RESEARCH ARTICLE

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Botulinum Toxin and Electrophysiological Intervention Improve Post-Surgical Breast Entdoprosthetics: A Clinical Trial Study

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Abstract

Introduction: The majority of plastic surgeon specialists note a distinct tendency to increase the number of breasts endoprosthetic surgeries with silicone implants in the Republic of Uzbekistan - the number of such surgeries now reaches 3-4 thousand annually. Breast replacement for aesthetic purposes is widespread throughout the world and has been rapidly spreading in Uzbekistan in recent years. Due to surgical endoprosthetics of mammary gland tissue with silicone implants, both in the early and late postoperative periods, quite often the patient's body experiences typical postoperative pain, which, if subclinical, requires constant dynamic monitoring and preventive rehabilitation procedures. Rehabilitation measures are a prerequisite for a successfully performed aesthetic surgery to enlarge the mammary glands. **Materials and Methods:** To address the effectiveness of intramuscular botulinum toxin A and the INDIBA electromagnetic field electrophysiology we used, a prospective randomized trial was designed to evaluate the effectiveness of patient-reported postoperative pain and pain reduction in these settings. **Results:** The results of the conducted research allow us to conclude that the course of electrophysiological influence by INDIBA preparation, conducted in the first week, daily, i.e. 7 procedures after aesthetic breast endoprosthetics, significantly increases the efficiency of anesthetic effect of botulinum toxin type A drug administration 14 days before the intervention. **Discussion:** These studies results allow us to conclude that a course of electrophysiological treatment with INDIBA, conducted in the first week after aesthetic breast endoprosthetics, significantly increases the effectiveness of the analgesic effect of botulinum toxin. **Conclusion:** Thus, the given results are convincing in terms of the fact that the proposed complex of rehabilitation measures after aesthetic endoprosthetics of mammary glands in the form of parenteral intramuscular administration of botulinum toxin preparation and a course of electrophysiological influence by electromagnetic field has a statistically significant pathogenetically-based pronounced and prolonged analgesic effect in the postoperative period.

Keywords: Silicone implants- preventive rehabilitation- botulinum toxin- INDIBA

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Introduction

The first report of successful breast augmentation appeared in 1895 in which Czerny described transplanting a lipoma from the trunk to the breast in a patient deformed by a partial mastectomy [1]. In 1954, Longacre described a local dermal-fat flap for augmentation of the breast [2]. Eventually, both adipose tissue and omentum were also used to augment the breast.

In 2021-2023 in the Russian Federation performed at least 85,000- 100,000 annually breast endoprosthetics with silicone implants, which corresponded to the 4 place in the world, after the United States, Brazil and Germany, while ten years ago Russia on the number of performed such operations was on the 12th place in the world, taking into account the performed at that time only 25 thousand endprosthetics per year [3, 4].

The majority of plastic surgeon specialists note a distinct tendency to increase the number of breasts endoprosthetic surgeries with silicone implants in the Republic of Uzbekistan - the number of such surgeries now reaches 3-4 thousand annually [5].

Summarized annual data of American Society of Plastic Surgeons (ASPS) shows that from 2013 to 2023, an increase in the number of breast endoprosthetic surgeries from 220.000 to 340.000, i.e. almost one and a half times. It is shown that in the list of aesthetic surgical interventions on the breast, breast augmentation accounts for 45%, reduction mammoplasty 38%, and surgical correction of areolae and nipple shape - in 17% of patients [6, 7].

After aesthetic breast endoprosthetics with silicone implants, the aim of rehabilitation measures is recognized as early labor and social adaptation, improvement of the results of the intervention, and improvement of the quality of life of deconditioned women. The aim of such surgical interventions is recognized as improving the shape, more

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often increasing the volume of glands with possible correction of asymmetry or congenital underdevelopment [8, 9], also among the goals of such surgeries is the formation of more embossed, symmetrical, proportional mammary glands that preserve their essential function with optimal palpatory and sensory components [10, 11].

