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RESEARCH

ANALYSIS OF RISK FACTORS FOR BLEEDING EVENTS IN ANTICOAGULATED PATIENTS

ANÁLISE DOS FATORES DE RISCO PARA EVENTOS HEMORRÁGICOS EM PACIENTES ANTICOAGULADOS

ANÁLISIS DE LOS FACTORES DE RIESGO PARA LAS HEMORRAGIAS EN PACIENTES ANTICOAGULADOS

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ABSTRACT

Objective: to analyze the risk factors related to the occurrence of bleeding events in anticoagulated patients. **Method:** this is a retrospective cohort study based on documentary analysis. A total of 867 medical records of hospitalized patients were investigated in 2011 and 2012, with a sample of 79 patients who received continuous intravenous heparin sodium administration. To calculate the probability of a bleeding event based on the different risk factors, non-parametric statistical treatments and association measures were performed. **Results:** the study recorded 21.52% (n = 17) bleeding events. Among the 17 patients who had bleeding events, 94.11% had one or more risk factors, with a prevalence of: activated partial thromboplastin time greater than 100 seconds (88.24%); age greater than 60 years (70.59%) and arterial hypertension 64.71%. Patients with a high activated partial thromboplastin time presented a 9.29-fold higher risk for bleeding events (p = 0.0008). **Conclusions:** among the six risk factors analyzed, five had a positive association with bleeding. Nursing care based on the identification of risk factors prevents bleeding events, increasing safety in the use of anticoagulants and consequently improvement of the quality of nursing care.

Keywords: Medication Errors; Nursing; Security Measures; Hemorrhage; Risk Factors.

RESUMO

Objetivo: *analisar os fatores de risco relacionados à ocorrência de eventos hemorrágicos em pacientes anticoagulados.* ***Método:*** *trata-se de estudo de coorte retrospectivo, a partir de análise documental. Foram investigados 867 prontuários de pacientes internados em 2011 e 2012, encontrando-se amostra de 79 pacientes que fizeram uso de heparina sódica em infusão contínua. Para quantificar a probabilidade do evento hemorrágico a partir dos diferentes fatores de risco, foram realizados tratamentos estatísticos não paramétricos e medidas de associação.* ***Resultados:*** *foi evidenciada taxa de 21,52% (n=17) eventos hemorrágicos. Dos 17 pacientes com eventos hemorrágicos, 94,11% apresentaram um ou mais fatores de risco, com prevalência para: tempo de tromboplastina parcial ativada superior a 100 segundos (88,24%); idade maior que 60 anos (70,59%) e hipertensão arterial 64,71%. Pacientes com tempo de tromboplastina parcial ativada elevada apresentaram risco 9,29 vezes maior para eventos hemorrágicos (p=0,0008).* ***Conclusões:*** *entre os seis fatores de risco analisados, cinco tiveram associação positiva com sangramento. Os cuidados de enfermagem fundamentados na identificação dos fatores de risco previnem eventos hemorrágicos, aumentando a segurança na utilização de anticoagulantes com consequente melhora da qualidade da assistência de enfermagem.*

Palavras-chave: *Erros de Medicação; Enfermagem; Medidas de Segurança; Hemorragia; Fatores de Risco.*

RESUMEN

Objetivo: *analizar los factores de riesgo relacionados con la incidencia de hemorragias en pacientes anticoagulados.* ***Método:*** *se trata de un estudio de cohorte retrospectivo, a partir de análisis documental. Se investigaron 867 expedientes de pacientes internados en 2011 y 2012, con una muestra de 79 pacientes que utilizaron heparina sódica en infusión continua. Para cuantificar la probabilidad de las hemorragias a partir de los diferentes factores de riesgo, se realizaron tratamientos estadísticos no paramétricos y medidas de asociación.* ***Resultados:*** *se evidenció una tasa de 21,52% (n = 17) de hemorragias. De los 17 pacientes con hemorragias, el 94,11% presentó uno o más factores de riesgo, con prevalencia de: tiempo de tromboplastina parcial activada superior a los 100 segundos (88,24%); edad mayor que 60 años (70,59%) e hipertensión arterial 64,71%. Los pacientes con tiempo de tromboplastina parcial activada elevada presentaron un riesgo 9,29 veces mayor para hemorragias (p = 0,0008).* ***Conclusión:*** *entre los seis factores de riesgo analizados, cinco presentaron asociación positiva con la incidencia de hemorragias. Los cuidados de enfermería basados en la identificación de los factores de riesgo previenen las hemorragias, aumentando la seguridad en la utilización de anticoagulantes y, por consiguiente, mejorando la calidad de la atención de enfermería.*

