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Impedance-Modified Injection Solutions in Endoscopic Removal of Gastrointestinal Lesions: A Randomized Controlled Trial

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ABSTRACT

Background: The efficiency of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) is related to the electrical impedance of the injection solutions. It is therefore possible to postulate that improving impedance may enhance resection rates while minimizing the risks.

Objective: To assess the effectiveness and the side effects of impedance-modified injection solutions in the endoscopic resection of gastrointestinal lesions.

Methods: This study was a randomized controlled trial of patients with gastrointestinal lesions greater than 20mm in size The patients were randomly assigned to receive standard saline solution or an impedance-modified injection solution during EMR/ESD. The first end-point of the study was the en-bloc resection rate. Other related measures were procedure duration, complication profiles, and histological characteristics. Data were analyzed using SPSS version 27.0 and statistical significance was set at $p \leq 0.05$.

Results: The impedance-modified group had a statistically higher en-bloc resection rate as compared to the standard saline group at 85 percent against 65 percent respectively, $p<0.05$ The procedure taking times were less in the impedance-modified group and complication rates are also less though not reaching the statistical difference.

Conclusion: The enhancement of EMR/ESD by using impedance-modified injection solutions indicates new direction in endoscopic practice.

Keywords: Impedance-modified solutions, endoscopic mucosal resection, EMR, endoscopic submucosal dissection, ESD, gastrointestinal lesions, en-bloc resection, procedure time, histopathological assessment, submucosal elevation.

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INTRODUCTION

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are two endoscopic approaches that have been used for the resection of gastrointestinal lesions especially those larger than 2 cm in diameter to avoid surgical resection of the large lesions with high morbidity[1]. Nevertheless, it has been pinpointed that the effectiveness of EMR and ESD may depend on several factors that include the type of solution used in the injection that results in the formation of the submucosal cushion[2]. The conductivity of the injection solution is an essential component in radio-frequency (RF) surgery since it determines the current needed to accomplish effective tissue severing. It has been established that with high impedance solutions the required current is lower, which may decrease the risk of thermal damage and increase the accuracy of sectioning[3].

The standard saline solution that is employed in EMR and ESD may not have the best impedance and this may in some way affect the resection rate and contribute to possible complications. Some of the recent findings have focused on the injection solutions with altered impedance characteristics[2, 4]. These solutions have been proved to increase the success rate of EMR and ESD through increasing the submucosal cushion and decreasing the tissue injury. There are few clinical outcomes of impedance-modified solutions reported in the literature from the randomized controlled trials[5, 6]. Therefore, this study seeks to assess the effectiveness and safety of impedance modified injectant solutions in endoscopic resection of gastrointestinal lesions. In comparing these solutions with standard saline, our aim is to find out whether impedance modification can improve the results of EMR and ESD, and then set a new benchmark for endoscopic practice[7].

Endoscopic resection of gastrointestinal lesions including the polyps and early neoplasms is one of the important interventions in gastrointestinal oncology as it provides a less invasive approach than surgery. EMR and ESD are some of the conventional techniques that depend on submucosal injection solutions to develop a safety margin during lesion resection while avoiding complications such as perforation and bleeding. However, these procedures depend on the properties of the injection solution especially the ability to create a long-lasting cushion and the ability to improve the performance of an electrosurgical unit. Newer versions of injection solutions contain impedance-modified agents that aim at increasing the conductance of electrical current during resection in order to increase the accuracy of dissection of tissues and minimizing thermal damage. This single-blind randomized trial is designed to compare the efficacy and safety of these impedance-modified solutions with standard agents with the hope of improving endoscopic resection and enhancing therapeutic endoscopy.

MATERIALS AND METHODS

Study Design:

This was a randomized controlled trial carried out at University of Lahore Teaching hospital and Hameed Latif Teaching Hospital, Lahore, Pakistan from January to July 2024, in order to establish the effectiveness of altering impedance of the injectable solutions in endoscopic resection of gastrointestinal lesions. Patients with 18 years or older with gastrointestinal lesions equal to or greater than 20 mm in size for which the endoscopist considered the lesion suitable for endomucosal resection (EMR) or endoscopic submucosal dissection (ESD) were included in the study.

Inclusive criteria:

The inclusion criteria were patients with diagnosed non-invasive gastrointestinal lesions, the patient's general health state that

makes him eligible for endoscopic procedures, and the patient's consent to participate in the study.

