

Evaluation of post-puncture bleeding time of arteriovenous fistulas with IRIS[®] bandage

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ABSTRACT

Purpose: Our aim was to evaluate the safety and effectiveness of the IRIS[®] bandage (Nephrokit[®]) on post-puncture bleeding compared to conventional manual compression.

Methods: Sixty-four patients, hemodialyzed with an arteriovenous fistula, were enrolled in a 3-week prospective study. Conventional manual compression was used during the first week, the IRIS[®] bandage during the second week and conventional manual compression again during the third week. The outcomes analyzed were the persistence or absence of bleeding 3 minutes post-puncture with IRIS[®] device compared to conventional manual compression. The safety of the IRIS[®] bandage was also evaluated.

Results: Rates of persistent bleeding 3 minutes post-puncture at arterial sites were 53±6% and 56±5%, respectively, during the first and third weeks (conventional compression) versus 18±5% during the second week (IRIS[®] bandage). Similarly, rates of persistent bleeding 3 minutes post-puncture at venous sites were 45±6% and 45±6%, respectively, with conventional compression versus 23±5% with the IRIS[®] bandage. The difference between the IRIS[®] device and conventional compression therefore proved highly statistically significant ($p<0.05$) for both arterial and venous puncture sites. No particular adverse events were observed with the IRIS[®] device.

Conclusions: Post-puncture bleeding time at arteriovenous fistula sites is significantly shortened by the IRIS[®] bandage in comparison with conventional manual compression.

Key words: Arteriovenous fistula, Conventional manual compression, Hemodialysis, IRIS[®] bandage, Post-puncture bleeding time

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INTRODUCTION

Since the use of the surgically created arteriovenous fistula first described in 1966 by Brescia and Cimino, post-puncture bleeding is still stopped using mechanical compression with simple or hemostatic bandages (1).

Bleeding control following needle removal is an important issue for both caregivers and patients. A long delay significantly impacts the patient's quality of life by extending time to discharge, increases nursing workload, consumes valuable staff time usually dedicated to monitoring patient treatments and is likely to disturb the overall dialysis schedule organization of the hemodialysis unit. In addition, excessive post-dialysis puncture site bleeding estimated by the gauze weigh method has been recently found to be significantly associated with lower hemoglobin levels in an observational study (2, 3). Conversely, excessive compression, especially with the use of hemostatic devices such as straps, tourniquets and rigid clamps, may damage vascular

access walls and has been claimed by some authors to favor late fistula thrombosis (4).

Post-dialysis puncture site bleeding could also be aggravated by the increasing prevalence of elderly patients in dialysis units. Elderly patients could be effectively prone to long bleeding time because of frequent use of antiplatelet agents and oral anticoagulants due to associated cardiovascular morbidity. Two randomized control trials, performed to prevent hemodialysis access graft thrombosis, by using warfarin or clopidogrel plus aspirin, have indeed been associated with a significant increased risk of bleeding and notably with a significant increase of bleeding from the cannulation site in the clopidogrel plus aspirin group compared to the placebo one (5, 6).

The objective of the present study was to evaluate the effectiveness of the IRIS[®] bandage (Nephrokit[®]), an innovative, non-impregnated device, in shortening post-puncture bleeding time at arteriovenous fistulas compared with manual compression using regular gauze.

MATERIALS AND METHODS

Patients

Sixty-four hemodialyzed adults from two French hemodialysis departments were enrolled in a prospective study. All patients provided written informed consent to participate in the study. Exclusion criteria were as follows: cognitive inability to provide informed consent and hemodialysis with central venous catheter. Inclusion criteria were as follows: hemodialysis using a functional native or prosthetic arteriovenous fistula. Among the 64 patients, whose mean age was 68 (22-88) years, 36 were males and 28 females, and 20 diabetic. Three patients were treated with oral anticoagulants (coumadin or fluidione) and 29 with antiplatelet agents (clopidogrel or aspirin). Dosages of oral anticoagulants (coumadin or fluidione) were adjusted to have an international normalized ratio between 2 and 3. Local anesthesia before puncture was used in 40 patients. Vascular accesses were native arteriovenous fistulas except in one case where a polytetrafluoroethylene brachioaxillary graft was used. Thirty-three patients had a radiocephalic arteriovenous fistula in the forearm, 14 a brachiocephalic arteriovenous fistula and 16 a brachio basilic arteriovenous fistula. Vascular access blood flow was measured by Doppler ultrasound in the brachial or radial artery feeding the arteriovenous fistula in 53 patients. Stenosis was also detected in these patients. No radiovascular or surgical interventions on the vascular access were performed during the study period since the vascular stenoses detected were not hemodynamically significant and had no particular impact or alteration on venous dialysis pressure, blood flow or increase in recirculation. Among the three types of puncture localization available (rope ladder, buttonhole and area puncture), the area puncture technique was the technique used in this study (7, 8). Needle size and dialysis modalities (conventional or convective) are reported in Table I.