Palabras clave*: Errores de Medicación; Enfermería, Medidas de Seguridad; Hemorragia; Factores de Riesgo.*

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INTRODUCTION

The World Health Organization (WHO) has recently emphasized that patient safety related to the use of medicines is a worldwide concern due to the high incidence of healthcare related incidents.[1] Sodium heparin is a drug that has been widely used in patients because it is indicated as an antithrombotic (prophylactic or therapeutic) medicine with scientific evidence of benefits. However, its use is often associated with a high rate of complications, such as bleeding.[2,3]

Studies have estimated that patients on heparin sodium therapy have a bleeding rate of 5-14.2%, including events such as hematuria, upper gastrointestinal bleeding, hemoptysis, epistaxis, ecchymosis, melena and hematomas.[2,4] In this scenario, it is necessary to look for solutions that can contribute to reducing such occurrences, minimizing the negative impact on patients, and to the health team and the institution.

Sodium heparin is administered at a controlled dosage and the adjustment of the therapeutic dose requires knowledge on the part of nurses about minimum and maximum dose, toxic dose, stability and compatibility, as well as the ability to detect the major adverse events caused by this drug. In most institutions, nursing care related to continuous infusion of sodium heparin is limited to the control of venous access (peripheral or central), and the preparation and administration of the drug.[5]

However, in clinical practice, heparin appears as one of the most common drugs involved in adverse events, preceded only by antibiotics, glucocorticoids, diuretics and digitalis drugs. Bleedings in critical patients are of concern because, depending on their origin and the volume of blood involved, they may potentiate hemodynamic and ventilatory instability, increase mortality and length of stay in intensive units.[6]

It is estimated that 5 to 10% of patients in intensive care units present some type of important bleeding. The impact that these bleeding events have on their prognosis makes it necessary to identify risk factors that may contribute to its occurrence.[7,8]

There are several risk factors reported in the literature to aid the analysis and prevention of bleeding events in patients using sodium heparin. The most frequently cited are: age greater than 60 years, systemic arterial hypertension (SAH), hepatic and renal insufficiency, previous use of oral anticoagulants, and activated partial thromboplastin time (aPTT) greater than 100 seconds.[2,4,6]

The contribution of this publication is based on the fact that it is the responsibility of the nurses to care for anticoagulated patients, and it is therefore their responsibility to recognize which risk factors are most associated with bleeding. Thus, this study may contribute to a specific and safer planning of care for anticoagulated patients allowing the prevention of bleeding events that may compromise their clinical improvement.

In view of this scenario, this research had as objective to analyze the risk factors related to bleeding events in anticoagulated patients.

METHOD

This is a retrospective cohort study based on a documentary analysis of medical records. Data collection took place in 2013 and 867 medical records from 2011 and 2012 were investigated. Due to the lack of previous data regarding the use of heparin and bleeding events, it was decided to investigate all medical records in the two-year period that met the selection criteria.

The selection criteria proposed by the *Institute for Healthcare Improvement*[9] for screening drug-related adverse events were applied in this study, namely: patients older than 18 years; length of hospitalization of two days or more; discharge or death record fully completed; and patients subjected to continuous intravenous infusion of sodium heparin for at least six hours. Patients using anticoagulants prior to intravenous heparin infusion and diagnosed with heparin-induced thrombocytopenia (HIT) were excluded. After the application of the selection criteria, the final sample of the study was 79 patients.

The study was developed in a large public hospital, located in the city of Rio de Janeiro, belonging to the Sentinela Network. Medical records of two intensive units (one with a cardiological and one general profile) and a semi-intensive (surgical) unit were tracked. The decision was to use all the units of the hospital that receive critical patients because it is believed that the severity of the clinical situation of patients in the studied universe would allow the amplification of the collected data, guaranteeing a reasonable sample and increasing the reliability and validity of results.