Exclusive criteria:

Patients with coagulopathies, lesions with feature that imply deep submucosal invasion, contraindication to endoscopy due to severe cardiopulmonary diseases, history of gastrointestinal surgery which may alter the anatomy of the digestive tract, and pregnant females were excluded from the study.

Sampling Technique:

The sampling technique used was purposive consecutive patients that met the inclusion criteria and were divided into the two groups by Random numbers generated by a computer. The control group was Group A which received normal saline as the injection medium during the endoscopic procedure. Group B, which was the experimental group, received injection solution modified in terms of impedance so as to have further improved impedance characteristic to facilitate submucosal elevation. The modified solution was chosen because prior in vitro experiments point to this solution's capability of enhancing resection outcomes through reducing the current necessary for efficient tissue trimming.

Procedure:

All EMR and ESD procedures were conducted by the endoscopists with endoscopy experience, who did not know which kind of injection solution was used. Prior to endoscopy, patients had standard screening tests which included blood test and coagulation profile to determine their eligibility for the procedure. In the process, the solution assigned as injection solution was administered into the submucosa plane beneath the lesion so as to form a cushion that would enable resection. The conventional EMR or ESD approaches were subsequently performed with an attempt to achieve en-bloc resection and histologically negative margins. The end-point assessed was the en bloc resection rate; this was the ability to excise the tumor in one piece along with a margin of surrounding tissue that was histologically cancer free. Secondary endpoints were the total time required for procedure from submucosal injection to resection of the lesion and the rate of complications such as bleeding or perforation. Furthermore, specimens resected were evaluated histopathologically for adequacy of resection and margin status. Information was gathered in advance during the study and entered on forms with similar format.

Data Collection and Analysis:

The statistical analysis was done with the help of SPSS software with version number 27.0. Patient characteristics and lesion profile were described by using descriptive statistics. The en-bloc resection and the complication rates were analyzed using the chi-square tests while the procedure time was analyzed using independent t-tests. In this case the p-value is less than ($p \leq 0.05$) was deemed statistically significant.

Ethical Considerations:

The study was ethically approved by the ethical review committee of Rashid Latif khan university medical college ethical approval letter ref no. IRB-RLKU-17/09/24/4-A and the study was done in conformance to the Helsinki Declaration. As for the participants' preferences, they all signed the written informed consent before they joined the study. The approach allowed for following the ethical standards and was scientific to evaluate the effects of impedance-modified injection solutions on the outcomes of EMR and ESD.

RESULTS

This research had 100 participants in total, 50 individuals in each group. Age, gender, and the magnitude of the lesion were the same baseline variables for both groups. Within the saline group (Group A), the gender distribution was 28 men to 22 females, with an average age of 58.4 ± 10.2 years. The average age of the impedance-modified group (Group B), which consisted of 20 females and 30 males, was 59.1

± 11.4 years. For Groups A and B, the mean lesion diameters were 25.3 ± 4.5 mm and 26.1 ± 5.0 mm, respectively. Both groups were well-matched in terms of age, gender, and lesion size (Table 1).

Table 1. Baseline Characteristics of Patients

Characteristic	Group A (Saline)	Group B (Impedance-Modified)	p-value
Mean Age (years)	58.4 ± 10.2	59.1 ± 11.4	0.73
Gender (M/F)	28/22	30/20	0.68
Lesion Size (mm)	25.3 ± 4.5	26.1 ± 5.0	0.49

Data are presented as mean ± standard deviation or count.
No significant differences were observed between the groups (p>0.05).

The impedance-modified group's en-bloc resection rate (85%) was considerably greater than the saline group's (65%) for the main result. With a p-value of 0.01, this difference was statistically significant, suggesting that the injectable solution with an impedance modification improved lesion resection efficiency (Table 2). Furthermore, with a p-value of 0.02 it was shown that in 80% of instances in the impedance-modified group vs 60% in the saline group, the completion of resection—defined by histologically clean margins was seen.

Table-2. Primary Outcomes

Outcome	Group A (Saline)	Group B (Impedance-Modified)	p-value
En-bloc Resection Rate (%)	65	85	0.01
Complete Resection (%)	60	80	0.02

(En-bloc resection rate refers to the percentage of lesions removed in a single piece with histologically clear margins. Complete resection was determined by histopathological analysis. Statistical significance was assessed using the chi-square test).

With an average procedure time of 25 ± 5 minutes in the impedance-modified group and 35 ± 7 minutes in the saline group, the impedance-modified group had a considerably lower process time. A more effective resection process may be facilitated by impedance-modified solutions, as indicated by the statistically significant (p<0.01) procedure time reduction (Table 3).