Medical devices

IRIS® is a non-impregnated bandage that contains neither hemostatic nor procoagulant substances, developed to shorten post-dialysis bleeding at dialysis puncture sites (Fig. 1). The first layer of the IRIS® bandage consists of a transparent microperforated adhesive strip which is stuck directly on the puncture site while the needle is partly removed. Absorbent gauze is then applied with slight pressure on the adhesive strip (in order to absorb blood through the pores of the adhesive strip) and the needle is removed. The second layer, a non-woven pad, is applied over the first strip at the end of bleeding (Fig. 2). The IRIS® bandage or conventional manual compression was applied first on the venous and subsequently on the arterial post-puncture

TABLE I - BASELINE CHARACTERISTICS OF THE OVERALL STUDY COHORT

Variables	Total numbers (n=64)	Percentage (%)
Age (years)	68 (22-88)	
Gender (male/female) (n, %)	36/28	56/44
Diabetes (n, %)	20	31
Antiplatelet agents (n, %)	29	45
Oral anticoagulants (n, %)	3	5
Local anesthesia (n, %)	40	63
Native distal radial-cephalic fistulae (n, %)	33	52
Native proximal humero-cephalic fistulae (n, %)	14	23
Native proximal humero-basilic fistulae (n, %)	16	23
Prosthetic fistulae (n, %)	1	2
Fistula blood flow (mL/min)	1007±520 (ND=11)	
Stenosis (n, %)	20	38
Aneurism (n, %)	23	43
Extracorporeal circuit anticoagulation (UFH/LMWH) (n, %)	5/59	8/92
Needle size (15G/16G) (n, %)	18/46	28/72
Dialysis modality (conventional/convective) (n, %)	36/28	56/44

Continuous variables are expressed as mean ± standard deviation. Vascular access blood flow, measured by Doppler ultrasound, was not determined (ND) in 11 patients. Needle size was expressed in gauge (G).

LMWH, low molecular weight heparin (Lovenox®, enoxaparin sodium); UFH, unfractionated heparin (Heparin®, Heparin sodium).

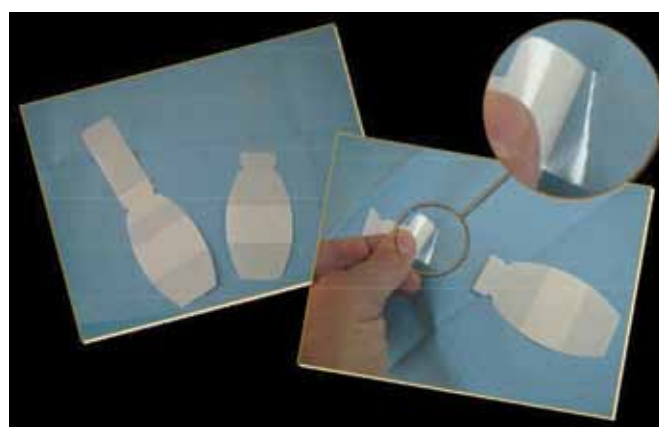


Fig. 1 - IRIS® microperforated adhesive bandage.

sites. The conventional method consisted in applying two-fold regular gauze (sterile, non-woven pad, 7.5×7.5 cm, manufactured by Innoset®) by manual compression on each puncture site. Conventional manual compression guidelines usually consist in removing the needles one at



Fig. 2 - Successive steps of IRIS® use.

the time, firstly the venous and secondly the arterial needle. It is usually recommended to wait at least 10 minutes until after the venous needle site has clotted before removing the arterial needle. The best hemostasis is achieved by applying mild, digital (using two fingers), localized, direct pressure over the needle site (9). IRIS® and conventional bandage were removed as usual, several hours after the end of the hemodialysis session. The patients did not compress themselves. The nurses performed all the compressions. Cannulation complications with excess bleeding time related to a vascular breach were noted when IRIS® bandage or regular gauze was used.

