New and more effective application assays for hemostatic disorder assessment: A systematic review

Faisal M Al-Zahrani

Background: Hemostasis research lacked novel platform assays for hemostatic disorder diagnosis. The current review study's goal is to compare various assays for evaluating the novel hemostatic techniques used in the diagnosis of coagulation disturbances and to highlight each method's strongest and weakest points.

Methods: The PRISMA guidelines and the recommendations for observational studies in epidemiology were both followed in the current systematic review. The PRISMA-compliant electronic databases (PubMed), a novel platform for evaluating hemostasis, were searched using the keywords. The electronic databases (PubMed), a cutting-edge platform to assess hemostasis, were searched using the keywords. Articles published between December 2016 and December 2021 were only included in searches; original articles were written in English. In order to assess hemostasis studies, we gathered bibliographies of abstracts that were published on the new and more effective application assays for assessments of hemostasis disorders.

Results: Following the removal of duplicates, articles were determined by examining the titles and abstracts. Disagreements were resolved through consensus and the application of novel hemostatic analysis methods. Then independently reviewed the relevant studies of the recognized records (n=503), excluding duplicates (n=9) and irrelevant studies (n=249). The remaining 254 studies were read in their entirety, the data from the seven included studies had been extracted.

Conclusions: When expressed as an anticoagulant for the in vivo assessment of on the complement system, nanotechnology-based study was more effective in some laboratory tests, and flow cytometer evaluation could be a promising platform approach for use in hemostasis management.

Keywords: novel platform, hemostasis assays, diagnosis, hemostatic disorders

INTRODUCTION

Novel platform assays for the diagnosis of hemostatic disorders were limited in hemostasis research during the drug acceleration phase of vitro-based therapeutics, particularly during the product design phase. An in vitro test flow was built in the year 2005 to evaluate the immune response stability of nanomaterials and devices for hemostatic evaluations [1]. 400 different nanotechnology devices were used to validate the hemostasis biomarker sequence. In addition to liposomes, emulsified, nanostructured lipid carriers, colloidal metals, metal oxides, nanotubes, fullerences, and polymeric nanotechnology were also taken into consideration. To prevent the blood clotting of the healthy donated blood used in such lab tests, a few assays were carried out using either traditional anticoagulants or hirudins. Earlier, a novel T2 magnetic resonance-based method for measuring hemostasis in whole blood was described (T2MR) [2]. One such method has a small blood volume requirement (35 l), is essentially straightforward because platelets are not really separated, and yields results quickly. Fibrinogen is essential for healing, bacteria-host interaction, and adhesion strength. Lower serum fibronectin levels have been suggested in some studies as a potential disease risk factor for the development of anti-PF4 and anti-heparin antibodies and professional HIT. In addition, fibronectin inhibited the formation of PF4 and PF4/heparin complexes on extracted platelets, complex disruption, downregulation of antibodies with high affinity for PF4/heparin complexes, and decreased expression of anti-PF4/heparin antibody-induced immune activation. These effects were all brought about by fibronectin. In addition, the Scientific and Standardization Committee of the International Society on Thrombosis and Hemostasis orders flow cytometer processing as more than just a method of processing when compared to routine diagnostic disorders, and it is demonstrated to be preferred to light transmission aggregometry throughout the diagnosis and treatment of platelet activity dysfunction [5, 6]. Even in the flow cytometer testing of mild routine diagnostic disorders, platelet granule identifiers, such as p-selectin, are used; however, platelet stimulation must occur prior to the analysis. The fluorescence-functionalized subset, which connects receptor nuclei, is frequently used to estimate platelet density. Reduced mepacrine fluorescence has been identified in patients with storage pool disorder (SPD) by several researchers [7, 8], and it is suggested that this finding

