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ORIGINAL ARTICLE

Comparing the Effect of Lidocaine 2% and Magnesium Sulphate on Relieving Intraoperative Vasospasm of Pedicled Island Flap in Male Albino Rats: An Experimental Study

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ABSTRACT

Background: Reconstruction using flap surgery has grown more dependable. It enables the restoration of nearly any area of the body damaged as a result of trauma or surgery. The present work aimed to detect the ability of lidocaine 2% and magnesium sulphate to decrease the duration of vasospasm as well as their overall efficacy and to review the evidence for the most effective pharmacological drugs for the management of intraoperative vascular spasm during microsurgery.

Methods: In an experimental study, 20 male albino rats with an average weight of 200-350 grams were used for flap pedicle based on inferior epigastric arteries that were harvested from all the rats. We measured the pedicle of the flap clinically with the caliber and under a microscope by the Shinwa crack scale clear type. The effects of the most potent drugs to relieve vasospasm were tested, and a direct comparison between lidocaine and magnesium sulphate was done.

Results: A significant decrease in the flap pedicle diameter was observed after vasospasm compared to the control at the right side ($P < 0.05$). No statistically significant differences were detected between the control and lidocaine effect on the right side, nor between the control and magnesium sulphate effect on the left side ($P \geq 0.05$). A statistically significant increased percentage of vasodilatation percentage was found after magnesium sulphate effect (mean = 103.2±13.04, range = 76.9–133.3%) when compared with that after lidocaine effect (mean = 93.5±9.2, range = 80–114.3%) ($P = 0.01$).

Conclusions: Based on our findings, the magnesium sulphate effect increased the percentage of vasodilatation when compared with the 2% lidocaine effect. Nevertheless, the small sample size of our study may limit drawing any firm conclusion, and we suggest conducting additional research with larger patient populations and extending the duration of follow-up to strengthen our findings.

Keywords: Lidocaine; Magnesium sulphate; Vasospasm; Male albino rat.

INTRODUCTION

Reconstruction using flap surgery has grown more dependable. It enables vascularized tissue regeneration of post-surgical and post-traumatic abnormalities anywhere in the body [1]. Reconstructive microsurgery using perforator flaps has grown commonplace, especially for areas without other local options, such as the head and neck, breast, trunk, and limbs (both upper and lower) [2]. When it comes to reconstructive surgery, microsurgery is becoming an essential option [3].

Vasospasm is a medical condition that can sometimes go away on its own. However, tissue hypoxia and flap failure can result from protracted vasospasm [4]. Direct manipulation of arteries or metabolic homeostasis are two examples of variable stimuli that can impact intraoperative vasospasm of the flap pedicle [3].In microvascular surgery, intraoperative vasospasm is frequent, difficult to anticipate, and could have a catastrophic effect on flap survival [5].

Because intraoperative surgical treatment of acute vasospasm is so ineffective, pharmacological

therapy is the treatment of choice [4]. Despite its continued popularity, surgeons performing microsurgery have had to experiment with various vasodilator medications due to the current global shortage of papaverine, which is used to treat intraoperative vasospasm [6]. To break intraoperative vasospasm during this shortage, topical medications such as magnesium sulphate and lidocaine 2% are utilized. Almost every drug that is now used to treat vasospasm has already been licensed for use elsewhere in the body [7].

To ascertain how the administration of intraoperative vasodilator medication affects flap perfusion, this study aimed to detect the ability of lidocaine 2% and magnesium sulphate to decrease the duration of vasospasm as well as their overall efficacy and to review the evidence for the most effective pharmacological drugs for the management of intraoperative vascular spasm during microsurgery at Zagazig University Hand and Microscopic Centre (ZUHMC).

METHODS

This experimental study was conducted on 20 Sprague-Dawley young adult male albino rats with an average weight of 200-350 grams. They were all subjected to the experiment during the study period from December 2023 to June 2024. We excluded all female rats that weighed below 200 gm or above 350 gm.

All the maneuvers carried out in this experiment concerning the rats were highly ethical and merciful. The Institutional Animal Care and Use Committee of the Faculty of Medicine, Zagazig University, approved the study (ZU-IACUC/3/F/146/2023). Following the recommendations of the Declarations of Helsinki as well as the European Community's rules for the use of experimental animals, the experiment was carried out.