Study design

Need to previously determine a cut-off compression time

Transparency of the IRIS® bandage enables the direct evaluation of post-puncture bleeding. The time required to achieve hemostasis can then be accurately noted down as a continuous quantitative variable, which is not possible with conventional methods because puncture sites are hidden by gauze. Furthermore, it is not possible to remove the gauze repeatedly to check if bleeding has stopped since it would decrease the effectiveness of the conventional method, which is based on sustained manual compression. The comparison of the effectiveness of conventional manual compression with that of the IRIS® bandage can therefore only be assessed according to qualitative criteria such as the persistence or absence of bleeding after a predetermined given time. During a 4-week preliminary study including 33 patients, from two dialysis units, both the minimum period of time needed to achieve hemostasis with regular gauze and the time during which hemostasis was not achieved were evaluated according to a step-by-step decrease in the duration of manual compression in subsequent dialysis sessions. Median values of both these parameters were 5 and 3 minutes, respectively. The cut-off compression time of 3 minutes was retained to perform a comparative study.

Comparative study

A multicentric prospective study, including 64 hemodialyzed patients from two hemodialysis units, was carried out to compare the hemostatic effectiveness of the IRIS® bandage with conventional manual compression at the cut-off value of 3 minutes. The nursing staff was trained to IRIS® bandage handling beforehand, until fully understood. Presence or absence of bleeding 3 minutes post-puncture was evaluated firstly at the venous site and secondly at the arterial site, in order to prevent any risk of retro blood spurting on the arterial site due to high venous compression. The 64 patients were successively treated with conventional manual gauze during the first week, IRIS® bandage during the second week and conventional manual gauze again during the third week. At each session and for each patient, a chronometer and a paper data recording sheet were provided to the nurses to enable them to record the persistence or absence of bleeding 3 minutes post-puncture. No nurse was specifically dedicated to one or another patient. The nurses who were handling IRIS® bandage or regular gauze of each patient during the different successive hemodialysis sessions were different and were not aware of the post-puncture bleeding time of each patient in the previous period. Furthermore, the patients did not compress the cannulation site themselves and consequently did not interfere in the post-puncture bleeding time.

Statistical analysis

Persistence and absence of bleeding at the cut-off time of 3 minutes were the two discontinuous variables tested. Cessation of bleeding was considered effective when achieved within 3 minutes in at least two sessions a week. The percentage of patients who achieved hemostasis with conventional manual compression during the first week, with IRIS® bandage during the second and with the conventional manual compression again during the third week were analyzed using McNemar's test (10). The confidence interval for the percentage of patients in whom bleeding persisted was determined using 500 biostrap iterations. P values <0.05 were considered statistically significant.

Safety

Safety of the IRIS® bandage was also evaluated. Two endpoints were specifically observed: firstly, possible occurrence of skin wound, attributable to iterative bandage removal, and secondly, rebleeding occurrence following bandage removal.

RESULTS

Baseline characteristics

Baseline demographic characteristics are presented in Table I.

Outcomes at bleeding sites 3 minutes post-puncture using the conventional method or IRIS bandage

For arterial puncture sites, rates of persistent bleeding 3 minutes post-puncture amounted to $53\pm 6\%$ and $56\pm 5\%$ during the first and third weeks, respectively, when conventional compression was used, as opposed to $18\pm 5\%$ with the IRIS® bandage during the second week. For venous puncture sites, rates of persistent bleeding 3 minutes post-puncture amounted to $45\pm 6\%$ and $45\pm 6\%$ during the first and third weeks, respectively, when manual compression was used, as opposed to $23\pm 5\%$ with the IRIS® bandage during the second week. For both arterial and venous puncture sites, differences between IRIS® bandage and conventional compression (during both the first and third weeks) were statistically significant ($p < 0.05$). On the other hand, bleeding rates with manual compression were not statistically different between the first and third weeks (Fig. 3).