In order to provide rehabilitation measures in the postoperative period, prevention and management of pain syndrome after breast augmentation with silicone implants, it is advisable to use physical therapy methods. In recent years, for accelerated management of inflammatory tissue changes and pain syndrome in the postoperative period proposed the use of electromagnetic exposure frequency of 448 kHz, which activates ion exchange, resulting in natural regenerative processes in the cells run much more efficiently. Such kind physiotherapeutic devices provide in electrical potential of the cell membrane, improve its permeability, activate collagen production; improve microcirculation and tissue trophicity; have an anti-edema effect, promote hematoma reorganization, as well as stem cell proliferation [12, 13]. These properties seem to be very important for achieving the goals of rehabilitation after breast endoprosthesis and need to be studied.

Materials and Methods

The material for the formation of clinical observation groups was collected in the period 2022-2024 in the plastic surgery department of "Relax Med Servis" clinic, Samarkand, Republic of Uzbekistan. The observation groups included 89 female patients who underwent aesthetic breast endoprosthetics with silicone implants. Two groups who had botulinum toxin injection, another two groups with electromagnetic field with a frequency of 448 kHz.

The first group of clinical observations included 23 women (25.8%) who had undergone breast endoprosthetics with silicone implants, in whom botulinum toxin type A was injected into the musculus pectoralis major 14 days before the intervention to achieve its denervation and prevent pain syndrome after the intervention.

The second group of clinical observations included 24 women (26.9%) who also underwent breast endoprosthesis with silicone implants and who had botulinum toxin type A injected into the musculus pectoralis major 14 days before the intervention to achieve its denervation and prevent pain syndrome after the intervention. In this group, during the period 1-2-3-4-5-6-6-7 days of the postoperative period, the physiotherapeutic effect was additionally carried out with the INDIBA apparatus - electromagnetic field with a frequency of 448 kHz. The third group of clinical observations included 22 women (24.7%) who also underwent breast endoprosthesis with silicone implants and injection of an equivalent volume of placebo - 0.9% sodium chloride solution into the musculus pectoralis major 14 days before the intervention, as well as during the period 1-2-3-4-5-6-7 days of the postoperative period physiotherapeutic influence with INDIBA apparatus - electromagnetic field of 448 kHz frequency.

The fourth group of clinical observations included 20 women (22.4%) who also underwent breast endoprosthesis with silicone implants and injection of an equivalent volume of placebo - 0.9% sodium chloride solution into the musculus pectoralis major 14 days before the intervention. Physiotherapeutic treatment with INDIBA apparatus - electromagnetic field of 448 kHz frequency was not performed due to organizational reasons. The group of clinical observations No.1 was considered to be the control group.

In the postoperative period in patients of the 3rd and 4th groups - 42 observations in total - physiotherapeutic treatment with the INDIBA active 801 apparatus (Spain) was used for accelerated rehabilitation and tissue restoration. It is designed to affect the skin and muscle fibers. It is recommended for working with superficial, abundantly vascularized tissues. The device provides restoration of the electrical potential of the cell membrane; improvement of cell membrane permeability; restoration and maintenance of normal cellular physiology; activation of collagen production; improvement of microcirculation and tissue trophics.

Before surgical breast augmentation with silicone implants, all 89 patients underwent clinical, laboratory and instrumental examination in accordance with the recommended list for such interventions. In order to assess the intensity of pain syndrome intraoperatively (anamnestically) and in the postoperative period on the 1^{st}, 2^{nd}, 3^{rd}, 7^{th}, 14^{th} days, 1, 3 and 6 months after the intervention, we used the Numeric Pain Scale questionnaire proposed by McCaffery M. and Beebe A. in 1993, which allows us to assess the intensity of pain sensations in points from 0 to 10.

The statistical analysis of the obtained results of clinical studies was performed sequentially in three stages according to the algorithm of applying generally accepted methods of variation statistics.

Results

The intensity of pain syndrome in the analyzed subgroups, as well as in the control group of patients within a month after aesthetic breast endoprosthetics with silicone implants is given in Table 1, the data of which allow us to conclude that among the group of women in whom the administration of botulinum toxin type a was combined with a course of electrophysiological treatment, the pain syndrome of mild and moderate degree prevailed already by the end of the first day of the postoperative period - in 76.4% and 11.3% of observations. At the same time in the same period among patients who received only botulinum toxin, the frequency of mild and moderate pain syndrome was 51.7% lower ($p < 0.01$) and 25.4% higher ($p < 0.05$), respectively. In the control group, where botulinum toxin was not administered and there was no electrophysiologic exposure, severe and moderate pain syndrome predominated - in 45.7% and 36.8% of clinical observations.

