups, respectively, without any statistically significant difference (P=0.37, Table VI).
Bleeding occurred in 2.4% of the total population studied: 1% and 3.9% of the control and study groups, respectively.

Table VI. Incidence of pseudoaneurysm formation

			Pseudoaneurysm		Total
			No	Yes	
Group	**Control**	Count	204	4	208
		% within group	98.1%	1.9%	100%
	Intervention	Count	204	1	205
		% within group	99.5%	5%	100%
Total		Count	408	5	413
		% within group	98.8%	1.2%	100%

There was a trend toward increased bleeding in the study group that it was marginally statistically significant (P=0.052, Table VII).

Table VII. Incidence of bleeding

			Bleeding		Total
			No	Yes	
Group	**Control**	Count	206	2	208
		% within group	99%	1%	100%
	Intervention	Count	197	8	205
		% within group	96.1%	3.9%	100%
Total		Count	403	10	413
		% within group	97.6%	2.4%	100%

There was neither any significant hemorrhage nor hematoma formation requiring transfusion or leading to a drop in hemoglobin or hemodynamic instability.
All of the cases of hemorrhage or hematoma formation were successfully managed by further manual compression and prolonging bed rest.

Also, there was no arteriovenous fistula or pseudoaneurysm formation requiring surgical intervention. All of the cases of arteriovenous fistulae and pseudoaneurysms were successfully managed by manual compression under guidance of Doppler ultrasound.
The hospital course was unremarkable for all the patients studied, and they were discharged uneventfully, including those with vascular complications.

Discussion

With a strategy of ambulation permitted at 6 hours post-procedure, we observed a low incidence of vascular complications with both methods of hemostasis. Thus, a strategy of N-Acetylglucosamine-facilitated manual compression for femoral artery access site hemostasis permitted early ambulation and was as safe as conventional manual compression. Furthermore, the benefit of N-Acetylglucosamine-facilitated manual compression with respect to less time necessary to achieve hemostasis led to more patient comfort and convenience. The cost effectiveness of this hemostasis strategy was not evaluated in this study however, and remains to be determined in future studies.
Our results demonstrate that the N-Acetylglucosamine-facilitated manual compression and early ambulation is safe in terms of complication rates when compared to currently used protocols.[17]
Several studies have suggested that shorter periods of groin pressure and earlier ambulation are safe in patients undergoing elective coronary angiography.[18-20] Reducing the period of immobilization has beneficial effects on patient comfort, particularly in terms of reduced back pain. Barkman directly compared ambulation at 3 and 6 hours and confirmed that patients with faster ambulation experienced significantly less back pain.[21]
The overall reported complication rates vary. This is undoubtedly due to the small numbers of patients in some of the studies. Pallord and coworkers reported a bleeding rate of 7.3%, a

hemotoma formation rate of 12.8%, and false aneurysm rate of 0.3%, quoting an overall complication rate of 19.2% at a mobilization time of 2.5 hours post procedure.[22] Our study demonstrated a total vascular complication rate of 5.1%, comparable to most other studies.

Issues related to understanding the role of patch use for hemostasis after arterial access include identifying the mechanism of action by which local hemostasis is achieved and demonstrating whether patch use adds any benefit beyond manual compression itself. Unfortunately, the evidence base available to help address these issues is limited. Hemostatic patches have been available for commercial use for years, but only recently have gained specific FDA approval for use as an external closure method for the management of femoral artery access sites. While multiple types of patches have been evaluated, including chitines, marine algae and thrombin, the exact mechanism by which they achieve hemostasis in patients is unclear.[23-25] After application on the skin over the femoral artery puncture site, topical agents mentioned above appear to promote coagulation within the upper aspects of the access tract.

Presumably, thrombus formation also occurs at the arteriotomy site with final hemostasis being achieved by a combination of these two phenomena.

Because each topical hemostatic agent requires a period of manual compression in addition to its application, it has not been clear whether there are hemostatic and clinical benefits beyond the manual compression itself. The extent to which manual compression contributes to hemostasis has not been specifically studied. [3]

This experience suggests, but is by no means conclusive, that manual compression is an essential component of hemostasis with N-Acetylglucosamine. However, N-Acetylglucosamine itself appears to be an active component contributing to hemostasis as well. There are only limited data evaluating outcomes after hemostatic patch use for femoral artery access site management. In small randomized trials, N-acetylglucosamine[26,27] reduced the time to hemostasis and ambulation compared to manual compression after cardiac procedures. In these studies, the incidence of vascular complications after topical hemostatic agent use was low and comparable to manual compression, as is the case in our study.

Nader et al. examined vascular complications in patients after catheterizations and percutaneous intervention procedures and electrophysiological studies. [28] They observed a low incidence of vascular complications, but did not include a control group for comparison.

The Chitoseal and Syvek patches were included in the phase II report of the ACC-NCDR[2] and appeared equally safe as manual compression alone. Nonetheless, details concerning time to hemostasis and ambulation were not provided in this report.

The present study demonstrates comparable incidences of pseudoaneurysms and arteriovenous fistulae, as well as total vascular complications in both control and study groups. Therefore, it appears that technical factors in the puncture of the femoral artery and access management are probably more important than the method of hemostasis with respect to vascular complications.

There was a trend toward increasing bleeding rates in the intervention group.

That was marginally statistically significant. All the cases of bleeding in the intervention group. Occurred at the first 6 hours of applying hemostatic agent but two cases. Thus it is meaningful to say that early ambulation per se does not increase the bleeding risk.

Several lines of reasoning suggest that potential confounding variables are unlikely to have significantly affected the findings. First, the incidence of factors known to affect the rate of vascular complications such as age,

gender, BMI, and sheath size were all similar between the two groups.

Moreover, the incidence of upstream glycoprotein IIb/IIIa blocker and clopidogrel use was also similar in both groups. Since the study was performed within the same time frame period for both control and study groups, neither a reporting bias nor a general improvement in vascular access management could have influenced the study results.

While the current study supports the conclusion that the risks of vascular complications after N-Acetylglucosamine-facilitated manual compression and manual compression alone are comparable, there are limitations to the study that should be discussed.

Ambulation by protocol after N-Acetylglucosamine-facilitated manual compression was permitted at 6 hours post procedure, compared to 12 hours post procedure for the manual compression group. The results would, therefore, have been biased towards lower vascular complications after manual compression alone because of longer bed rest. Similar to any other study, the current results may be subject to unrecognized biases in patient selection and/or procedures not accounted for in this analysis.

The cost-effectiveness of this method of hemostasis remains to be determined.

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Conflict of Interest

No conflicts of interest have been claimed by the authors.

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