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COMPARISON OF THE EFFECTIVENESS OF BOTULINUM TOXIN A (BoNTA) INJECTION THERAPY AND DEEP BRAIN STIMULATION (DBS) IN CERVICAL DYSTONIA: A META-ANALYSIS

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ABSTRACT

Cervical dystonia is a debilitating movement disorder, and both Deep Brain Stimulation (DBS) and Botulinum Toxin A (BoNTA) are commonly used treatments. However, their comparative effectiveness remains unclear. This study aims to evaluate the effectiveness of DBS versus BoNTA in improving TWSTRS scores and to explore factors influencing treatment outcomes. A meta-analysis was conducted, including subgroup analyses and meta-regression to assess the efficacy of both treatments across various demographics and study designs. The results indicate that DBS significantly improves TWSTRS scores by an average of 54.48% (95% CI 45.01–63.95), compared to BoNTA's 28.96% (95% CI 24.12–33.80). High heterogeneity was noted, but no significant differences were found across intervention types or patient demographics. These findings suggest that DBS is a more effective treatment for cervical dystonia than BoNTA, regardless of patient age or follow-up duration. Future research should investigate the mechanisms behind these differences to optimize treatment strategies.

KEYWORDS *Cervical Dystonia, BoNTA, Deep Brain Stimulation (DBS)*

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INTRODUCTION

Dystonia was first introduced by Oppenheim in 1911. Dystonia is a movement disorder characterized by continuous or intermittent muscle contractions, resulting in abnormal and often repetitive movements, postures, or both (Albanese et al., 2019; Raisa, 2024). Dystonia is a syndrome with diverse causes, anatomical distributions, and heterogeneous clinical manifestations that lead to varying degrees of disability. Initially considered a basal ganglia disorder, the

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pathophysiology of dystonia has been found to involve circuits between the cortex, basal ganglia, cerebellum, and spinal cord (Albanese et al., 2019).

Based on body distribution, dystonia is classified into focal, segmental, multifocal, generalized, and hemidystonia types. Identifying the affected body part is crucial in assessing dystonia (Raisa, 2024; Albanese et al., 2019). Cervical dystonia is the most common type and represents a focal form of dystonia. It is localized to the neck and surrounding muscles. The incidence of cervical dystonia in the United States is 1.18 per 100,000 population, predominantly affecting women, with a peak incidence in the fifth decade of life (Raisa, 2024). Currently, no prevalence data for cervical dystonia are available in Indonesia.

Cervical dystonia impacts not only physical health but also mental and social aspects, affecting daily activities, health conditions, and patient care. Social factors, such as stigma, insecurity, isolation, and abnormal postural changes, contribute to the development of depressive symptoms. Non-motor symptoms like pain, sleep disturbances, depression, and anxiety exacerbate motor symptoms.

The management of cervical dystonia is symptomatic, aimed at improving posture, functionality, and pain relief. Despite limited understanding of the etiology and pathophysiology of dystonia, symptom treatment has improved, especially since the introduction of botulinum toxin (BoNT).

BoNT injections are the primary therapy or gold standard for cervical dystonia. Periodic injections into multiple affected muscle sites every 3 to 6 months remain the most effective treatment. Four main BoNT products are commercially available worldwide, derived from the Clostridium botulinum strain: onabotulinum toxin A (Ona-BoNTA), abobotulinum toxin A (Abo-BoNTA), incobotulinum toxin A (Inco-BoNTA), and rimabotulinum toxin B (Rima-BoNTB). Abo-BoNTA and Rima-BoNTB are classified as Level A treatments in the American Academy of Neurology (AAN) clinical practice guidelines for cervical dystonia. Rima-BoNTB is sometimes chosen for patients who respond poorly to BoNTA, although it carries risks of side effects such as dry mouth and dysphagia.

Meta-analysis results indicate that BoNTA therapy provides significant clinical improvement for cervical dystonia patients, with an average reduction of 8.09 points on the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) compared to placebo four weeks post-injection. However, the therapy increases the risk of side effects, including dysphagia (11%), neck weakness (14%), and generalized fatigue (8%).

For cervical dystonia patients with suboptimal responses to BoNTA injections, Deep Brain Stimulation (DBS) is an effective second-line treatment. DBS typically targets the globus pallidus internus (GPi), a brain region controlling muscle movement, and significantly reduces dystonia severity while improving quality of life. DBS outcomes include a 50-70% reduction in symptoms after months or years post-implantation, with some cases showing sustained benefits for over a decade. However, DBS is not without risks; some patients experience mild neuropsychological changes without significant impacts on daily life.

Tsuboi et al. (2020) 's meta-analysis of cervical dystonia patients undergoing DBS in the GPi or STN regions revealed significant improvements in motor symptoms, disability, and pain. Average reductions in TWSTRS scores for total,

severity, disability, and pain categories were 58.8%, 53.9%, 61.3%, and 46.6%, respectively, approximately 23.3 months post-DBS implantation. While no significant differences were found between GPi and STN targets in effectiveness, each demonstrated unique side effect profiles.

Current studies assess BoNTA and DBS effectiveness separately, without direct comparison, even though BoNTA is the first-line therapy, and DBS is reserved for refractory cases. Long-term data on BoNTA's effectiveness with repeated injections remain limited, leaving its comparison with DBS in terms of clinical outcomes and patient quality of life unclear.