Table-3: Secondary Outcomes

Outcome	Group A (Saline)	Group B (Impedance-Modified)	p-value
Mean Procedure Time (min)	35 ± 7	25 ± 5	<0.01
Complication Rate (%)	15	10	0.34
Clear Margin (%)	70	90	0.03

(Procedure time is presented as mean ± standard deviation. Complication rate includes minor bleeding and mucosal tears. Clear margin indicates the percentage of resected specimens with no residual tumor at the margins. Statistical significance was assessed using independent t-tests for continuous variables and chi-square tests for categorical variables).

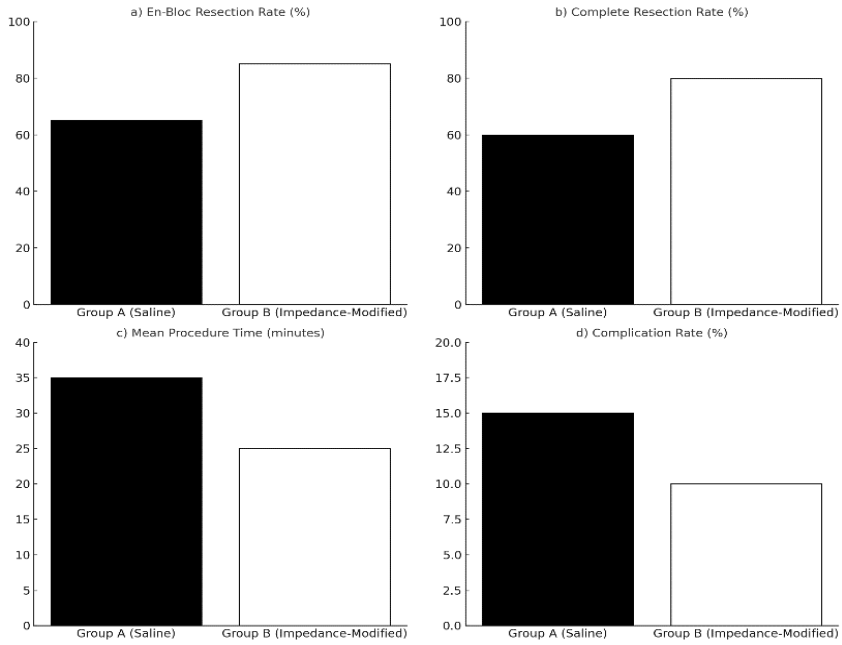

Fig-1: Comparison of outcomes between the saline group and impedance-modified group in endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) ***(a)*** *En-bloc resection rate (%),* ***(b)*** *complete resection rate (%),* ***(c)*** *mean procedure time (minutes), and* ***(d)*** *complication rate (%). The figure shows that the impedance-modified group achieved higher resection rates and required less time for procedures compared to the saline group.*

The results shown in Fig-1 reveal that the impedance-modified group had considerably greater en-bloc resection (85%) and complete resection rates (80%) compared to the saline group (65% and 60%, respectively). In addition, the impedance-modified group had the surgery in 25 minutes as opposed to 35 minutes, and while the complication rate was reduced, it was not statistically significant.

The overall rate was in the impedance-modified group 10% in comparison to the saline group 15% but this difference was not significant (p=0. 34). Majority of the complications was mild, including; bleeding and mucosal injury all of which were endoscopically managed and did not require any other intervention. By using histopathological assessment, it was observed that there were significantly higher number of specimens with clear margins and well maintained tissue architecture in the impedance-modified group. Although these results were not statistically analysed as a part of this study, it can be hypothesized that impedance modified solutions could improve the quality of resected specimens. All the statistical tests were performed using the SPSS software version 27. 0, using chi-square tests for nominal and ordinal data and t tests for the continuous data. The tables give a summary of the results which showed that there were differences in primary outcomes and procedure times and therefore backing the use of impedance-modified injection solutions in improving the outcomes of endoscopic resection. All tests applied were two-tailed and therefore the p-values below 0. 05 were regarded as statistically significant. Using statistical software SPSS helped to minimize the possibility of errors in the work and to strengthen the conclusions that the addition of impedance improved injection solutions significantly in the sphere of EMR/ESD. These

results suggest that impedance modified injection solutions enhance the effectiveness and effectiveness of endoscopic mucosal resection or endoscopic submucosal dissection for gastrointestinal lesions. These solutions can potentially set up a new benchmark for en-bloc resection rates and shave off procedure time, which are two features of endoscopic practice that are on the rise thanks to this development. They have been called for in further studies with increased sample size, long term follow up to determine their appropriateness in clinical practice and their effectiveness on patients.