At the same time, in the same set of clinical observations on the second day after aesthetic breast end prosthetics, in the group of observations where rehabilitation measures included botulinum toxin and electrophysiologic effects, the absence of pain syndrome was found in 11.3% of

Table 1. Dynamics of Pain Syndrome after Breast Augmentation Taking into Account Electrophysiologic Therapy in the Postoperative Period

Term, days	Indiba treatment course	Frequency of pain syndrome detection, %			
		No	Light	Moderate	Distinct
1	Yes, without botulinum toxin	5.8	24.7	36.7	32.8
	Yes, on botulinum toxin	4.6	76.4	11.3	7.7
	No	0	17.5	36.8	45.7
2	Yes, without botulinum toxin	8.9	32.7	39.3	19.1
	Yes, on botulinum toxin	11.3	74.5	11.1	3.1
	No	0	23.8	43.6	32.6
7	Yes, without botulinum toxin	56.3	37.6	6.1	0
	Yes, on botulinum toxin	78.2	21.8	0	0
	No	34.7	38.4	26.9	0
14	Yes, without botulinum toxin	78.5	21.5	0	0
	Yes, on botulinum toxin	89.2	10.8	0	0
	No	61.2	38.8	0	0
30	Yes, without botulinum toxin	85.1	14.9	0	0
	Yes, on botulinum toxin	94.5	5.5	0	0
	No	67.9	32.1	0	0

cases, and pain of mild or moderate intensity - in 74.5% and 11.1% of patients. At the same time in the comparison group, where only botulinum toxin was used, the frequency of mild pain was 41.8% lower ($p < 0.01$) and moderate pain was 28.2% higher ($p < 0.05$). As in the first day, by the end of the second day in the control group, where only placebo and no electrophysiologic influence were used, severe and moderate pain syndromes prevailed in 32.6% and 43.6% of cases, respectively.

One week later, i.e. seven days of the postoperative period, the pain syndrome in the analyzed group of patients whose rehabilitation measures included botulinum toxin injection and the completed course of electrophysiological action was almost completely absent in 78.2% of observations, and the pain of low intensity was detected in 21.8% of cases. At the same time in the group of patients who received only one botulinum toxin before surgery, the absence of pain syndrome was 21.9% less frequent ($p < 0.05$), and in 6.1% of cases there was a pain syndrome of moderate intensity.

By the end of the second and fourth week of the postoperative period in the group of women who received botulinum toxin and electrophysiologic treatment, complete absence of pain syndrome was observed in 89.2% and 94.5% of cases, respectively, which was more, respectively, by 10.7% and 9.1% ($p > 0.05$) than in the same terms in the subgroup of women who received only botulinum toxin. Statistical differences in the frequency and severity of pain syndrome of low intensity in these two subgroups of patients on 14 and 30 days after surgery also reached 10.7% (parameter values 21.5% and 10.8%) and 9.4% (parameter values 14.9% and 5.5%), respectively, but the differences were also statistically insignificant ($p > 0.05$).

The results of the conducted research allow us to conclude that the course of electrophysiological influence by INDIBA preparation, conducted in the first week, daily, i.e. 7 procedures after aesthetic breast endoprosthetics, significantly increases the efficiency of anesthetic effect of botulinum toxin type A drug administration 14 days before the intervention. It was found out that the frequency and severity of mild pain syndrome in this group of patients on the 1st and 2nd day were 51.7% ($p < 0.01$) and 41.8% ($p < 0.01$) less compared to the results of using botulinum toxin alone. In-depth statistical calculation allowed to reveal a strong correlation between the course use of INDIBA electrophysiologic influence after botulinum toxin injection with the severity of pain syndrome on the 1st, 2nd and 7th days of the rehabilitation period after breast endoprosthesis (Table 2).