This study aims to evaluate and compare the effectiveness of BoNTA and DBS in reducing symptoms of cervical dystonia, using a meta-analysis approach. By analyzing TWSTRS scores, the research seeks to determine which therapy provides the most optimal patient outcomes. The research addresses three key questions: BoNTA's effectiveness, DBS's effectiveness, and potential differences in their therapeutic impacts. The study's contributions span multiple domains. Education enhances the understanding of cervical dystonia and the application of BoNTA and DBS therapies, laying the groundwork for future research. In public service, it provides valuable insights to healthcare facilities for selecting appropriate treatment strategies to improve the quality of life for patients. Lastly, in research, it serves as a reference for identifying effective interventions that lead to better outcomes in managing cervical dystonia.

The current research presents several novel aspects compared to previous studies on the effectiveness of Deep Brain Stimulation (DBS) and Botulinum Toxin A (BoNTA) in treating cervical dystonia. Firstly, it quantitatively demonstrates a significant difference in average improvement in TWSTRS scores between DBS and BoNTA, with DBS showing a greater efficacy (54.48% vs. 28.96%) and providing robust statistical evidence through meta-regression analysis. Secondly, the study addresses the high heterogeneity observed in previous research by conducting subgroup analyses, revealing that the effectiveness of both treatments is consistent across various intervention types and study designs. Additionally, the investigation into patient age and follow-up duration as predictors of treatment outcomes adds a new dimension to understanding treatment efficacy, indicating that these factors do not significantly influence results. This research lays the groundwork for future studies to explore the underlying mechanisms of treatment efficacy, which has not been extensively covered in prior literature.

RESEARCH METHOD

The research design is a systematic review and meta-analysis with an observational approach, focusing on the effectiveness of BoNTA injections and DBS in cervical dystonia. A systematic review involves systematically examining, evaluating, classifying, and categorizing findings from previous primary studies. Meta-analysis is an analytical method that combines primary data extracted in alignment with similar research objectives and hypotheses, resulting in new evidence-based conclusions. The study was conducted from October to December 2024.

RESULT AND DISCUSSION

Meta-Analysis of TWSTRS Score Improvement Based on Intervention Type

1. DBS

This forest plot presents the results of a meta-analysis of several studies on the use of DBS for cervical dystonia. Each study provides an estimated average improvement in TWSTRS scores along with 95% confidence intervals (95% CI) (Figure 16).

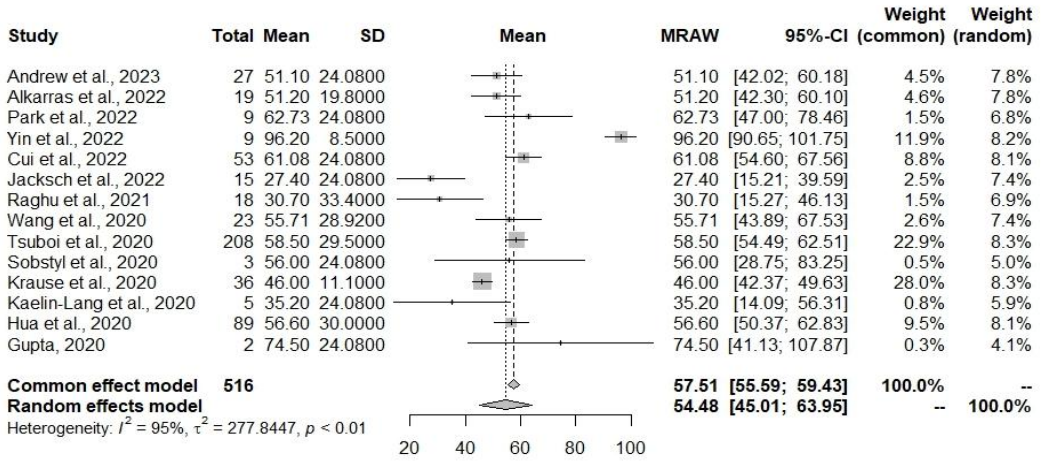

Figure 1. Meta-Analysis Results of Studies on DBS for Cervical Dystonia

Each row represents a study included in the analysis. The box size in each row reflects the study's weight in the random-effects model, with larger weights assigned to studies with larger sample sizes and lower variability. Studies such as Tsuboi et al. (2020) and Krause et al. (2020) carry greater weight due to their larger sample sizes, contributing more significantly to the overall estimate. Conversely, studies with smaller sample sizes, such as Kaelin-Lang et al. (2020) and Gupta (2020), carry smaller weights.