The technique used for data collection was documentary analysis based on original documents that have not yet received analytical treatment, being considered primary sources. The instrument of data collection was prepared so as to contemplate all the objectives of the thesis, from which this article originated. However, in order to respond to the objectives in question, data regarding risk factors specifically were used (activated partial thromboplastin time - aPTT above 100 seconds, age above 60 years, previous use of anticoagulants, renal insufficiency, systemic arterial hypertension, and hepatic insufficiency). Data were collected from clinical evolutions, water balance sheets, laboratory tests, medical prescriptions, and identification data of the patient.

Data collection took place in two stages: in the first moment, all medical records (n = 867) of the patients hospitalized in the study period were retrospectively traced; among these records, patients who received continuous infusion of sodium heparin were selected (n = 87). In a second moment, all medical

records of patients who used heparin were read and analyzed in a systematized manner. During data collection, eight irreplaceable losses occurred, most of them due to incomplete filling (n = 7) and one due to the non-location of the record in the archive sector (n = 1). Thus, 79 medical records of patients who used sodium heparin in continuous infusion were analyzed.

The data obtained were organized in Microsoft Excel® spreadsheets and later transferred into the *Statistical Package for the Social Sciences* used for statistical tests. In order to guarantee the quality control of the data typed, the process of double typing was used, counting on two independent typists.

Bivariate analysis using the Mann Whitney test was performed in order to evaluate the association between the predisposing factors and the bleeding event, which is used when the sample is small and when numerical variables do not present a normal distribution.[10]

The relative risk (RR) was calculated to quantify the probability of occurrence of a bleeding event in patients with factors predisposing to bleeding, which is a measure of association between the disease in exposed and non-exposed patients (values below one suggest protection against exposure and values above one suggest a deleterious effect of exposure). All relative risk calculations were done in a 2 x 2 table, using the *OpenEpi*® program available free of charge on the internet. The Fisher's exact test, which is used to analyze discrete (nominal or ordinal) and non-parametric[11] data, was applied here to calculate the relative risk. A confidence level of 95.0% ($p < 0.05$) was adopted in all analyses.

All the ethical precepts related to the development of research with human beings regulated by Brazilian Resolution 466/12 were obeyed in the present study. The work was approved by the Research Ethics Committee under number 3083/2011.

RESULTS

Among the 79 patients who used sodium heparin, a rate of 21.52% (n = 17) of bleeding events was found, with a confidence interval varying from 13.5% to 31.5%. Predisposing factors are presented by groups with and without bleeding events (Table 1).

For the group of patients with bleeding events, the prevalent risk factors were aPTT > 100s with 88.24% (n = 15), followed by age greater than 60 years with 70.59% (n = 12) and SAH with 64.71% (n = 11).

From the 17 patients with bleeding events, 94.11% had one or more predisposing factors and only one patient had bleeding without having an associated predisposing factor.

Predisposing factors for bleeding event and the measure of association of relative risk (RR) obtained from the ratio between the risk of bleeding in the exposed and unexposed patients to the predisposing factors. The p-value expresses the statistical significance related to the predisposing factor and bleeding (Table 2).

The only predisposing factor with statistical significance (0.00008) was aPTT > 100. Patients exposed to this factor presented a 9.29-fold higher risk for bleeding events.

Patients older than 60 years are 1.24-fold more likely to bleed than patients younger than 60 years. SAH was associated with a 1.45-fold greater risk for bleeding events when compared to non-hypertensive patients. Patients who had made previous use of anticoagulants presented 1.38-fold higher risk of bleeding than patients who had not used anticoagulants.

The only predisposing factor that had no association with bleeding events was hepatic insufficiency. Other predisposing factors such as age over 60 years, SAH, renal insufficiency and previous use of anticoagulants, despite presenting no statistically significant association, showed a positive association with bleeding events.

Table 1 - Distribution of predisposing factors associated with bleeding events. Rio de Janeiro, Brazil, 2014 (n = 79)

