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By Ashari Bahar

WORD COUNT 2575
TIME SUBMITTED 02-DEC-2024 02:16AM
PAPER ID 113263582

AMALTEA MEDICAL PUBLISHING HOUSE

https://medscience.center/journals/
Words count – 2,572

TYPE OF ARTICLE: Reviews

Comparative analysis of onyx, squid, and n-butyl cyanoacrylate in intracranial arteriovenous malformation embolization

Ashari Bahar[1,2], Amaludin Jaelani[2], Wijoyo Halim[2]

[1] Department of Neurology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia

[2] Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia

Corresponding author:

Ashari Bahar

E-mail: asharibahar@med.unhas.ac.id

ABSTRACT

Background and Objectives: The use of embolization for treating arteriovenous malformations (AVMs) is pivotal, with a variety of liquid embolic agents such as Onyx, Squid, and N-Butyl Cyanoacrylate (NBCA) being widely utilized. This review aims to provide a comparative analysis of these agents, focusing on their efficacy, safety, and clinical applications to inform the choice of treatment in AVM management.

Materials and Methods: A literature review was conducted, analyzing data from studies examining the use of Onyx, Squid, and NBCA as embolic agents in AVM treatment. The findings were categorized based on outcomes such as obliteration rates, complication profiles, and procedural characteristics.

Results: Studies on Squid reported mean obliteration rates ranging from 33% to complete occlusion in specific cases, with minor complications. Onyx demonstrated high obliteration rates with fewer complications when used preoperatively, contributing to reduced surgical risks. NBCA, while effective, required multiple sessions to achieve results comparable to Onyx, with some studies highlighting a higher risk of complications. Comparative studies showed similar efficacy between Onyx and NBCA, though Onyx offered a more favorable safety profile in several reports.

Conclusions: Onyx and Squid exhibit promising potential as embolic agents for AVMs, with Onyx being particularly advantageous for preoperative embolization. NBCA remains effective but may be associated with higher risks. However, limitations such as selection, measurement, and confirmation biases in existing studies warrant caution in interpreting these findings and underline the need for more standardized and robust research methodologies.

Keywords: arteriovenous malformation, onyx, squid, *N*-butyl cyanoacrylate, embolization

Abbreviations:

Arteriovenous malformations (AVMs)

N-Butyl Cyanoacrylate (NBCA)

INTRODUCTION

Arteriovenous malformations (AVMs) are complex vascular anomalies characterized by abnormal connections between arteries and veins, bypassing the capillary system. These lesions pose significant clinical risks, including intracranial hemorrhage, seizures, and progressive neurological deficits. Effective management of AVMs often requires a multimodal approach combining surgical, endovascular, and radiosurgical techniques, with embolization serving as a cornerstone intervention to reduce nidus size and mitigate the risk of rupture.[1]

In recent years, pre-operative endovascular embolization for cerebral arteriovenous malformations (AVMs) has been extensively conducted, with favorable therapeutic outcomes, with a variety of materials traditionally employed for AVM embolization. [2]

The choice of embolic agent is a critical factor in the success of AVM embolization. Among the available options, Onyx, Squid, and N-Butyl Cyanoacrylate (NBCA) are the most frequently employed due to their unique properties and clinical versatility. Onyx, composed of ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide, offers controlled polymerization and superior penetration into the AVM nidus. Squid, a newer agent similar to Onyx, incorporates advanced formulations to reduce risks such as microcatheter adhesion. In contrast, NBCA, a cyanoacrylate-based adhesive, rapidly polymerizes upon contact with blood, making it effective for small AVMs but challenging to control in larger lesions.[1,3]

Despite their widespread use, limited comparative data exist to guide clinicians in selecting the most appropriate agent for specific AVM characteristics. This study aims to provide a comprehensive review of the efficacy, safety, and clinical applications of Onyx, Squid, and NBCA, offering evidence-based recommendations for optimizing embolization strategies in AVM management.[1,4]

MATERIALS AND METHODS

The method used in this literature review is through a systematic approach to analyze data in a simplified approach. The articles used are focused on original empirical research articles or research articles that contain results from actual observations or experiments where there are abstracts, introductions, methods, results, and discussions.

The article search strategy used relevant keywords, as mentioned earlier, to ensure that the literature found covered various aspects relevant to the topic, databases available on reputable and trusted academic and medical literature searches such as: PubMed, Scopus, Google Scholar. Inclusion criteria to determine the criteria for literature review materials, namely: 1) experimental research, 2) Original articles from primary sources. 3) Research articles published from 2010 to 2024 4) Full text articles in English, The exclusion data are: 1) Articles outside the use of extracranial malformation arterial embolic agents, 2) Articles published above the last 14 years / before 2010, 3) Articles in Indonesian. 4) The article only contains part of the abstract or part of the text.

RESULTS

The results section synthesizes findings from multiple studies to offer a comparative analysis of the efficacy and safety of embolic agents used in treating arteriovenous malformations (AVMs) show in table 1.