The estimated average TWSTRS score improvements varied across studies, with Yin et al. (2022) reporting the most significant improvement at approximately 96.2% (CI 90.65–101.75), while Kaelin-Lang et al. (2020) reported a smaller improvement of around 35.2% (CI 14.09–56.31). Overall, the fixed-effects model indicated an average TWSTRS score improvement of 57.51% (95% CI 55.59–59.43), while the random-effects model showed an average of 54.48% (95% CI 45.01–63.95), reflecting variability between studies.

a. Subgroup Analysis Based on Intervention Type

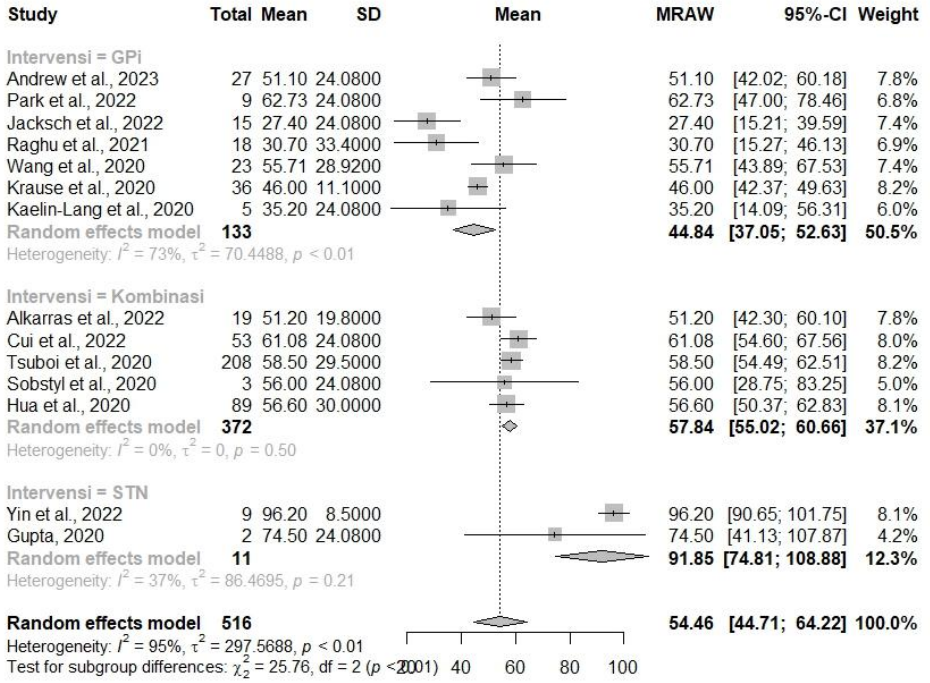

Figure 2 Forest Plot of Meta-Analysis Comparing Effects of Three Intervention Groups

Figure 2 illustrates the meta-analysis results for three types of interventions: GPi, Combination, and STN, analyzed using a random-effects model. GPi Interventions: Six studies with a total sample of 133 participants yielded a combined mean effect of 44.84 (95% CI: 37.05–52.63) with high heterogeneity (I^2 = 73%, p < 0.01), indicating significant variation between studies. Combination Interventions: Five studies with a total sample of 372 participants showed a combined mean effect of 57.84 (95% CI: 55.02–60.66) with no heterogeneity (I^2 = 0%, p = 0.50), suggesting consistent results. STN Interventions: Two studies with a small total sample (11 participants) produced the highest combined mean effect of 91.85 (95% CI: 74.81–108.88) with moderate heterogeneity (I^2 = 37%, p = 0.21).

b. Subgroup Analysis Based on Study Design

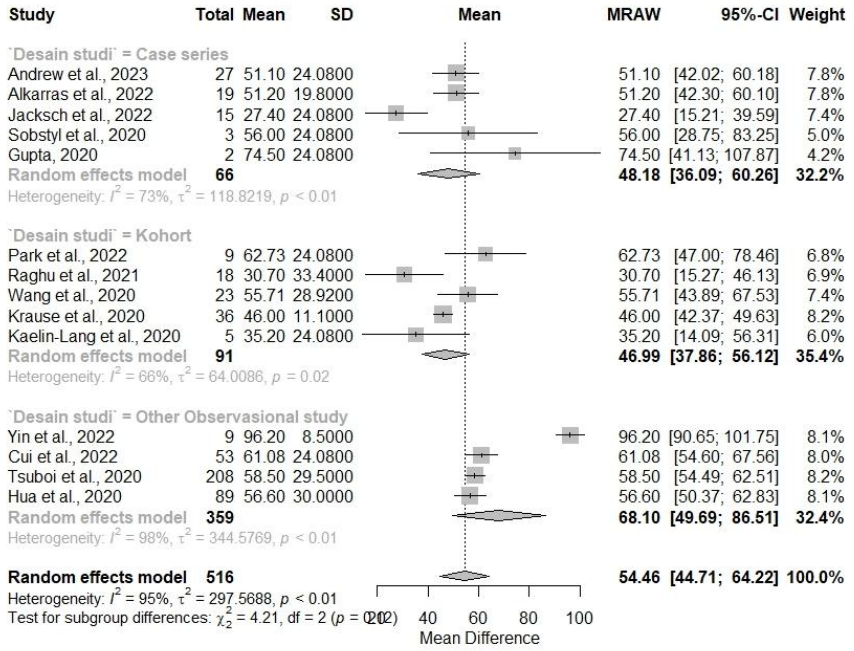

Figure 3. Forest Plot of Meta-Analysis Comparing Effects of Three Study Designs

Figure 3 represents the meta-analysis results based on different study designs, detailing the variability and outcomes across methodological approaches. Figure 3 is a forest plot from the meta-analysis comparing the effects of three study designs: Case Series, Cohort, and Other Observational Studies. The meta-analysis results indicate combined effect sizes for each subgroup: 48.18 [36.09; 60.26] for Case Series, 46.99 [37.86; 56.12] for Cohort, and 68.10 [49.69; 86.51] for Other Observational Studies. All three subgroups exhibited high levels of heterogeneity, particularly in the Other Observational Studies group (I^2 = 98%), indicating significant variation among studies within this group. A test for differences between subgroups yielded non-significant results (p = 0.12), suggesting no significant differences in effects among the three study designs.