be incorporated into a screening methodology for common diagnostic disorders. It remains to be seen whether ongoing fluorescent records will be successful in a real-world medical setting, especially when compared to customary SPD screening procedures [9, 10]. Oceans are abounding with natural resources. A crucial aspect of aquatic active ingredient analysis would be the fact that many marine products are made from naturally occurring active ingredients with specific properties, including marine-appropriate peptides. Marine active peptides have been found to have antimicrobial, hemo­static, and wound-healing properties [11-13]. In order to transform enzyme inhibitor peptides and antioxidant peptides, oyster peptides (OP), which are active substances present in marine organisms, include angiotensin I and antiseptic peptides [14, 15]. In studies, it has been shown to have exceptional biological properties, including antibacterial, antioxidant, hypoglycemic, anti­aging, and anti-tumor activity [16, 17]. OP too has typical physical and chemical properties, such as various compositions, ease of adaptation, and non-toxic and non-harmful properties [14, 15]. Besides that, because of their readily available nutrition and poor bio­ stability, they are exposed to microorganism invasion, resulting in the loss of biological processes [18]. Platelet abnormalities should always be monitored in order to diagnose mild bleeding disorders, which are characterized by grossly disproportionate bleeding after trauma, menorrhagia, severe and frequent mucocutaneous hemorrhage, and easy bruising [19, 20]. Although this technique has been used in diagnostic laboratories for more than four decades, it still lacks sensitivity for mild platelet function defects (PFDs) and does not predict the risk of bleeding health problems in patients with certain clinical diagnostic defects [21-26]. The difficulties of transmission aggregrometry may include poor standardization, but besides existing guidelines, the need for a large amount of fresh blood, the realization that it is periodical and time-consuming, and that it is not applicable for analyzing platelet count [27-32]. As a result, alternative techniques for measuring platelet aggregation have just been developed, but despite potential advantages, neither of these techniques raced with light transmission aggregrometry (LTA) in terms of bleeding diagnostics [33]. Alternative methods for providing additional data about mild PFDs are desperately needed. The whole normal platelet initiation test, developed by [34], is a flow cytometric approach that enables platelets to just be stimulated with various agonists and platelet stimulation to be quantified using different kinds of activation markers such as granule official launch, glycoprotein activation, and phospholipid expression. Because many research laboratories do not have both aggregrometry and flow cytometer capabilities, records based on the agreed methodologies are as previously published [35, 36]. Using synthetic and natural polymers such as chitosan, electro spinning allows us to create three-dimensional porous and fibrous materials [37]. This method is used in biomedicine and tissue engineering in conjunction with 3D printing [38]. While the extracellular matrix is modeled by electrode position scaffolds for rapid cell proliferation and tissue regeneration [39], early literature has shown that electro-spin chitosan membranes have high blood clot-forming activity as well as biocompatibility. Furthermore, the composition of hydrogen bonds formed after chitosan dissolves in an acid solution complicates the spinning process, limiting the use of pure chitosan [40]. Extra added polymers, like caprolactone (PCL), polyvinyl alcohol (PVA), or polyethylene oxide (PEO), are now used to improve chitosan spinning, reduce conductivity, or produce thinner fibers [41]. The best way to stabilize the chitosan electroprocessing route would have been to add PEO, a water-soluble synthetic polymer with good biocompatibility and low toxicity [42]. In a previous study, PEO was used, which binds to chitosan via hydrogen bonds, lowering the viscosity and interfacial of the chitosan solution. The purpose of the present review study would be to make a comparison between several assays for assessing the novel hemostatic techniques used in the diagnosis of coagulation disturbance and to point out the most advantageous and disadvantageous aspects of each method as a predictor of morbidity and mortality to determine hemostatic efficacy as well as biological safety.

METHODS

Study Selection

The current systematic review follows the guidelines for observational studies in epidemiology [8] and the PRISMA guidelines. Figure 1 depicts a high-level overview of the methodology. The keywords were used to search the electronic databases (PubMed) (a novel platform to evaluate hemostasis). Searches were restricted to articles published between December 2016 and December 2021; original articles were written in English. To summarize, we collected bibliographies of abstract articles published on a novel platform to evaluate laboratory techniques used for hemostasis studies, and no attempt was made to contact the original article’s authors for information. This study does not require ethical approval because the included data is based on previously reported articles, and no identifying information about participants will be revealed. IBM (IBM Corp., USA) software was used for statistical analysis in this study.

RESULTS

Following the removal of duplicates, articles were determined by examining the titles and abstracts. Conflicts were settled through consensus and the use of novel hemostatic analysis methods. The relevant studies of the recognized records (n=503) were reviewed, excluding duplicates (n=9) and irrelevant studies (n=249). The remaining 254 studies were read in all of them, and data from the seven included studies were extracted (Figure 1 represents the search strategy and screening procedures). The incidence rate of new platforms to analyze hemostasis is summarized in Table 1 for the reported studies. The total number of patients considered in the present review (seven studies) was 216, with an absolute max of 161 patients and a minimum of 0.01, as follows: fibronectin modulates formation (n=42), T2 magnetic resonance (n=1), electrospun chitosan-based (n=2), flow cytometric mepacrine fluorescence (n=3), chitosan-based thermo-sensitive (n=1), and nanotechnology-based formulation. The benefits of nanotechnology-based formulations as a novel platform would be optimal in vitro assays demonstrating anticoagulant for nanoparticle effects on the complement system, but less ideal and would require emphasis in test results dependent on the specific anticoagulant being used. While the flow cytometric analytical method has been used for many different measurements, specific, small amounts of blood have been required for such
Figure 1. Preferred reporting studies for systematic reviews (Source: Author’s own elaboration)

Table 1. The estimated prevalence of a new platform for analyzing hemostasis in the studies investigated