The procedure

All rats received proper anesthesia, "ketamine Intra-peritoneal (0.08-0.09 mg/g body weight), during all surgical procedures. The hair on the abdomen was shaved using electric clippers. The skin was then disinfected with a povidone-iodine solution. The rats were divided into two groups of flap pedicles based on the inferior epigastric artery that was harvested from all the rats. Flaps pedicle used lidocaine 2% on the right side and magnesium sulphate on the left side. The vasospasm of the pedicle was made by using iced saline. Vasodilator drugs were applied locally at a rate of 0.5 ml/minute for two minutes. Flap pedicle monitoring was assessed to determine the duration of flap pedicle reperfusion. We measured the pedicle of the flap clinically with a caliber by the Shinwa crack scale clear type and under a microscope. The effects of the most potent drugs were tested, and a direct comparison between drugs was carried out. Using an isoflurane overdose, we euthanized the subjects after the experiment. All biosafety laws and ethical considerations about animal experimentation were adhered to (Figures 1 & 2).

Statistical analysis

We used SPSS version 28 (IBM Co., Armonk, NY, USA) to complete the statistical analysis. We used the terms mean, standard deviation (SD), and range to display quantitative parametric data. A statistically significant result was defined as a P-value less than 0.05, and an independent t-test was used to compare the normal distribution between the studied groups.

RESULTS

Twenty male rats survived the operation and the follow-up period without major complications. Two groups of flap pedicles based on the inferior epigastric artery were harvested from all the rats. We measured the pedicle of the flap clinically with the caliber and under a microscope with a Shinwa crack scale clear.

A statistically significant decreased flap pedicle diameter was found after vasospasm (mean = 0.24±0.08, range = 0.1-0.4 mm) when compared with control diameter (mean = 0.46±0.09, range = 0.35–0.65 mm) on the right side ($P < 0.001$) (Table 1).

A non-statistically significant difference in flap pedicle diameter was found between the control diameter (mean = 0.46±0.09, range = 0.35-0.65 mm) and after lidocaine effect (mean = 0.43±0.09, range = 0.3–0.6 mm) on the right side ($P = 0.316$) (Table 2).

A high statistically significant decreased flap pedicle diameter was revealed after vasospasm (mean = 0.27±0.05, range = 0.15-0.4 mm) when compared with control diameter (mean = 0.48±0.1, range = 0.3–0.65 mm) on the left side ($P < 0.001$) (Table 3).

A non-statistically significant difference in flap pedicle diameter was found between the control diameter (mean = 0.48±0.1, range = 0.30-0.65 mm) and after the magnesium sulphate effect (mean = 0.48±0.06, range = 0.4–0.6 mm) on the left side ($P = 0.852$) (Table 4).

A statistically significant increased percentage of vasodilatation was revealed after magnesium sulphate effect (mean = 103.2±13.04, range = 76.9–133.3%) when compared with that after lidocaine effect (mean = 93.5±9.2, range = 80–114.3%) (P = 0.01) (Table 5).

Table (1): Comparison of flap pedicle diameter at right Side between control diameter and after vasospasm

Right side		Control (N = 20)	After vasospasm (N = 20)	t	P-value
Flap pedicle diameter (mm)	**Mean ±SD**	0.46 ± 0.09	0.24 ± 0.08	7.5	< 0.001*
	Range	0.35 – 0.65	0.1 – 0.4		

t: Independent sample t-test
** P-value < 0.001 was considered highly significant*

Table (2): Comparison of flap pedicle diameter at right side between control diameter and after Lidocaine effect

Right side		Control (N = 20)	After lidocaine (N = 20)	t	P-value
Flap pedicle diameter (mm)	**Mean ±SD**	0.46 ± 0.09	0.43 ± 0.09	1.01	0.316
	Range	0.35 – 0.65	0.3 – 0.6		

t: Independent sample t-test
P-value > 0.05 was considered non-significant

Table (3): Comparison of flap pedicle diameter at left side between control diameter and after vasospasm.