2. BoNTA

This forest plot illustrates the meta-analysis results of several studies on the effects of BoNTA in cervical dystonia, measured as a percentage improvement in TWSTRS scores with 95% confidence intervals (95% CI) (Figure 4).

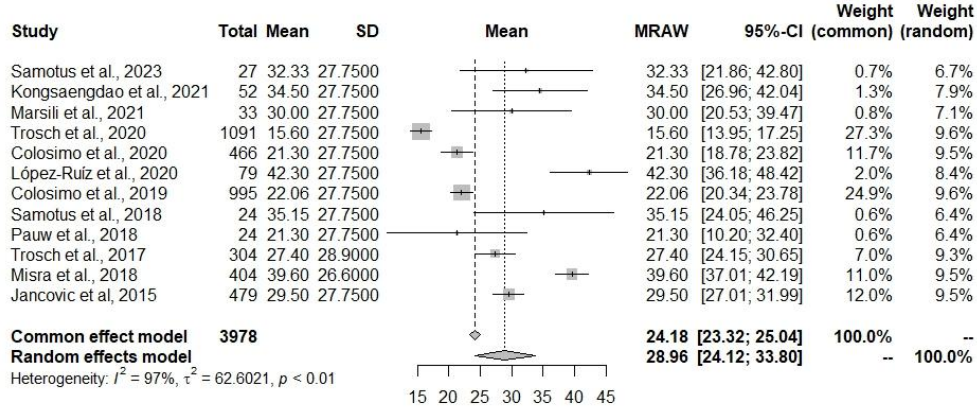

Figure 4. Meta-Analysis Results of Studies on the Effects of BoNTA in Cervical Dystonia

Each row represents a study included in the analysis. The box size in each row reflects the study's weight in the random-effects model, with larger weights assigned to studies with larger sample sizes and lower variability. Studies such as Trosch et al. (2020) and Colosimo et al. (2019) contributed significantly to the overall estimate due to their large sample sizes. Conversely, smaller studies like Samotus et al. (2018) and De Pauw et al. (2018) carried smaller weights.

The average improvement in TWSTRS scores varied across studies. For example, Samotus et al. (2023) reported a 32.33% improvement (CI 21.86–42.80), while Trosch et al. (2020) reported a lower improvement of 15.60% (CI 13.95–17.25). The overall average improvement in TWSTRS scores for the fixed-effects model was 24.18% (95% CI 23.32–25.04), while the random-effects model showed an average of 28.96% (95% CI 24.12–33.80), accounting for variability between studies.

This forest plot indicates very high heterogeneity among the studies, with I^2 = 97% and $p < 0.01$, suggesting that most of the variability in study outcomes may be attributed to differences in methodology, population characteristics, or variations in the implementation of BoNTA interventions in cervical dystonia patients.

a. Subgroup Analysis Based on Intervention Type

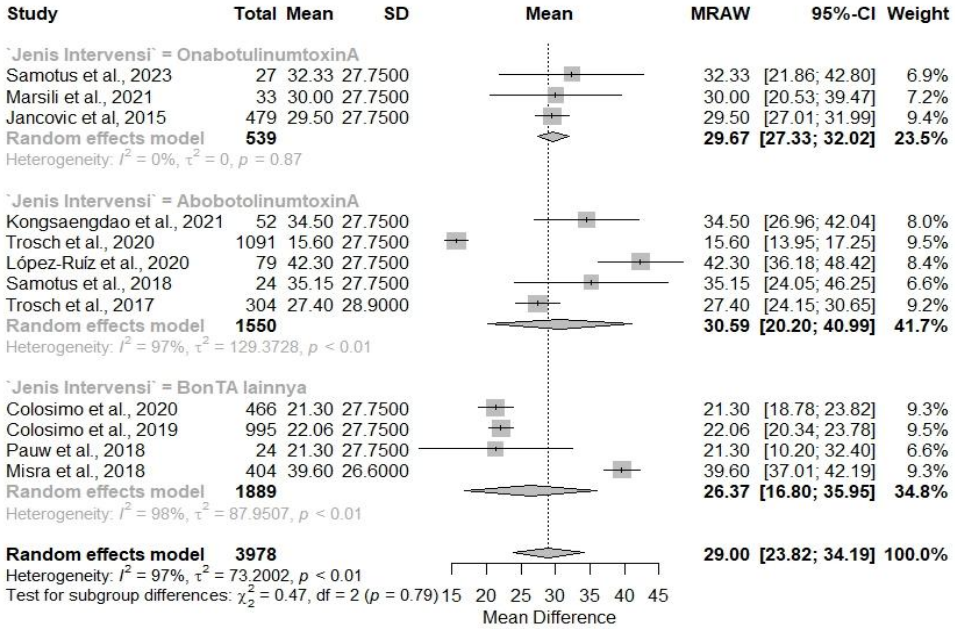

Figure 5. Forest Plot from Meta-Analysis Comparing the Effects of Three Types of Botulinum Toxin Interventions