<table>
<thead>
<tr>
<th>Novel platform</th>
<th>Study</th>
<th>No. of Patients</th>
<th>Positive (%)</th>
<th>Negative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibronectin modulates formation</td>
<td>[43]</td>
<td>42</td>
<td>18 (42.8)</td>
<td>24 (57.2)</td>
</tr>
<tr>
<td>T2 Magnetic Resonance</td>
<td>[44]</td>
<td>1</td>
<td>1 (100)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Electrospun Chitosan-Based</td>
<td>[45]</td>
<td>2</td>
<td>2 (100)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Flow cytometric mepracrine fluorescence</td>
<td>[46]</td>
<td>3</td>
<td>3 (100)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Chitosan-Based Thermo-Sensitive</td>
<td>[47]</td>
<td>1</td>
<td>1 (100)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Nanotechnology-Based Formulations</td>
<td>[48]</td>
<td>6</td>
<td>5 (83.3)</td>
<td>1 (16.7)</td>
</tr>
<tr>
<td>Flow cytometric analysis</td>
<td>[49]</td>
<td>161</td>
<td>116 (72.0)</td>
<td>45 (28.0)</td>
</tr>
</tbody>
</table>

tests but depended on skilled personnel, increased cost, short- time reagents, complicated samples, low sensitivity tests, and short-term indicator molecules. While T2 magnetic resonance might indeed enable the identification of platelet disorders in whole blood to extend to assessments of hemostasis, it even had some disadvantages in basic analytic techniques. Other novel platforms for evaluating hemostasis used in the current studies may require further evaluation to determine their benefits and drawbacks in hemostasis assessment (Table 2).

DISCUSSION

Observing the mechanical and physical properties of clotting blood is perhaps the most effective method for monitoring blood coagulation. In fact, the formation of blood clots is monitored in order to prevent platelet aggregation from interfering with the coagulation process [50, 51]. Coagulation can also be caused by an individual’s inner stimulation reagent, including ellagic acid or phospholipid [52], an extrinsic inducer solution, such as tissue factor [53], or all of these can be triggered by clotting inhibitors, such as cytochalasin D in combination with an exterior activator [54]. Previous analyses [55, 56] evaluated various point-of-care (POC) devices for test results but instead briefly described their scanning principles, although this systematic looked into other blood clotting checking methodologies. Experimental measurements of various technologies can provide biologists with ideas on the obvious benefits of certain tools in identifying disorders and future performance for clinical management and treatments. Furthermore, the role of nanotechnology in detection and diagnosis, as well as commonly available devices, future trends in checking of novel treatments, artificial intelligence in diagnostic testing, and monitoring for greater predictive value
have both been explained. As a result, both industrial and academic parts have been enclosed, allowing for the filling of present gaps in blood coagulation monitoring as well as new plans for prolonged hemostasis monitoring. HIT Serum monitoring research of heparin-treated patient population’s shows that only a subset of patients develops platelet-activating anti-PF4/heparin antibodies [57, 58] another initially described a novel T2 magnetic resonance platform for measuring hemostasis for whole blood (T2MR) requires small blood (35 mL), and was indeed basically simple, but since platelets are not separated, it actually works in minutes [2]. As a result, the aim of this systematic review would be to contrast certain novel methods for evaluating hemostasis and platelet advantages and disadvantages of this platform for evaluating blood clotting [8, 59]. Another request was made to assess the biocompatibility and hemostatic and tissue properties by using the regeneration performance of copolymers prepared by electro spinning technique in order to develop new techniques to reduce the biodegradation time of their based material properties for hemostatic application. Flow cytometer fluorescence is being used to rule out platelet dense granule shortage, but this test is time-consuming and requires a large blood volume [60]. It can also be used for the analysis of platelets as a potential alternative, but it lacks confirmation, preventing it from being used in a diagnostic setting [61]. Another of the leading causes of death in trauma emergency cases is unregulated massive hemorrhage. At a specific temperature, chitosan-based thermo-sensitive hydrogel loading OP was prepared using catechol-modified chitosan (CS-C) as the matrix material as a thermo-sensitive agent. Hemostasis performance has been measured in vivo and in vitro, as well as its biological safety. The findings revealed that hemostasis experiments, the hemostasis time, and indeed the amount of blood loss in post-operative models were improved due to the small quantities of nano-materials usable for such studies. In vitro analysis of novel nanotechnology-based pharmaceutical formulations is of vital importance, particularly during the product development phase. Almost all immune tests necessitate the use of blood donors [61]. To perform such test results, blood must be kept from coagulating, which itself is an attachment, by adding an anticoagulant to blood testing tubes. The most widely used anticoagulants are heparin, ethylene diamine tetra acetic acid, and citrate [62]. New anticoagulants, including hirudin, are also available but rarely used. Although certain anticoagulants may influence assay results, there is currently very little systematic correlation of traditional and novel anticoagulants in vitro experiments aimed at immunological identification of nano medicine formulations, whereas traditional anticoagulants, such as citrate and hirudin, are more relevant for coagulation and cytokine secretion assays. The research suggests that this technology is likely to be favorable mostly in the medical field of hemostasis, and those variations in lab tests between and traditional mechanisms involving blood for nanostructures have all been observed at a time when no such results were observed with traditional controls [63]. As a result, it is critical to understand the benefits and drawbacks of each anticoagulant and to establish appropriate nanoparticles on a case-by-case basis. Introduction LTA has been the gold standard for identifying bleeding disorders and might be useful in standardizing diagnostic work-up studies. A parameter estimation that excluded single studies had no effect on the significance of this association. Several limitations of the research must be considered carefully. First, our findings are useful because of confounding factors such as patient clinical characteristics, sample size, and hemostatic defect estimation procedure [1, 62]. The aforementioned confounders, on the other hand, fully described the observed. As a result, some authors suggested that some studies have not been provided, and we have had to estimate the value based on the data. There may be small variations between the precise methodology used and the extrapolated data obtained using the laboratory method. Despite the fact that we did not impose a language restriction, only studies in English were included in the review. Subsequently, studies with insufficient data have been omitted. Besides this, several additional studies were unable to be published due to negative or null results; these studies were, in fact, excluded from the current analysis. Each of these factors could have contributed to the limitations observed in this review study.