Adverse events

The IRIS® bandage proved to be well tolerated; in particular, no adverse events such as skin abrasion or increase in rebleeding occurrences following removal of the IRIS® bandage were observed.

DISCUSSION

This study showed that the IRIS® bandage was statistically more effective in reducing the post-puncture bleeding time than conventional manual compression with gauze. Among the 64 patients enrolled in the study, the percentage of persistent bleeding 3 minutes post-puncture was approximately 50% in the case of manual compression with conventional bandage versus 25% with IRIS® bandage. Absence of significant difference between the first and third weeks during which conventional compression was used supports the perfect reproducibility of the experiment.

Besides this significant and clinically relevant result, this study provided evidence of additional findings.

The first finding is related to the post-puncture manual compression time usually considered necessary to achieve hemostasis. From general expert opinions, it is usually recommended to apply mild, digital (with two fingers), localized and direct pressure over the needle site for at least 10 minutes (9). In this study, hemostasis was achieved

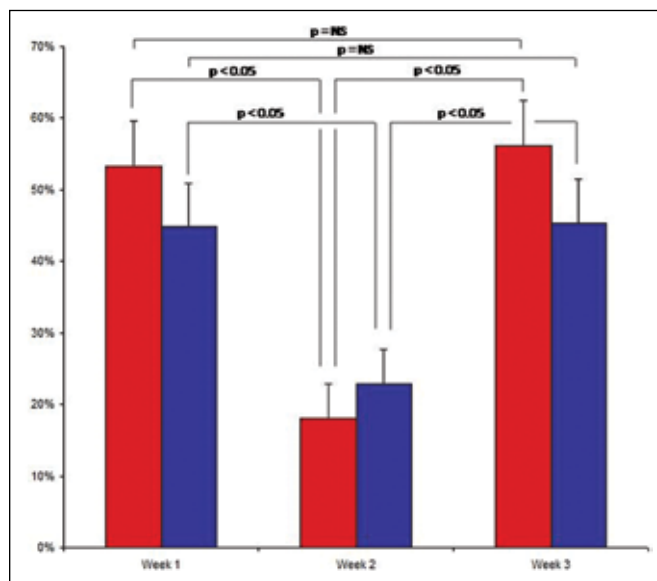


Fig. 3 - Persistent bleeding 3 minutes post-puncture, expressed as a percentage of hemodialyzed patients, using conventional compression (weeks 1 and 3) or IRIS® bandage (week 2) at arterial (red bars) and venous (blue bars) puncture sites.

within 3 minutes in 50% of patients, hence showing that extending compression time on puncture site to 10 minutes was probably unnecessary. In addition, given that the IRIS® bandage enables to check hemostasis directly, this approach is intrinsically time-saving.

The second finding deals with the intrinsic hemostatic properties of the IRIS® bandage. Several hemostatic dressings which have been developed to promote hemostasis at dialysis access puncture sites are currently available, usually resulting from surgical and interventional vascular radiology experience. These usually consist of compressive dressings impregnated with hemostatic substance or procoagulant factor (11). Calcium alginate dressings such as Coalgan®, Algosteril® or Kaltostat®, whose hemostatic improvement is related to calcium release and, to a lesser extent, to alginate, have been used for many years as hemostatics, especially to control bleeding in oral, nasal and neurosurgery but also to control post-puncture bleeding in dialysis patients (12). Cellulose-based fiber dressings are largely used in wound management to control post-surgical bleeding (Surgicel®) and post-dialysis puncture bleeding (Pushban®). Other dressings made of collagen, such as Pangen®, are also used in surgery and dialysis. Recently, costly new dressings made of polysaccharides have further enlarged the arsenal of hemostatic bandages such as the chitosan-based hemostatic dressings, HemCon® bandage (mainly tested for combat injuries and war trauma) and Syvek® Patch (mainly used for local management of wound bleeding at vascular access puncture site). Both the latter dressings have also been used for the management of post-puncture bleeding in dialysis patients (13-15).