Left side		Control (N = 20)	After vasospasm (N = 20)	t	P-value
Flap pedicle diameter (mm)	**Mean ±SD**	0.48 ± 0.1	0.27 ± 0.05	8.07	< 0.001*
	Range	0.30 – 0.65	0.15 – 0.4		

t: Independent sample t-test
** P-value < 0.001 was considered highly significant*

Table (4): Comparison of flap pedicle diameter at left side between control diameter and after magnesium (Mg) sulphate effect

Left side		Control (N = 20)	After Mg sulphate (N = 20)	t	P-value
Flap pedicle diameter (mm)	**Mean ±SD**	0.48 ± 0.1	0.48 ± 0.06	0.18	0.852
	Range	0.30 – 0.65	0.4 – 0.6		

t: Independent sample t-test
P-value > 0.05 was considered non-significant

Table 5: Comparison of vasodilatation (VD) percentage after Lidocaine effect on right side flap pedicle and magnesium (Mg) sulphate effect on left side flap pedicle

VD percentage (%)	After Lidocaine (N = 20)	After Mg sulphate (N = 20)	t	P-value
Mean ±SD	93.5 ± 9.2	103.2 ± 13.04	2.7	0.01*
Range	80 – 114.3	76.9 – 133.3		

t: Independent sample t-test
** P-value < 0.05 was considered significant*

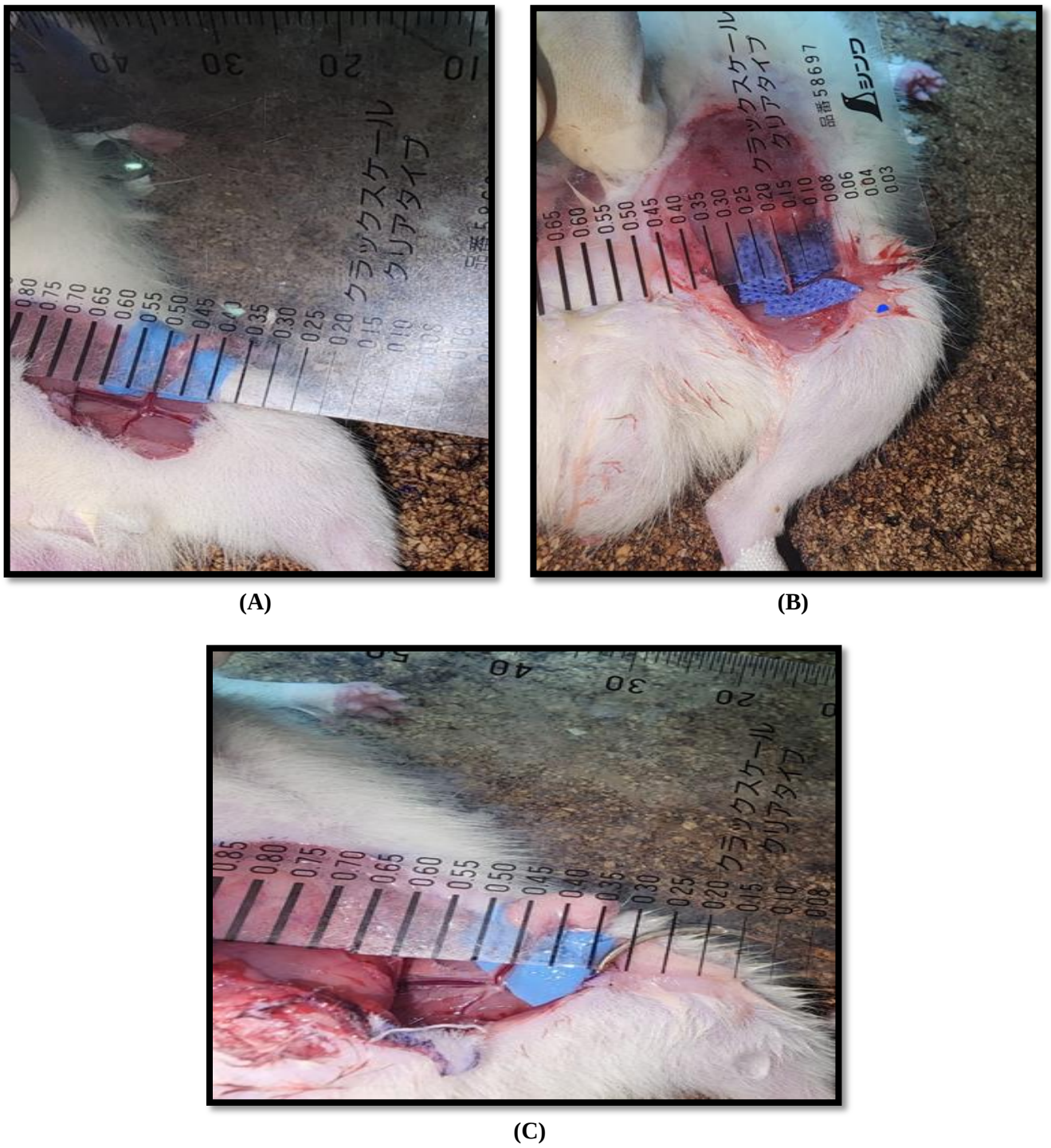
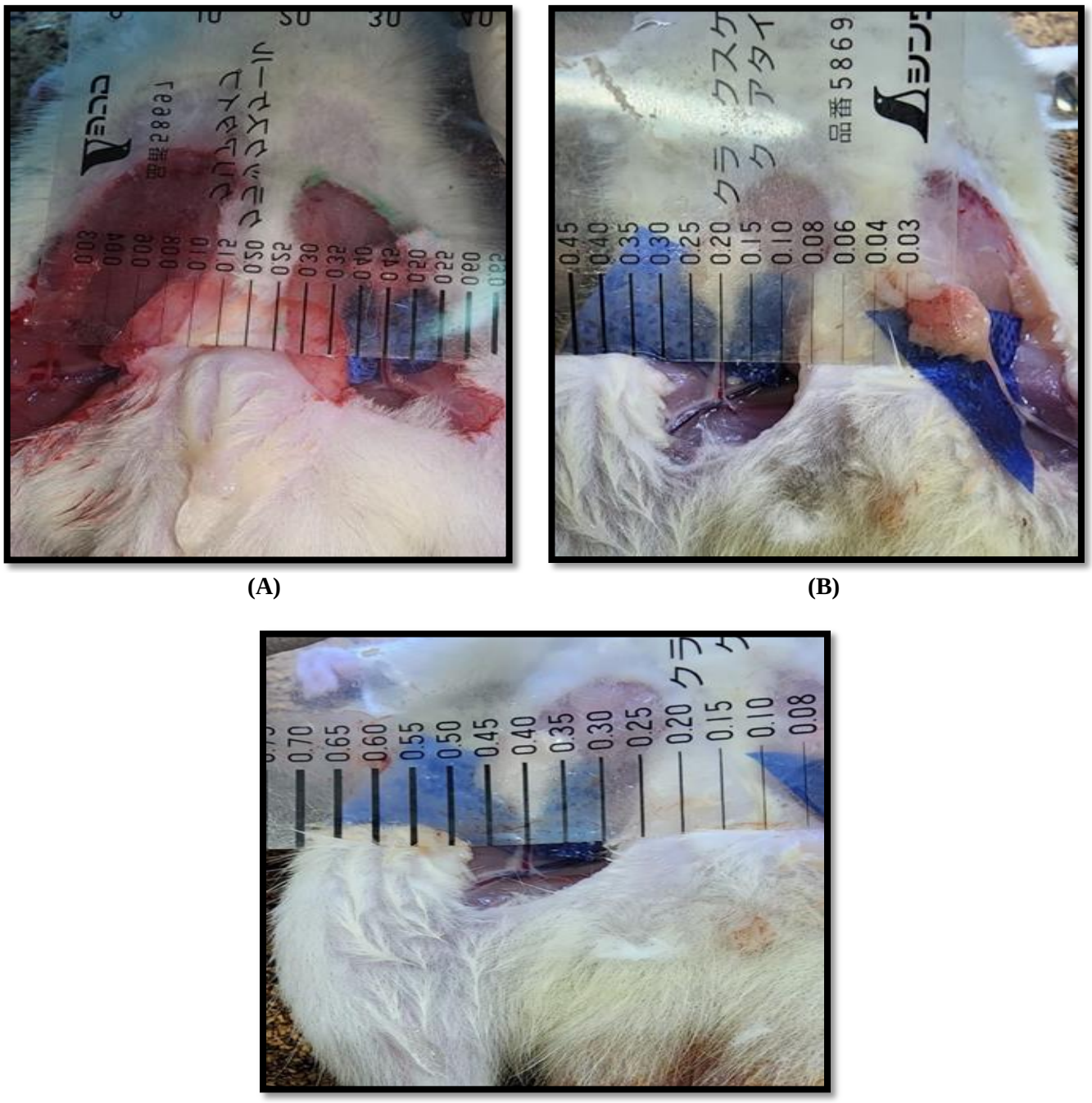