Figure 5 is a forest plot from the meta-analysis comparing the effects of three types of BoNTA interventions: Ona-BoNTA, Abo-BoNTA, and other BoNTA types. The meta-analysis results show the combined effect sizes (Mean Difference) for each subgroup: Ona-BoNTA at 29.67 [27.33; 32.02] with low heterogeneity (I^2 = 0%, p = 0.87); Abo-BoNTA at 30.59 [20.20; 40.99] with high heterogeneity (I^2 = 97%, p < 0.01), indicating significant variation among studies; and other BoNTA types at 26.37 [16.80; 35.95] with similarly high heterogeneity (I^2 = 98%, p < 0.01). A subgroup difference test (p = 0.79) revealed no significant effect differences among the three intervention types.

b. Subgroup Analysis Based on Study Design

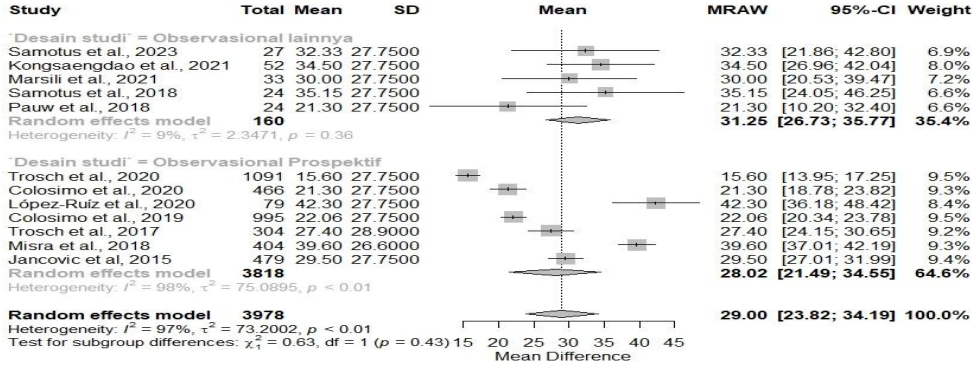

Figure 6. Forest Plot from Meta-Analysis Comparing Effects Based on Two Study Designs

Figure 6 presents a forest plot from the meta-analysis comparing effects based on two study designs: Other Observational and Prospective Observational Studies. The combined effect size (Mean Difference) for Other Observational Studies was 31.25 [26.73; 35.77] with low heterogeneity ($I^2 = 9\%$, $p = 0.36$), indicating minimal variation among studies in this group. Meanwhile, Prospective Observational Studies had a combined effect size of 28.02 [21.49; 34.55] with very high heterogeneity ($I^2 = 98\%$, $p < 0.01$), reflecting substantial variation among studies. A subgroup difference test ($p = 0.43$) indicated no significant effect differences between the two study designs.

Meta-Regression: Relationship Between Intervention Type and TWSTRS Score Improvement

1. Univariate Analysis

Table 20 shows the univariate meta-regression analysis examining the relationship between intervention type and TWSTRS score improvement. The intercept (baseline value) had a coefficient estimate of 3.61 with a standard error (SE) of 8.59, a z-value of 0.42, and a p-value of 0.674, indicating statistical insignificance. The 95% confidence interval for the intercept ranged from -13.22 to 20.45, covering zero, further supporting its insignificance.

Table 1. Univariate Meta-Regression: Relationship Between Intervention Type and TWSTRS Score Improvement

Variable	Coefficient estimation	Standard error (SE)	Z-value	Value p	Confidence intervals
Intercept (intrcpt)	3.61	8.59	0.42	0.674	-13.22:20.45
Types of Interventions (DBS)	24.53	5.44	4.69	<0.001	14.85:36.20

For the intervention type variable (DBS), the coefficient estimate was 24.53 with an SE of 5.44, a z-value of 4.69, and a p-value of <0.001, indicating a statistically significant relationship between DBS and TWSTRS score improvement. The 95% confidence interval for DBS was 14.85 to 36.20, demonstrating consistent and significant score improvements with this intervention.

2. Multivariate Analysis

Table 21 presents the multivariate meta-regression analysis evaluating the relationships among intervention type, average patient age, and follow-up duration with TWSTRS score improvement. The intercept had a coefficient estimate of 46.32 with an SE of 20.86, a z-value of 2.22, and a p-value of 0.026, indicating statistical significance. The 95% confidence interval for the intercept ranged from 5.43 to 87.21, suggesting that TWSTRS score improvement lies within this range when all other variables are zero.

Table 2. Multivariate Meta-Regression: Relationship Between Intervention Type and TWSTRS Score Improvement

Variable	Coefficient estimation	Standard error (SE)	Z-value	Value p	Confidence intervals
Intercept (intrcpt)	46.32	20.86	2.22	0.026	5.43:87.21
Jenis Intervensi (DBS)	22.51	6.32	3.56	<0.001	10.12:34.90
Average age of patients (years)	-0.33	0.37	-0.90	0.369	-01.06:0.39
Duration of follow-up (months)	0.08	0.17	0.47	0.604	-0.24:0.42

For the intervention type variable (DBS), the coefficient estimate was 22.51 with an SE of 6.32, a z-value of 3.56, and a p-value of <0.001, indicating a significant relationship between DBS and TWSTRS score improvement. The 95% confidence interval for DBS was 10.12 to 34.90, confirming its consistent contribution to score improvement.

