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Low Dose Oxybutin in Primary Hyperhydrosis: A Prospective Study from a Tertiary Care Center in Nepal

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Abstract

Introduction: Hyperhydrosis is a clinical condition where there is excessive sweating beyond the physiological need of the patient's body.This can directly or indirectly affect the quality of patients life.Oxybutin is widely used in urology as anticholinergic medication for bladder urge incontinence.It can be used safely at a high dose (over 15 mg/day) to treat urological disorder. It also acts against excessive sweating and can be used in cases of hyperhidrosis.

Objectives: To evaluate effectiveness of oxybutin at low dose and to assess the Hyperhidrosis Disease SeverityScale (HDSS).

Materials and Methods: This is a hospital based cross-sectional study in primary hyperhydrosis. Oxybutin was prescribed to all patients of primary hyperhydrosis with gradual increment of dosage of 2.5 mg orally once a day to 5 mg twice a day. Patients were evaluatedat zero wk (baseline), 4wk, 8 wk, 12 wk and follow-up in 16 wks with Hyperhidrosis Disease Severity Scale (HDSS) along with adverse effects were noted.

Results: There wasa significant difference in HDSS at zero wk(baseline) and 4thwk(p=0.001) at a dose of 2.5 mg once a day of oxybutynin. Also, a significant difference was noted (p=0.022) in HDSS between zero wk(baseline) and 12 wk. Similarly,a significant difference between HDSS at zero wk(baseline) versus the 16th wk was also noted.

Conclusion: Oxybutin is an anticholinergic drug with an emerging role in hyperhydrosis. Low doses have shown significant results with minimal side effects. The dose requirement varies among authors. Studies with long-term follow-ups with ideal protocol need to be established in the future.

Keywords: Anti-cholinergic; Hyperhydrosis; Scoring system; Oxybutin

Introduction

Hyperhydrosis is a clinical condition where there is excessive sweating beyond the physiological need of the patient's body.[1] This can directly or indirectly affect the quality of a patient's life.[2] Clinically hyperhydrosis is divided into two types primary (idiopathic) and secondary to any medication or disease like hyperthyroidism, hyperpituitarism, diabetes mellitus, neurological disease, sympathetic dystrophy.[1]

Primary hyperhydrosis is characterized by symmetrical involvement with a frequency of at least once a week and develops during childhood before the age of twenty-five. It tends to persist throughout adult life.[3] The main affected areas are the palms, soles, face, and axilla.

The etiology of primary hyperhydrosis is fully not known, and has been attributed to increased cholinergic stimulation, as there is no hypertrophy or hyperplasia of sweat gland.[3] Family history has been reported, supporting a genetic basis.[4]

According to the Canadian Hyperhidrosis Advisory Committee, the criteria for primary hyperhydrosis are:[5]

1. Excessive sweating of 6 months or more in duration
2. Primarily involving eccrine-dense sites (axillae/palms/soles/craniofacial sites)
3. Bilateral and symmetric
4. Absent nocturnally
5. Episodes at least weekly
6. Onset at the age of 25 years or younger; a positive family history, and impairment of daily activities

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There are various treatment modalities including topical therapy iontophiresis, oral medication(α-adernergic blockers),surgical treatment like video assisted thoracic sympathectomy(VATS). Surgical treatment can lead to complication like compensatory hyperhydrosis.[6]

Oxybutin is widely used in urology as an anticholinergic medication for bladder urge incontinence.[6] Sweat gland are stimulated by acetylcholine; thus the anticholonergic effect of oxybutin is responsible against excessive sweating. It can be used safely at a high dose (over 15 mg/day) to treat the urological disorder.[7] The objectives of our study was to evaluate the effectiveness of oxybutynin in hyperhidrosis and evaluate patient satisfaction using the Hyperhydrosis Disease Severity Scale (HDSS) with the use of oxybutin at lower doses.

Materials and Methods

This is a hospital based cross-sectional study conducted in the Department of Dermatology, Venereology, and Leprology in Kathmandu Medical College Teaching Hospital in Kathmandu. The proposal was first submitted to Ethical Review Board and ethical clearance was taken. Patients clinically presenting with the feature of primary hyperhydrosis in dermatology OPD, fulfilling the inclusion criteria,with individual consent to participate in this study were enrolled. All primary hyperhydrosis patients were examined and diagnosed by qualified registered dermatologists and werefurther investigated by Iodine-starch test. The study was conducted from December 2020 to December 2021.The non-probability convenience sampling technique was applied and data was collected on printed proforma, then analyzed using Microsoft excel 2016 and SPSS Version 20.0.