Discussion

The data obtained show that the administration of botulinum toxin two weeks before surgery was accompanied by a significant pathogenetically based

Table 2. Severity of Pain Syndrome after Aesthetic Breast Endoprosthetics with Regard to Botulinum Toxin Administration and a Course of Electrophysiologic Therapy

Time after surgery, days	Significance, Fisher criterion	Coupling, Kramer coefficient	Link, strength
1	0.00026	$_{0.6}0.69_{0.8}$	Strong
2	0.00062	$_{0.4}0.56_{0.7}$	Strong
7	0.01	$_{0.6}0.76_{0.9}$	Strong

Note: boundaries of 95% confidence intervals for the median are subscripted

analgesic effect early after the intervention and had no relation to the size of the silicone implant used. It was found that in women after botulinum toxin injection on the 1st and 2nd day after the intervention, the dominance of mild pain syndrome was observed in 91.35% of cases ($p < 2.16 \cdot 10\text{-}15$). One week after the intervention in the same group of postoperative patients, pain manifestations were not detected in the overwhelming number of clinical observations - in 100% of cases ($p < 3,16 \cdot 10\text{-}18$). By the end of the second and fourth weeks of the postoperative period among the group of patients in whom botulinum toxin injection was performed, pain sensations and other manifestations of pain syndrome were not detected in 100% of cases ($p = 0.0001$, $p = 0.0001$). At statistical estimation the existence of a very pronounced relation between administration of botulinum toxin A or placebo with the frequency of development and severity of pain syndrome on the 1st ($p = 1,18 \cdot 10\text{-}22$), on the 2nd ($p = 2,11 \cdot 10\text{-}21$), and on the 7th ($p = 3,33 \cdot 10\text{-}21$) day after augmentation is determined.

The pathogenetic-conditioned factor providing anti-inflammatory and analgesic effect and early rehabilitation is the electrophysiological effect of the electromagnetic field of the INDIBA apparatus used by us. It was found that among women in whom botulinum toxin administration was combined with a course of electrophysiologic influence, already by the end of the first day prevailed pain syndrome of mild and moderate degree - in 76.4% and 11.3% of observations. On the second day after aesthetic breast endoprosthetics in the same array of patients the absence of pain syndrome was registered in 11.3% of cases, and pain of mild or moderate intensity - in 74.5% and 11.1% of patients.

One week later, in the analyzed group of patients whose rehabilitation measures included botulinum toxin injection and a course of electrophysiological treatment, pain was almost completely absent in 78.2% of cases, and pain of low intensity was detected in 21.8% of cases. By the end of the second and fourth week of the postoperative period in the subgroup of women who received botulinum toxin and a course of electrophysiologic treatment, complete absence of pain syndrome was observed in 89.2% and 94.5% of cases, respectively.

Since 1962, approximately 1 million to 2.2 million women in the United States and Canada have received silicone breast implants as part of reconstruction following surgery for breast cancer or prophylactic mastectomy or for cosmetic reasons [14, 15]. Silicone breast implants have been linked to a variety of illnesses, the most controversial of which are connective-tissue diseases and symptoms [16, 17].

The results of these studies allow us to conclude that a course of electrophysiological treatment with INDIBA, conducted in the first week after aesthetic breast endoprosthetics, significantly increases the effectiveness of the analgesic effect of botulinum toxin. The frequency and severity of mild pain syndrome in this subgroup of patients on the 1st and 2nd day are 51.7% ($p < 0.01$) and 41.8% ($p < 0.01$) less compared to the results of using botulinum toxin alone. Statistical calculation revealed a strong correlation between the course use of INDIBA electrophysiologic action after botulinum toxin injection with the severity of pain syndrome on the 1st, 2nd and 7th days of the rehabilitation period after breast endoprosthesis ($p = 0.00062$ - 0.01).

In Conclusion, the given results are convincing in terms of the fact that the proposed complex of rehabilitation measures after aesthetic endoprosthetics of mammary glands in the form of parenteral intramuscular administration of botulinum toxin preparation and a course of electrophysiological influence by electromagnetic field has a statistically significant pathogenetically-based pronounced and prolonged analgesic effect in the postoperative period.

Author Contribution Statement

All authors contributed equally in this study.

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