The average patient age had a coefficient estimate of -0.33 with an SE of 0.37, a z-value of -0.90, and a p-value of 0.369, indicating no statistically significant relationship between age and TWSTRS score improvement. The 95% confidence interval for age ranged from -1.06 to 0.39, showing no meaningful impact on scores.

The follow-up duration had a coefficient estimate of 0.08 with an SE of 0.17, a z-value of 0.47, and a p-value of 0.604, indicating no statistically significant relationship. The 95% confidence interval for follow-up duration ranged from -0.24 to 0.42, suggesting no significant influence on TWSTRS score improvement.

Assessment of Publication Bias Risk

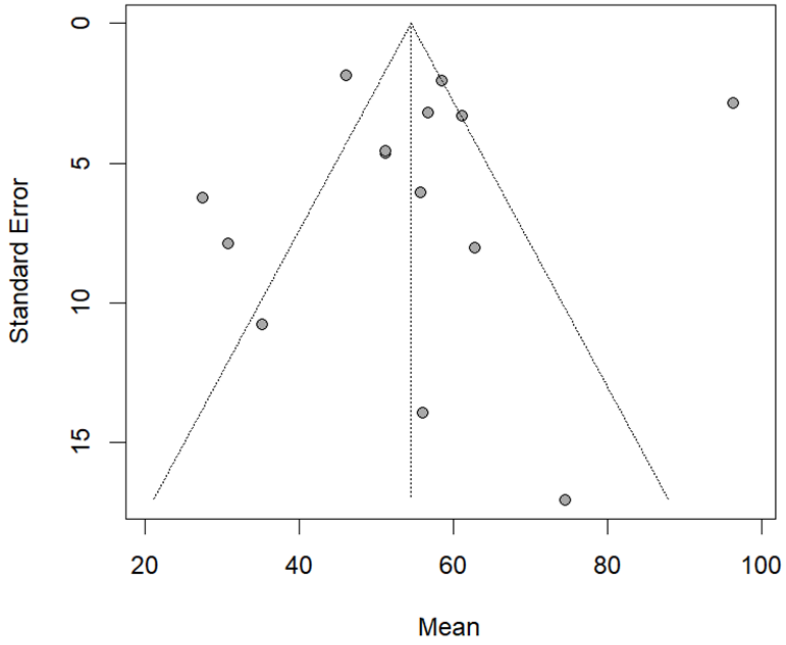

Figure 7. Funnel Plot of DBS Studies

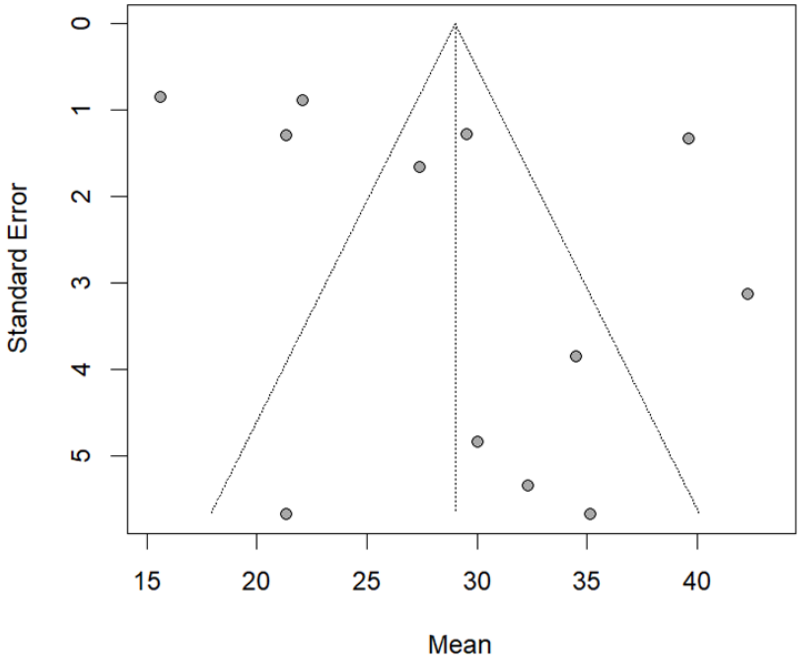

Figure 8. Funnel Plot of BoNTA Studies

Figures 7 and 8 display funnel plots from the meta-analysis of DBS and BoNTA studies, with the mean effect size on the horizontal axis and the standard error on the vertical axis. Each dot represents an individual study included in the meta-analysis. Funnel plots assess publication bias, typically evident when the dots

are asymmetrically distributed around the vertical line (representing the average effect).