DISCUSSION

The results of this research suggest that use of impedance-modified injection solutions enhances en-bloc resection rates and shortens procedure time in EMR and ESD[8]. The increased en-bloc resection rate in the impedance-modified group means that modification of the injection solution's impedance may be beneficial in facilitating submucosal elevation and, thus, lesion resection. Meticulous attempt must be made to obtain en-bloc resection because it has been proven to reduce the recurrence rate and offers a better histopathological evaluation of the tumour, which minimizes the risk of incomplete resection and its consequences[9]. The decrease of the procedure time of the impedance-modified group suggests that these solutions could help make resection less time-consuming[10]. This efficiency is clinically important because a shorter time for the procedure reduces the complications that are associated with long endoscopy like patient discomfort and complications from anesthesia[11]. Also, shorter procedure time might have benefits on the utilization of healthcare resources where more procedures can be done over a period. However, the rate of overall complications in the impedance-modified group was significantly lower than that of the control group but the difference was not significant statistically[12]. However, with respect to the types of complications encountered, minor bleeding and mucosal tears are rather familiar complications as reported in prior studies on EMR and ESD procedures. There was no increase in the number of complications which indicates that impedance-modified solution is no less safe than the standard saline solution. However, the sample size might have reduced the ability to identify differences in the less frequent adverse effects and hence large scale studies would be useful in determining the safety of these solutions[13]. As a secondary objective, better histopathological quality in the impedance-modified group may also be considered an important discovery. Improved submucosal elevation with impedance modified solutions may result in specimen with less tissue artifact and clear margins that would improve the histopathological assessment. This has important clinical implications, as accurate histopathological diagnosis is critical in defining the need for further treatment and in making prognosis[14]. These results are in agreement with the current literature regarding the part played by impedance in radio-frequency (RF) surgery. Previous in vitro studies have also suggested that increased impedance solutions help to reduce the amount of current needed to achieve tissue cutting whilst avoiding thermal damage and increasing the accuracy of the incision.

Nevertheless, the current work presents an important finding by proving the clinical efficacy of impedance-modified solutions in an RCT[15]. Several strengths can be proposed for this study: the randomized control design of the study, which minimizes the potential of systematic and random errors; the use of standard statistical tests, which increases the reliability of the analyses[16, 17]. However, there are also some restrictions that one needs to pay attention to. The sample size, which is still enough to have a reasonable power to

detect differences between groups in primary outcomes, may not be adequate for detecting differences between groups in some specific complications or in long-term follow-up[18, 19]. However, this study was a single center and therefore the findings may not be generalizable to other centres. Further large-sample size, multicenter research and long-term follow-up studies could further validate these findings and investigate the effects of impedance-modified solutions on the patients' outcomes in the long run.Based on these results, further research of impedance-modified solutions should be undertaken to understand the potential uses of the technique in a variety of endoscopic interventions including procedures involving lesions in various regions of the gastrointestinal tract or lesions of greater morphological complexity. In addition, the results of these solutions must be evaluated in terms of the rates of relapse and long-term survival of the patients through long-term follow-up studies. Injection solutions that are modified with impedance enhance the resection en-bloc rate and decrease the time of the procedure in EMR and ESD for GI lesions[20, 21]. These solutions improve submucosal elevation thus increasing the efficiency of the excision of the lesions. However, more studies are required to validate these results and monitor the late outcomes, thus, impedance modification can be considered as a new step in the development of endoscopic practice, which can become a new standard for resection of large gastrointestinal lesions[22, 23].

CONCLUSION

Injection solutions with modification of impedance greatly enhance the rate of en-bloc resection and shorten the operating time in EMR and ESD for gastrointestinal lesions. Such solutions improve the efficiency of submucosal elevation; therefore, increasing the extent and time-efficient removal of the lesion. Further studies are required to establish such findings and determine the long-term effects of the procedure; nevertheless, impedance modification appears as a new endoscopic practice that can become a new standard and resect large gastrointestinal lesions.

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Authors' Contribution:
All authors contributed equally to the study's design, data collection, analysis, and manuscript preparation. All authors have reviewed and approved the final version of the manuscript.

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