DISCUSSION

Endovascular embolization is a cornerstone in the treatment of arteriovenous malformations (AVMs), serving to reduce nidus size, mitigate hemorrhagic risk, and facilitate surgical resection when necessary. A range of embolic agents is utilized, each with unique properties that influence treatment outcomes. This review examines the roles of Onyx, Squid, and N-Butyl Cyanoacrylate (NBCA) in AVM embolization, synthesizing findings from key studies to provide insights into their clinical applications, benefits, and limitations. The literature reviewed includes three articles on Onyx, three on Squid, one on NBCA, and four comparing Onyx and NBCA.

Squid, a relatively newer EVOH-based embolic agent, has shown promise in the treatment of AVMs. Ilkay et, al. demonstrated that nearly one-third of AVM lesions achieved effective occlusion following embolization with Squid. The study emphasizes Squid's role as a viable alternative to Onyx and NBCA, particularly for cases requiring nuanced approaches. However, complications such as bleeding, thromboembolic events, and neurological impairments were reported, underscoring the importance of patient selection and procedural expertise.[3]
Andrade et al. specifically investigated Squid 18® in the context of micro-AVMs. All patients achieved complete obliteration of the malformations, with no significant complications reported during or after the procedure. These findings suggest that Squid may offer advantages in treating smaller or more intricate AVM cases, providing a targeted and safe option for specific clinical scenarios.[8]

Ch'ng et al. expanded on Squid's efficacy in brain AVM embolization, with obliteration rates ranging from 10% to 100% and an average of 33%. While these results highlight variability in outcomes, the majority of patients benefited from substantial lesion reduction. Importantly, no severe complications were reported, reinforcing Squid's safety profile. Despite this, its comparative effectiveness in larger or more complex AVMs warrants further exploration.[4]

Onyx has been extensively studied and remains a leading choice for AVM embolization. Maimon et al. provided critical insights into its effectiveness, showing high obliteration rates with the use of detachable microcatheters. The study also reported low complication rates, establishing Onyx as a safe and reliable option for managing AVMs with favorable angioarchitecture.[12]
Preoperative embolization with Onyx offers distinct advantages in reducing intraoperative challenges. By effectively occluding feeder vessels and the nidus, Onyx significantly decreases intraoperative hemorrhage and shortens surgical duration. Studies have reported favorable neurological outcomes following resection of AVMs pretreated with Onyx, further supporting its role in multimodal treatment strategies.[2]
Onyx has also shown efficacy in standalone treatment for small to medium AVMs, where its unique properties enable gradual and controlled embolization. This minimizes the risk of nontarget embolization and provides superior nidus penetration compared to NBCA. However, concerns remain regarding its potential for delayed complications, such as foreign body reactions and postprocedural inflammation, which merit continued vigilance.[7]

NBCA, one of the earliest liquid embolic agents used for AVMs, continues to be a viable option in specific contexts. A Japanese study highlighted its efficacy, demonstrating a significantly higher success rate in cases achieving >50% nidus penetration ($p < 0.001$). These findings underscore the importance of technical expertise and precise delivery in optimizing NBCA's performance.[5]
Despite its advantages, NBCA has limitations compared to newer agents like Onyx and Squid. Its rapid polymerization requires meticulous planning and execution, leaving little margin for error. However, its affordability and wide availability make it an attractive choice, particularly in resource-constrained settings.[1]

Several studies have compared the performance of Onyx and NBCA in AVM embolization. Loh Y et al. reported a 96% volume reduction with Onyx compared to 85% with NBCA, though the difference was not statistically significant. Both agents demonstrated efficacy in presurgical embolization, with Onyx offering superior handling and ease of use.[9]
Lv X et, al. examined complication rates, finding a slightly higher incidence of adverse events with Onyx, including bleeding, ischemia, and neurological deficits. However, these outcomes were influenced by demographic and angiographic variables, suggesting that patient-specific factors play a crucial role in determining the optimal embolic agent.[6]

Behzadi et al. conducted a longitudinal comparison from 2002 to 2019, concluding that while both agents are effective, NBCA often requires multiple sessions to achieve results comparable to Onyx. Moreover, Onyx exhibited a better complication profile in later studies, reflecting advancements in technique and delivery systems over time. Nonetheless, earlier studies associated Onyx with higher complication rates, indicating the learning curve associated with its use.[11]

Several limitations and biases were noted in the reviewed studies. Selection bias may arise from the inclusion of studies reporting favorable outcomes for Onyx, Squid, or NBCA, potentially excluding data on more complex AVM cases. This could result in an overly optimistic portrayal of these embolic agents' efficacy and safety.

Measurement bias was also a concern, as varying methodologies for assessing obliteration and complications hindered direct comparisons across studies. For example, differences in angiographic follow-up protocols and criteria for defining obliteration may skew results, making it difficult to draw definitive conclusions about each agent's relative performance.

Additionally, confirmation bias may influence findings. Researchers may favor data supporting the efficacy of newer agents like Onyx and Squid, potentially overlooking studies that highlight NBCA's effectiveness or report adverse outcomes associated with newer agents. This could lead to an imbalanced understanding of the comparative roles of these embolic agents in AVM management.