<table>
<thead>
<tr>
<th>Method platform</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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<tbody>
<tr>
<td>Fibronectin modulates formation</td>
<td>The decline in fibronectin leads to an increase in PF4, potentially immunizing PF4/heparin complexes in heparin-treated patients.</td>
<td>Fibronectin inhibits platelet activation by anti-PF4/heparin antibodies by interfering with the formation of PF4/heparin complexes.</td>
</tr>
<tr>
<td>T2 Magnetic Resonance</td>
<td>T2MR may subsequently facilitate the identification and identification of platelet disorders in whole blood, extending to global haemostatic assessments.</td>
<td>Basic and clinical research is required to determine whether latest technique will provide a more biological systems and quantifiable measure of poor platelet activation.</td>
</tr>
<tr>
<td>Electrospun Chitosan-Based</td>
<td>Particles with significantly higher porosity also show high biocompatibility and adequate in vitro blood clotting blood interaction.</td>
<td>The application really wasn’t useful for parenchymal bleeding because it had a lower immunogenicity with an acceptable host-tissue response.</td>
</tr>
<tr>
<td>Flow cytometric mepacrine fluorescence</td>
<td>It has the ability to be used in the testing of platelet dense granules.</td>
<td>It is not a quick screening and contains a low amount of whole blood.</td>
</tr>
<tr>
<td>Chitosan-Based Thermo-Sensitive</td>
<td>It rapidly takes up water and stays focused on blood, resulting in extremely rapid platelet aggregation, which can be used to identify patients with severe laboratory tests.</td>
<td>The safety evaluations required to ensure the specific hemostasis pathways remain a significant challenge.</td>
</tr>
<tr>
<td>Nanotechnology-Based Formulations</td>
<td>In vitro analysis has shown that nanoparticles have anticoagulant consequences on the signaling pathway.</td>
<td>It’s much less ideal but also necessary to distinguish differences throughout findings depending on the nature of the anticoagulant in use.</td>
</tr>
<tr>
<td>Flow cytometric analysis</td>
<td>So several various measurements were recorded with this device, and only a smaller amount is required for the test.</td>
<td>Short-term reagents, processing conditions, higher sensitivity check, short-term highlighter molecule, specialized workers, and higher prices.</td>
</tr>
</tbody>
</table>
CONCLUSIONS

Nanotechnology-based published study formulations discovered it is more optimal for some laboratory tests when expressed as an anticoagulant for the in vivo evaluation of nanoparticle implications on the complement system, and flow cytometer evaluation could be a promising platform approach for use in hemostasis mangers. However, because of the limitations identified in the current study, the results of the systematic review may be estimated. To clarify our outcomes, linearly increasing basic study is needed in the future. One of the most serious issues with both of these novel assays would be a lack of consistency and variation in marker parameters. If we try to describe and select patient groups with different reports focusing on assay factors, the actual increase might not have been large enough here to impair clinical benefit. Several of the novel assays show improvement in terms of increased sensitivity, though their clinical efficacy remains unknown. There are various designs of each strategy, and clinical studies frequently use diverse perspectives, and assay response is heavily dependent on the used procedure. As a result, the findings of the various papers cited in this analysis may be hard to interpret and reproduce. The ongoing efforts at quality control for several of the stronger organizations mean that it can be settled mostly in the nearest future.

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REFERENCES