Predisposing factors		With bleeding event (17)		Without bleeding event (62)		Total (79)		
		n	%	n	%	p valor	n	%
Age > 60 years	yes	12.00	70.59	40.00	64.52	0.642	52.00	65.82
	no	5.00	29.41	22.00	35.48		27.00	34.18
SAH	yes	11.00	64.71	33.00	53.23	0.402	44.00	55.70
	no	6.00	35.29	29.00	46.77		35.00	44.30
Renal insufficiency	yes	4.00	23.53	14.00	22.58	0.935	18.00	22.78
	no	13.00	76.47	48.00	77.42		61.00	77.22
Hepatic insufficiency	yes	1.00	5.88	4.00	6.45	0.932	5.00	6.33
	no	16.00	94.12	58.00	93.55		74.00	93.67
Previous use of anticoagulants	yes	11.00	64.71	34.00	54.84	0.469	45.00	56.96
	no	6.00	35.29	28.00	45.16		34.00	43.04
PT > 100	yes	15.00	88.24	20.00	32.26	0.000	35.00	44.30
	no	2.00	11.76	42.00	67.74		44.00	55.70

*p-value calculated by the Mann-Whitney test.

Table 2 - Association of predisposing factors with relative risk for the occurrence of bleeding. Rio de Janeiro, 2014 (n = 17)

Predisposing factors	p-value*	RR	Risk in exposed patients	Risk in non-exposed patients
Age > 60 years	0.8722	1.24	23.08	18.52
HAS	0.573	1.45	25.00	17.00
Renal insufficiency	0.99	1.04	22.22	21.31
Hepatic insufficiency	0.99	0.92	20.00	21.62
Previous use of anticoagulants	0.65	1.38	24.44	17.65
aPTT > 100	0.000008	9.29	42.86	4.54

* p-value obtained by the Fisher's exact test.

DISCUSSION

It is understood that this study presents limitations inherent to the technique of data collection, since the quality of data depends directly on the quality of the filling of the medical records. The size of the population also represents a limitation because, despite the time period of two years of hospitalizations, the number of patients receiving sodium heparin was low (n = 79), which may be justified by the fact that heparin is a potentially dangerous drug and its use is restricted to a small population with well-defined indications.

The only risk factor presenting statistically significant association with bleeding events was aPTT above 100 seconds. According to the *Institute for Healthcare Improvement* (IHI), aPTT greater than 100 seconds is considered a predisposing factor for bleeding. The IHI emphasizes that the increase of aPTT is not considered an adverse event in itself, but rather an indicator (a trigger tool) for the detection of adverse events, such as bleeding with hematocrit fall, hemoglobin fall or hematomas.[9,11]

An indicator is considered an alert that helps the health care provider and health care organization to identify/prevent adverse events and assess any possible harm caused during the care process. Therefore, according to the IHI identification, indicators are related to the processes of care, surgical procedures and drug administration.[12]

The results obtained in this study corroborate that aPTT > 100 seconds is a significant predisposing factor for bleeding in patients receiving sodium heparin in continuous infusion, since 88.24% of the patients with bleeding events present at some point aPTT above 100 seconds.

According to research, sometimes an increased aPTT may occur despite adequate monitoring of heparin infusion, in this case turning it an unavoidable predisposing factor.[13] However, what is most evident is an increased aPTT due to improper monitoring or incorrectly programmed infusion rate, which is an avoidable predisposing factor.

As highlighted in the results, each patient could present one or more predisposing factors to bleeding; six patients presented two predisposing factors, three patients presented three predisposing factors, and seven presented one predisposing factor, which demonstrates the multifactorial nature of bleeding events and the complexity of the patients studied.

Age above 60 years was the second most prevalent predisposing factor in patients with bleeding, when compared to patients without bleeding (70.59: 64.52). Although this difference was not statistically significant (p-value = 0.642), RR was found to be 1.24.

Elderly patients aged more than 60 years are classified as a risk group for bleeding events because they generally present a different risk profile than that of non-elderly patients. Elderly patients, in general, have a higher prevalence of hypertension, diabetes mellitus, previous myocardial infarction, angina, peripheral vascular disease, stroke, multiple arterial disease and heart failure.[13,14]

Besides the high risk profile resulting from the higher prevalence of diseases, the elderly are highly sensitivity since they have less iron absorption, less body fluids, and a great number of them use regular platelet antiaggregant.[15]

Study reveals that the elderly are among the patients who most benefit from the treatment with anticoagulants. However, they are also among those who more often experience bleeding complications.[16] Thus, as demonstrated in the present study, elderly people represent a population with a higher risk of bleeding complications when compared to the non-elderly.