CONCLUSION

This review highlights the evolving landscape of embolic agents in AVM management, with Onyx and Squid emerging as strong contenders alongside the established NBCA. While Onyx offers superior handling and nidus penetration, Squid's safety profile and efficacy in specific scenarios position it as a valuable alternative. NBCA, despite its limitations, remains relevant due to its cost-effectiveness and proven track record.

Future research should prioritize multicenter, randomized studies to eliminate biases and standardize outcome assessments. Additionally, exploring the long-term effects of embolic agents and their role in combination therapies will be crucial in optimizing AVM management. By addressing these gaps, clinicians can better tailor treatments to individual patients, maximizing efficacy while minimizing risks.

CONFLICT OF INTEREST

The authors declare no conflict interest in this study

AUTHOR'S CONTRIBUTIONS

AB: conceptualization, investigation, writing-original draft, writing-review, editing and supervision, AJ: investigation, writing-review and editing, WH: conceptualization, investigation, writing-review and editing.

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TABLES

Table 1. Comparative Analysis of Onyx, Squid, and N-Butyl Cyanoacrylate in Intracranial Arteriovenous Malformation Embolization

Study	Research Method	Patient Demographics	Embolization Material	Outcomes	Complications
Miyachi S, et al. (2017). [5]	Retrospective	73 patients; Group S: 44 (successful occlusion); Group N: 29 (residual nidus); Average size: 31.6 mm	N/A	Successful occlusion in >50% nidus penetration (P<0.001). Larger AVMs correlated with lower occlusion rates.	No major complications reported.
Lv X, et al. (2011. [6]	Retrospective	147 patients; Average size: 4.0 cm; Hemorrhage: 46.9%; Seizures: 29.3%	NBCA & Onyx	396 pedicles embolized; hemorrhage in 2 cases, ischemic complications in 5 cases.	Hemiparesis (3 cases), ataxia (1 case), visual impairment (1 case).
Van Rooij WJ, et al. (2012). [7]	Observational	24 patients; Average size: 2.2 cm; Hemorrhage: 14; Seizures: 10	Onyx	100% complete obliteration in one session; No hemorrhagic or ischemic complications.	No complications reported.
Izumo T, et al. (2022). [2]	Retrospective	NBCA: 16; Onyx: 22; AVMs in eloquent areas (NBCA: 43.8%; Onyx: 72.7%)	NBCA & Onyx	Onyx reduced intraoperative hemorrhage; better outcomes (mRS<3) in Onyx group.	None significant.
Ch'ng LS, et al. (2023). [4]	Retrospective	25 patients; Mean age: 34 years; AVM obliteration: 10%-100%	Squid-18 & Squid-12	Squid-12 better penetrated embolic bulk; Mean obliteration rate: 33%.	Hemorrhage (4 cases), catheter perforation (7 cases), catheter breakage (1 case).

Study	Research Method	Patient Demographics	Embolization Material	Outcomes	Complications
Andrade GCD, et al. (2020). [8]	Case Study	3 patients with micro-AVMs; Complete obliteration achieved	EVOH (SQUID 18®)	mRS: 0 in all patients; 50% reduction in seizures for epilepsy cases.	None reported.
Ilkay A, et al. (2014). [3]	Observational	28 patients; AVMs: 16; AVFs: 9; Tumors: 2; Aneurysm: 1	Squid-18 & Squid-12	AVM obliteration rate: 37.5%; AVFs: 6/9 achieved full closure with combined treatments.	Two hemorrhages; three thromboembolic complications.
Loh Y, et, al (2010). [9]	RCT	125 patients; NBCA: 63; Onyx: 54	NBCA & Onyx	AVM volume reduction ≥50%: Onyx: 96%, NBCA: 85%. Comparable complication rates between groups.	Adverse events occurred equally in both groups.
Lv X, et al. (2012). [10]	Retrospective	147 patients; NBCA: 79; Onyx: 68; AVM obliteration: 19.7%	NBCA & Onyx	Onyx achieved higher obliteration rates; NBCA required more sessions for similar outcomes.	ICH (1 case), temporary neurological deficits (5 cases).
Behzadi F, et al. (2022). [11]	Retrospective	30 patients; NBCA: 12; Onyx: 18	NBCA & Onyx	Mean AVM volume reduction: NBCA: 52%; Onyx: 51%. Onyx required fewer sessions.	NBCA: 2 complications; Onyx: No complications.
Maimon S, et al. (2010). [12]	Observational	43 patients; Onyx: 40; Combined Onyx + NBCA: 3	Onyx	Complete eradication: 37% of total cohort; Average Onyx volume: 2.5 mL	Clinical complications: 9.2% per procedure; permanent deficits: 6.9%.

Study	Research Method	Patient Demographics	Embolization Material	Outcomes	Complications
				(detachable catheter); 1.7 mL (non-detachable catheter).	