Figure (1): Right flap based on inferior epigastric artery; (**A**) shows normal diameter of the pedicle, (**B**) shows the diameter of the pedicle after vasospasm, (**C**) shows the diameter after using Lidocaine 2%.



(A) **(B)**

(C)

Figure (2): Left flap based on inferior epigastric artery; (**A**) shows normal diameter of the pedicle, (**B**) shows the diameter of the pedicle after vasospasm, (**C**) shows the diameter after using magnesium sulphate.

DISCUSSION

Reconstruction using flap surgery has grown more dependable. Vascularized tissue can be used to mend abnormalities that have occurred as a result of surgery or trauma frequently in the body [1]. Reconstructive microsurgery frequently employs perforator flaps to cover wounds in the breast, trunk, head, and neck, as well as lower and upper limbs when no other local options are available [2].

As a functional condition, vasospasm typically goes away on its own. Prolonged vasospasm drastically reduces tissue blood flow, which might lead to flap failure. Direct manipulation of arteries or metabolic homeostasis are two examples of variable stimuli that can impact intraoperative vasospasm of the flap pedicle. Regarding the viability of microvascular

flaps, intraoperative vasospasm is still a prevalent, unpredictable, and perhaps fatal complication [5].

Complete blockage of blood flow to the flap and the potential production of thrombi, leading to irreversible ischemia, are consequences of prolonged vasospasm. It is recommended to offer pharmaceutical therapy for acute vasospasm since surgical treatment during surgery is rarely beneficial. There have been numerous evaluations of pharmacologic medications to prevent or minimize vasospasm during microsurgery, but the exact mechanism by which it occurs remains unknown [8].

Although 94% of UK plastic surgeons regularly employed vasodilators intra-operatively, the agent(s) chosen and method of administration differed substantially, according to a recent survey [4].

The present study aimed at detecting the ability of lidocaine 2% and magnesium sulphate to decrease the duration of vasospasm as well as their overall efficacy and to review the evidence for the most effective pharmacological drugs for the management of the intraoperative vascular spasm during microsurgery.

In this experimental study, twenty male rats survived the operation and the follow-up period without major complications. Two groups of flap pedicles based on the inferior epigastric artery were harvested from all the rats. We measured the pedicle of the flap clinically with the caliber and under a microscope by the Shinwa crack scale clear type. The effects of most patent drugs were tested, and a direct comparison between lidocaine and magnesium sulphate was done.

Our data showed a high statistically significant ($P < 0.001$) decrease in flap pedicle diameter after vasospasm (mean = 0.24±0.08, range = 0.1-0.4 mm) when compared with control diameter (mean = 0.46±0.09, range = 0.35–0.65 mm) at the right side. Moreover, our data showed a high statistically significant ($P < 0.001$) decrease in flap pedicle diameter after vasospasm (mean = 0.27±0.05, range = 0.15-0.4 mm) when compared with control diameter (mean = 0.48±0.1, range = 0.3–0.65 mm) at the left side.

It is still unclear what causes the pathogenesis of vasospasm when the pedicle is pulled. Direct myogenic reaction of the smooth vascular wall muscle is one reason that could explain it. When the length of artery smooth muscle is stretched to 1.2 times its resting length, the muscles contract, and the myosin light chains are maximally phosphorylated [5].