Systemic arterial hypertension is also a non-modifiable predisposing factor for bleeding.[17] In the present study, 64.71% of patients with bleeding events presented this predisposing factor. Although this percentage was not statistically significant (p-value = 0.402), hypertension was associated with a 1.45-fold (RR = 1.45) higher risk of bleeding events when compared to non-hypertensive patients. The results show that hypertensive patients have a 25% risk of having a bleeding event, whereas non-hypertensive patients, 17%.

In most patients, blood pressure increases with age, unless the patient presents healthy lifestyle habits (a low-salt diet, not overweight, and practicing physical activity). A study estimated that about 60 to 90% of the elderly population had increased blood pressure values.[18]

The pressure exerted on the vessels related to the use of anticoagulants can considerably increase the risk of occurrence of bleeding. Therefore, the higher the blood pressure, the greater is the risk of any bleeding event[18], corroborating the results presented herein, where 64.71% of the patients who had bleeding were hypertensive.

The other risk factor analyzed was renal insufficiency, which represented a predisposing factor of low incidence in the study (22.78%). It is known that elimination of sodium heparin may occur through some ways; a portion of sodium heparin is taken up by the lungs and the liver, but most of it is filtered into the urine.[19]

There are some other factors that can modify the elimination of heparin. Hypothermia, especially below 25°C, may delay the elimination of heparin.[20] However, renal failure is the major factor related to elimination and may prolong the anticoagulant effect of heparin.[19] Therefore, patients with renal impairment are at an increased risk of bleeding complications, which is confirmed in the results of this study. It has been identified that patients with renal failure have a 1.04-fold greater risk of bleeding events.

As for hepatic insufficiency, it is known that 25% of the metabolism of sodium heparin takes place in the liver. So, hepatic impairment may compromise the metabolism of heparin and increase the risk of bleeding. According to research, unfractionated sodium heparin is related to asymptomatic elevation of transaminases and it has been proven that the majority of patients who used heparin had laboratory abnormalities in liver function.[21]

The results obtained in this study contradict what the literature says, because hepatic insufficiency was the only predisposing factor that, besides not presenting statistical significance with regard to the presence or not of bleeding event, it was not positively associated with bleeding. In this sense, an important limitation of this research needs to be highlighted, that is, among the 79 patients who used sodium heparin, five had hepatic insufficiency, and this this result may likely have been influenced by the reduced number of patients in the study.

The use of anticoagulant agents prior to infusion of sodium heparin is also considered a predisposing factor to bleeding because the risk of bleeding is directly related to the intensity of anticoagulation; therefore, the association of anticoagulants of different natures may potentiate its effect.

The results on the previous use of anticoagulants, although not statistically significant (p-value = 0.469), showed that patients who had made this use presented a 1.38-fold higher risk of bleeding than patients who did not use them. This corroborates the literature on that the use of oral anticoagulants prior to the use of heparin may increase the risk of bleeding.[22]

However, it is often understood that bleeding events depend not only on the characteristics of the patients, but also on the therapeutic decisions taken, the time the medicine was given, and the serum level of the medicine. All these factors linked to therapy can be influenced and modified by early identification of hemorrhage.[23,24]

Therefore, some predisposing factors are attributed to factors inherent in the nursing care. Nursing care processes can be modified to reduce the risk of adverse events, including communication strategies, correct drug administration, workflow and staffing, continuing education, and proper guidance and selection of equipment.[24]

Ultimately, continuous assessment of predisposing factors may contribute to the reduction of bleeding events and allow nurses and other health professionals to individualize the care provided and interventions.

In this sense, we understood that when nurses provide care for patients who receive continuous infusion of sodium heparin, they must know the main factors predisposing to the occurrence of bleeding, with the objective of identify as soon as possible patients at high risk and act in a way to prevent the bleeding event.

CONCLUSION

Due to the multifactorial nature of hemorrhage, the knowledge of the predisposing factors is fundamental for the adoption of preventive and therapeutic measures. Among the 17 patients with bleeding events, 94.16% presented one or more risk factors for bleeding.

All risk factors except for hepatic insufficiency were positively associated with bleeding events. This means that the predisposing factor increases the probability of a bleeding event. The variable aPTT greater than 100 seconds was statistically associated with the studied event, since patients exposed to aPTT greater than 100 seconds had a 9.29-fold higher risk of bleeding.

Therefore, in order to ensure the safe use of heparin in continuous infusion, we recommend that nursing actions be based on the identification of predisposing factors and on the clinical indication of each patient.

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