Oxybutin was prescribed to all patients of primary hyperhydrosis with a gradual increment of dosage starting at 2.5 mg orally once a day for four weekswith gradual increment to 2.5 mg twice in a day for next four weeks and again increasing the doseto 5 mg twice a day for next four weeks. Patients were evaluated every four weekly using the HDSS startingfrom zero wk (baseline) up to 16 wks along with the recording of adverse effects.

The Hyperhidrosis Disease Severity Scale (HDSS) was chosen to assess the disease severity, according to the Canadian Hyperhidrosis Advisory Committee.5 HDSS consist of simple and straight forward questionnaire with a 4 point scale on which the patients rate the tolerability of their hyperhidrosis symptoms and the degree of interference with their activities. A score of 3 or 4 indicates severe hyperhidrosis, and a score of 1 or 2 indicate moderate hyperhidrosis. HDSS was analyzed by ANOVA.

HDSS was evaluated prior to treatment with oxybutin and then every four weeks for sixteen weeks.Moreover, the extension of hyperhidrotic area was assessed by the iodine starch test (Figure 1), in which an iodine solution was spread on the area of skin to be tested. After the solution dries, thestarch powder was applied. Sweat production then caused the mixture to turn dark blue, identifying the exact location of sweating.

Results

In our study 46 patients of primary hyperhydrosis were enrolled. The mean age of patients was 23± 5.7, with male 31(67.4%) predominant.In our study 23(50%) had education of bachelor level followed by higher secondary level 15(32.6%). Regarding ethinicity, almost 25(54.3%) were Bharmin followed by Chhetri 16(34.8%). Out of 46 patients, 28(60.9%) had a positive family history of hyperhidrosis. The mean duration of hyperhydrosis was 2.11± 60. Palmo-plantar 21(45.7%) was the most common area followed by cranio-facial 12(26.1%),axilla 8(17.4%)andfocal5(10.9%)(Table 1).

We found a significant difference at zero wk(baseline) and 4th wk(p=0.001) at a dose of 2.5 mg once a day. Similarly, there was no significant difference when comparing between zero wk(baseline) and 8 wk(p=0.6) at dose of 2.5 mg twice aday. On follow-up the dosage was gradually increased to 5 mg twice a day.There was a significant difference noted (p=0.022) between zero wk(baseline) and 12 wk. Similarly, when the patients were reevaluated at 16 wk on follow-up, we found there was a significant difference between zero wk(baseline) versus 16th wk. There was a significant difference in HDSS in zero wk(p=0.03) and 16 wk (p=0.005)(Table 2). Mild adverse effects of oxybutin were observed throughout the duration of treatment. The most common side effect was a dry mouth and blurred vision (Table 3). Most side effects were observed during 12 wk, at a dose of 10 mg. All the side effectswere mild and managed accordingly. None of the patients withdrew from the study.

Discussion

Hyperhydrosis can cause severe psychosocial disorder in patients and can lead to a substantial burden, interfering with daily activities and can cause social embarrassment.In our study there is a higher predominance of women which is consistence with other study.8 This can be explained as womenbeing more concern in esthetic engagement in social search for treatment more often than men.

In this study oxybutin was prescribed in a low dose of 2.5mg once a day for 4 wk and gradually increasedto 10 mg at end of the study with a duration of 3 months. As a result, there were very less side effect with a significant difference in HDSS.Our result was comparable with the study done by Wolosker *et al*., where the maximum dose of oxybutin 10 mg /day was reached over a period of 3 months peroid with fewer side effects and good compliance.[9] Similarly, in the French trial study, oxybutin was used in generalized hyperhydrosis in 30 patients, starting with a low dose of 1.25 mg and gradually increased to a maximum dose of7.5 mg, where the treatment was considered “very efficient” in 80% of the patients.[10]

Wolosker *et al*., reported several papers on the use of oxybutin in large groups of patients for the treatment

of hyperhydrosis in its various location, and assessment was performed by questionnaires completed by patients where more than 80% individuals with improvememt in quality of life was noted.[11-13] Oxybutin was given at a dose of 5 mg daily in children aged 7 to 14 years, improvement was seen after treatment in relation to pretreatment period, in 65.5% patients.[14]

In several studies done by Wolosker, 70% of patients had dry mouth, followed by blurred vision, which was comparable with our study.11-13 Major adverse effect and discontinuation of patients in our study was not observed as mentioned in the literature and minor side effect was managed accordingly.