For DBS studies, Egger's test for asymmetry in the funnel plot resulted in t = 1.62, df = 10, and p-value = 0.1365. Since the p-value is greater than 0.05, the results are not statistically significant, suggesting no strong evidence of asymmetry in the funnel plot and a low likelihood of publication bias in this meta-analysis. The bias estimate (4.2768) indicates a small effect size for asymmetry, but it is not statistically significant to be considered publication bias. Residual heterogeneity variance (tau^2) was 25.4284, indicating considerable variability among studies, although this variation was not significantly correlated with study size according to Egger's test.

For BoNTA studies, Egger's test for asymmetry in the funnel plot yielded t = -0.33, df = 12, and p-value = 0.7436. The high p-value (above 0.05) suggests no statistically significant evidence of asymmetry in the plot, indicating a low likelihood of publication bias in this meta-analysis. The bias estimate (-0.7963) was also relatively small.

Discussion

General Effectiveness of DBS and BoNTA Interventions for Cervical Dystonia

The meta-analysis results demonstrate that DBS and BoNTA effectively improve TWSTRS scores, which measure the severity of cervical dystonia symptoms. Based on a random-effects model, the average improvement in TWSTRS scores for the DBS group was 54.48% (95% CI 45.01–63.95%). While this range indicates considerable variability among studies, the overall effect remains positive. In contrast, the BoNTA group showed a lower average TWSTRS score improvement of 28.96% (95% CI 24.12–33.80%), also reflecting variability but with consistently positive outcomes.

Studies involving DBS, such as Andrew et al. (2023) and Park et al. (2022), reported significant TWSTRS score improvements of approximately 51.10% and 62.73%, respectively. Yin et al. (2022) observed the highest improvement among DBS studies, at 96.2%, indicating DBS's success in reducing symptoms, particularly when targeting specific brain regions like the GPi. However, other DBS studies, such as Jacksch et al. (2022) and Raghu et al. (2021), reported lower improvements (27.4% and 30.7%, respectively), possibly due to variations in stimulation techniques, target locations, or patient characteristics.

BoNTA studies, such as those by Samotus et al. (2023) and Kongsaengdao et al. (2021), reported TWSTRS score improvements of approximately 32.33% and 34.5%, demonstrating BoNTA's effectiveness, albeit with generally lower effects compared to DBS. Trosch et al. (2020), involving a large sample of 1,091 patients, reported only a 15.6% improvement, while López-Ruíz et al. (2020) observed a higher improvement of 42.3%. These differences may result from variations in dosage, injection techniques, or targeted muscle areas, affecting BoNTA's efficacy for cervical dystonia patients.

Comparison of Effectiveness Between DBS and BoNTA

Univariate meta-regression results show a significant association between DBS intervention and TWSTRS score improvement compared to BoNTA. The coefficient estimate for DBS was 22.51, indicating that patients receiving DBS experienced an average TWSTRS score improvement of 22.51 points higher than those receiving BoNTA. This value is statistically significant (p-value < 0.001), suggesting that this difference is unlikely due to chance. The 95% confidence interval for the DBS coefficient (10.12 to 34.90) further supports the conclusion that DBS provides greater benefits in improving TWSTRS scores than BoNTA.

Subgroup analysis showed no significant differences in effects between DBS and BoNTA based on intervention type, toxin type, or study design. However, high heterogeneity in some subgroups (e.g., Prospective Observational designs and non-Ona-BoNTA toxin types) highlights significant study variations, potentially due to methodological differences, sample populations, or uncontrolled factors. These findings warrant cautious interpretation, especially for subgroups with high heterogeneity.

The differences in effectiveness between DBS and BoNTA for dystonia, particularly cervical dystonia, stem from their distinct mechanisms of action. DBS stimulates specific brain areas involved in motor regulation, such as the GPi or STN. This stimulation reorganizes disrupted motor circuits, allowing for better long-term symptom control. Studies show that GPi-targeted DBS can reduce motor symptoms by up to 60%, particularly for hereditary dystonia, with improvements lasting several years. For example, Chen et al. (2021) reported significant motor symptom improvement in complex dystonia cases treated with DBS.

In contrast, BoNTA inhibits neuromuscular transmission in spasmodic muscles, temporarily relaxing them. BoNTA is highly effective for focal or segmental dystonia, where symptoms are localized. However, its effects are temporary and require repeated injections every few months. Research by Odorfer & Volkmann (2023) demonstrated BoNTA's efficacy in managing localized dystonia symptoms, but the limited duration of its effects makes it less ideal for widespread or complex symptoms. For patients no longer responding to BoNTA, DBS is often considered a subsequent option due to its more stable long-term outcomes for complex and widespread symptoms.

While DBS offers greater long-term benefits, it is more invasive than BoNTA and carries risks such as infections and device-related complications. Therefore, DBS should be carefully considered, taking into account patient conditions and their readiness for a complex procedure. As noted by Rodrigues et al. (2019), patient acceptance of DBS for dystonia is influenced by procedural risks and the need for comprehensive preoperative evaluations. Overall, DBS is generally more effective for complex and generalized dystonia, while BoNTA is better suited for managing localized symptoms. Treatment decisions should be tailored to clinical conditions and patient preferences.