In the study of Ma et al. [7], an $87.26 \pm 1.32\%$ decrease in perfusion of the femoral artery and a $75.96 \pm 1.47\%$ decrease in perfusion of the vein were noted following vasospasm induction, respectively. Furthermore, following vasospasm, none of the ten groups showed statistically different perfusion rates in the femoral artery ($P = 0.863$) or vein ($P = 0.180$).

In the current work, no statistically significant difference ($P = 0.316$) in flap pedicle diameter was found between control diameter (mean = 0.46±0.09, range = 0.35-0.65 mm) and after lidocaine effect (mean = 0.43±0.09, range = 0.3–0.6 mm) at the right side.

There is debate over whether or not it is effective when used as a vasodilating medicine. Our findings are in line with those of Ricc et al. [6], who suggested that 2% lidocaine could reduce vasospasm and Evans et al. [9], who found that 2% lidocaine had a negative impact on preexisting vasospasm.

According to Ma et al. [7], the mechanically produced vasospasm paradigm does show a dose-dependent pattern for lidocaine, but it is not biphasic. In terms of relieving femoral artery spasms quickly, nothing beats high-concentration 2% lidocaine. Resolving arterial vasospasm with 2% lidocaine was more effective, stabilizing hyperperfusion in the femoral artery in 1100 ± 22 seconds.

In the current study, a non-statistically significant difference ($P = 0.852$) in flap pedicle diameter was found between the control diameter (mean = 0.48±0.1, range = 0.30-0.65 mm) and after magnesium sulphate effect (mean = 0.48±0.06, range = 0.4–0.6 mm) at the left side.

Because of its potential to decrease Ca^{2+} concentration in vascular smooth muscle cells, magnesium sulphate has been utilized for the treatment of cerebral and coronary vasospasm [10, 11]. There have been inconsistent results when using it in microvascular surgery.

Although its direct capacity to dilate the inner diameter and increase perfusion of the arteries in the pedicle has not been investigated, Hyza et al. [5] revealed that restoring flap perfusion with topical magnesium sulphate therapy was a highly reliable option.

Research conducted by Ma et al. [7] aimed to assess the beneficial effects of magnesium sulphate vasodilatation effects on arterial vasospasm and

showed that 10% magnesium sulphate acts swiftly, reversing constricted femoral artery and vein in approximately half a minute. The study also shows that the femoral artery hyperperfusion occurs in 620 ± 29 seconds and the vein hyperperfusion occurs in 1142 ± 45 seconds.

For cerebral vasospasm, similar results were corroborated in pilot prospective randomized controlled trials by Van den Bergh et al. [12] and Wong et al. [13]. Preventative magnesium administration to guard against vasospasm, as opposed to treatment of an already-established vasospasm, may yield better results from magnesium therapy.

The current study findings showed a statistically significant (P = 0.01) increased percentage of vasodilatation after magnesium sulphate effect (mean = 103.2±13.04, range = 76.9–133.3%) when compared with that after lidocaine effect (mean = 93.5±9.2, range = 80–114.3 %).

Ma et al. [7] found that out of ten drugs that might shorten the time it takes to escape a spasm in the femoral vein or artery, magnesium sulphate and 2% lidocaine were the most effective spasmolytics. The two drugs were statistically indistinguishable; however, the 10% magnesium sulphate group required less time than the 2% lidocaine group. While both magnesium sulphate and 2% lidocaine have the potential to increase blood flow to the femoral artery, the latter takes far less time to do the former. Additionally, hyperperfusion of the femoral vein can only be achieved by using magnesium sulphate. Consequently, the best antispasmodic to use is magnesium sulphate.

In the same context, according to Hyza et al. [5], with the highest level of significance and reliability, 10% magnesium sulphate was shown to be the most efficient in reducing the duration of surgically induced vasospasm (P < 0.01). The authors concluded that locally applied magnesium sulphate had the best potential to alleviate the condition. Alternatively, after 2% lidocaine was applied locally, the duration of vasospasm was prolonged (P < 0.01).

CONCLUSION

Based on our data, the magnesium sulphate effect increased the percentage of vasodilatation when compared with the 2% lidocaine effect. Nevertheless, the small sample size of our study may limit drawing any firm conclusion, and we suggest conducting additional research with larger patient populations and extending the duration of follow-up to strengthen our findings.

Conflict of interest: None.

Financial disclosures: None.

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