International Hyperhidrosis Society[5] developed Hyperhidrosis Disease Severity Scale (HDSS) as a quick method with simple and straight forward questions with four available answers related to the implications of patient's daily routine and the degree of tolerance to the symptoms. The advantage of this scale is that the questions are simple and easy to respond to, reducing the number of errors and optimizing medical evaluation, potential self-filling, and large-scale application.

Conclusion

Oxybutin is an anticholinergic drug with an emerging role in hyperhydrosis. Low doses have significant results with minimal side effects. The dose requirement varies among authors. Studies with long-term follow-ups and ideal protocols need to be established in the future regarding the effective management of hyperhidrosis.

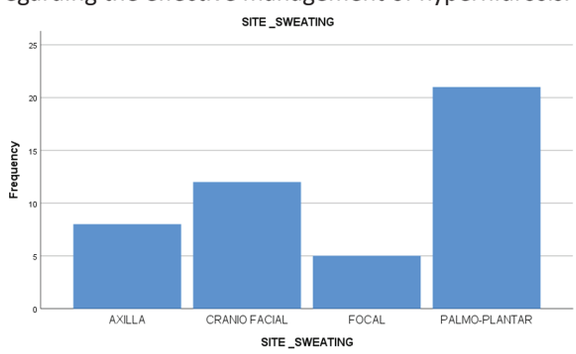

Table 1 : Site of hyperhidrosis

ANOVA						
		Sum of Squares	Df	Mean Square	F	Sig.
HDSS 4WK	Between Groups	11.536	2	5.768	46.505	.000
	Within Groups	5.333	43	.124		
	Total	16.870	45			
HDSS 8 WK	Between Groups	.706	2	.353	.516	.600
	Within Groups	29.403	43	.684		
	Total	30.109	45			
HDSS 12WK	Between Groups	3.310	2	1.655	4.155	.022
	Within Groups	17.125	43	.398		
	Total	20.435	45			
HDSS 16 WK	Between Groups	.368	2	.184	1.060	.355
	Within Groups	7.458	43	.173		
	Total	7.826	45			

Table 2 : Hyperhidrosis Disease Severity Scale (HDSS)

Side Effect	4 wk(2.5mg)	8wk(2.5 mg BD)	12wk(5mg BD)	16wk(follow-up)
Dry mouth	9(19.6)	11(23.9)	10(21.7)	15(32.6)
Dry Eye	0	3(6.5)	7(15.2)	8(17.4)
Blurred Vision	5(10.9)	12(26.1)	9(19.6)	1(2.2)
Headache	3(6.5)	7(15.2)	9(19.6)	6(13)
Sommolence	0	1(2.2)	1(2.2)	4(8.7)
Constipation	0	0	5(10.9)	5(10.9)

Table 3 : Adverse effects as per dose

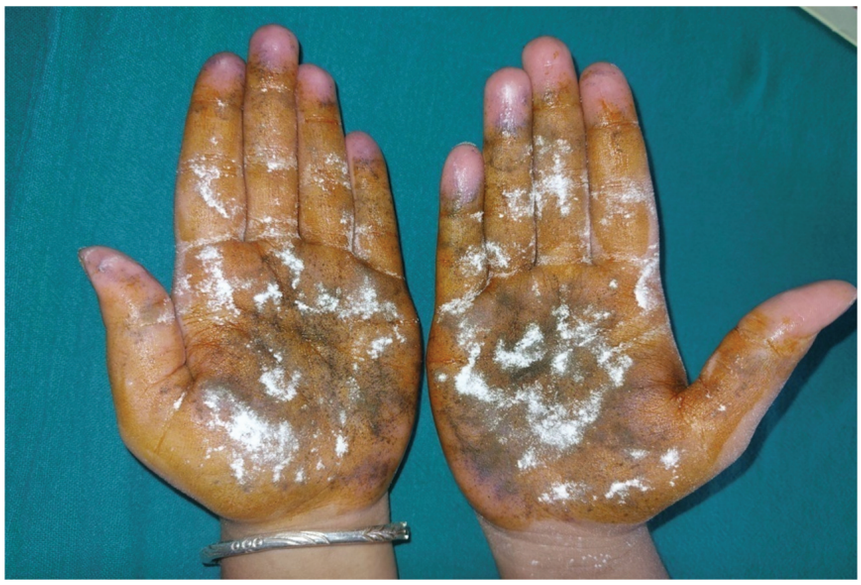

Figure 1 : Iodine starch test: areas of excessive sweating (hyperhidrosis) show bluish-purplish discoloration

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