Influence of Patient Age and Follow-Up Duration

The univariate meta-regression results indicate that the average patient age and follow-up duration do not significantly impact TWSTRS score improvement in

cervical dystonia interventions using DBS and BoNTA. The coefficient estimate for age was -0.33, suggesting a slight negative trend where increasing age might be associated with a minor decrease in TWSTRS scores. However, this value was not statistically significant ($p = 0.369$), and the 95% confidence interval (-1.06 to 0.39) included zero, indicating that this relationship is likely coincidental rather than a true effect. Similarly, the coefficient estimate for follow-up duration was 0.08, suggesting a trend of increased TWSTRS scores over time. However, like age, this value was insignificant ($p = 0.604$), and the confidence interval (- -0.24 to 0.42) also included zero, indicating no meaningful influence.

The insignificance of age and follow-up duration suggests that the effectiveness of DBS and BoNTA in improving cervical dystonia symptoms is relatively consistent across different age groups and follow-up durations. These findings have important clinical implications, indicating that both interventions can be applied to patients of various ages without reduced effectiveness in older age groups. Furthermore, the stability of TWSTRS score improvements across different follow-up periods allows for greater flexibility in clinical monitoring schedules, as treatment outcomes remain stable regardless of follow-up duration.

Heterogeneity and Variability of Results

The high levels of heterogeneity observed in the meta-analysis results, with I^2 values of 95% for DBS and 97% for BoNTA, suggest that most of the variability among study results is not due to random fluctuations but rather to methodological differences and population characteristics in each study. This high heterogeneity indicates that individual study outcomes may be influenced by various factors, making it difficult to generalize findings comprehensively.

Potential contributors to heterogeneity include differences in DBS or BoNTA techniques, BoNTA dosages, DBS stimulation sites (e.g., globus pallidus internus or subthalamic nucleus), and patient characteristics such as dystonia severity, disease duration, or comorbidities. Additionally, differences in study design may play a significant role in heterogeneity. For example, some studies may use observational designs with smaller sample sizes and less representative sampling methods, while others employ more rigorous designs with larger samples and more reliable outcome measures. Other factors, such as variations in follow-up duration, TWSTRS scoring methods, and the presence or absence of blinding in outcome assessments, may also contribute to significant result variability.

This high heterogeneity warrants cautious interpretation of the meta-analysis results. While the analysis provides an overall picture of DBS and BoNTA effectiveness, it may not yield highly specific conclusions applicable to the cervical dystonia patient population. These findings highlight the need for further research with standardized protocols or randomized controlled trials to reduce heterogeneity and provide more definitive evidence on the effectiveness of DBS and BoNTA.

Clinical Implications

The findings of this meta-analysis have significant clinical implications, particularly in selecting interventions for cervical dystonia treatment. The analysis indicates that DBS tends to produce more substantial improvements in TWSTRS

scores compared to BoNTA, suggesting that DBS may be a more effective treatment option in cases where cervical dystonia symptoms are severe or unresponsive to BoNTA. However, it is important to note that DBS is a more invasive procedure, involving brain surgery and electrode implantation, which requires intensive postoperative monitoring and carries potential risks such as infection, bleeding, or device-related issues. Therefore, despite its higher effectiveness, DBS should be carefully considered based on the patient's physical condition and preferences.

On the other hand, BoNTA, while slightly less effective, is a simpler, non-invasive procedure that can be administered on an outpatient basis. BoNTA may be more suitable for patients with mild to moderate cervical dystonia or those who are unwilling or unsuitable for surgical procedures. BoNTA works by inhibiting neuromuscular transmission in spasmodic muscles, providing localized relief of symptoms, though its effects are temporary and require repeated injections every few months to maintain results.

Strengths and Limitations of the Study

This study has several strengths, including comprehensive literature coverage and meta-analysis, which integrates data from multiple studies to provide a robust overview of DBS and BoNTA effectiveness in cervical dystonia. Additionally, the meta-regression analysis offers insights into variability based on factors such as intervention type, age, and follow-up duration. Another strength is the selection of recent studies from the past 10 years, ensuring relevance and up-to-date data in evaluating the effectiveness of these interventions.

However, the study also has limitations. First, the high heterogeneity among studies may affect the reliability of results and make it challenging to generalize findings. This variability could be attributed to differences in BoNTA types, dosages, injection sites, methods, or patient characteristics. Some studies employed blind injection techniques, while others used EMG or ultrasound guidance, which could influence outcomes. The lack of consistent protocols in dosage and administration techniques also adds to the variability, making direct comparisons between studies difficult. Most studies analyzed were observational, which carries a higher risk of selection bias and confounding, increasing heterogeneity among studies.

CONCLUSION

The study concludes that both Deep Brain Stimulation (DBS) and Botulinum Toxin A (BoNTA) effectively improve TWSTRS scores in cervical dystonia, with DBS demonstrating a greater average improvement of 54.48% compared to BoNTA's 28.96%, despite high heterogeneity in results. Subgroup analyses showed no significant differences in effectiveness across various intervention types or study designs, and meta-regression confirmed DBS's superior efficacy. Factors such as patient age and follow-up duration did not significantly predict treatment outcomes, indicating consistent effectiveness across diverse groups. Future research should focus on understanding the mechanisms behind the differential efficacy of DBS and BoNTA, including neurophysiological changes, biomarker identification, long-

term effects, psychosocial factors, comparative effectiveness, and cost-effectiveness analyses to optimize treatment strategies for cervical dystonia.

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