Very few studies have compared the effectiveness and safety of available hemostatic bandages in dialysis patients. A recent observational study was performed with the different hemostatic bandages currently available, but did not specifically look at the potential hemostatic advantage of one bandage over another (16). Rationales are derived from experimental studies performed *in vitro* and *in vivo* in animal models and in human clinical trials in surgery and vascular interventional radiology. To our knowledge, only two studies have been carried out in dialyzed patients to investigate and compare the different hemostatic dressings available. The first study, dating back to 1999, demonstrated the statistical improvement in the time to achieve hemostasis post-puncture using Syvek® Patch dressing as compared to a conventional dressing. However, this study was only published as an abstract at the American Society of Nephrology and the original article was never published. The second study, conducted in 2006, investigated the effects of a chitosan-based dressing in comparison with conventional dressing, but failed to clearly establish its statistical superiority (15). The results obtained with the IRIS® bandage, which is not impregnated with hemostatic or procoagulant substances, raise the issue of its underlying biophysical mechanism which enables to achieve hemostasis. The IRIS® bandage is thought to achieve hemostasis through the following steps: closing the puncture site outflow with adhesive dressing, extracting blood serum through the micropores, hence improving blood cell concentration and accumulation in the subcutaneous channel created by the needle. However, the exact biophysical mechanism aiming at improving hemostasis should be investigated further.

The safety of IRIS® is also an important issue. The transparent properties of the IRIS bandage allow complete visualization of the bleeding stopping. Such a transparent property also eliminates the need for repeated bandage removal hence reducing traditional blood spray. It can then be assumed that the IRIS® bandage may decrease the risk of blood exposure accidents. In addition, no adverse events such as skin abrasion or rebleeding occurrences were observed following IRIS® removal. Nevertheless, we are aware that the time of our study may be too short to definitively confirm the good tolerance of IRIS® bandage.

Cost is another issue to consider. IRIS bandage manufacturing costs are indeed higher than those of conventional bandages. However, such a difference in cost might be offset by the amount of time gained: blood stopping occurs only after three minutes among 75% of patients, whereas conventional bandages take up to 10 minutes to stop the bleeding process. Should nurses compress all the 64 hemodialyzed patients of the study with the IRIS bandage on a period of one month, at one puncture site, the medical staff would gain 70 hours over bleeding reduction compared to conventional dressing. In reality, the majority of the hemodialyzed patients compress themselves. However, there is always a group of patients in a dialysis unit unable to compress themselves

because of neurologic troubles, blindness secondary to diabetes and increasing age. For these patients, the bleeding time reduction obtained with IRIS® bandage saves time for the medical staff and can therefore be cost saving.

Fistula stenosis can affect the bleeding time. However, as noted above, these stenoses were not hemodynamically significant. Moreover, given that the fistula stenoses are present without any alteration at the three steps of the study (regular gauze, Iris bandage and again regular gauze) and that the patients with stenosis were their own witness, it should not have any impact on the results of the study. Cannulation complications such as vascular breach can also significantly affect bleeding time independently of other parameters (such as fistula stenosis or antiplatelet agents and oral anticoagulant prescription) and can therefore also affect bleeding time in one group compared to another. The number of excess of bleeding time due to vascular breach was not particularly different between the regular gauze and the IRIS® bandage group.

Lastly, it would have been particularly interesting to compare the effectiveness of the IRIS® bandage to regular gauze in different subgroups of patients, such as patients under platelet inhibitors or oral anticoagulants, patients with proximal or distal arteriovenous fistula, patients with high or low arteriovenous fistula blood flow, and patients with arteriovenous fistula stenosis or aneurysm. Besides, the impact of needle size and interdialytic weight gain related to fluid retention on bleeding time should have also been investigated. Unfortunately, due to the small number of patients included in this study, these questions could not be answered.

CONCLUSION

This study demonstrates that the IRIS® bandage proves to be an effective and time-saving method to stop bleeding at the end of each hemodialysis session as compared to regular dressings. It is therefore of great advantage to both patients and dialysis teams. Moreover, the original approach adopted to develop the IRIS® bandage opens up new perspectives for the improvement of bandages dedicated to post-puncture hemostasis and for further research about the biophysical mechanisms of hemostasis.

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Conflict of interest: None.

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