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A Randomised Comparison Trial Comparing Topical Betamethasone Diproprionate Lotion with Topical Latanoprost for the Treatment of Localised Alopecia Areata

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KEYWORDS
Teleophthalmology Practice, Anterior/Posterior

ABSTRACT:

Background: The conventional treatment for alopecia areata is topical corticosteroids. Eyelash alopecia areata has recently been reported to respond well to topical latanoprost therapy.

Objectives: This research aimed to assess the effectiveness of topical betamethasone diproprionate lotion (group 2) and topical latanoprost ophthalmic solution (group 1) in the treatment of localised alopecia areata.

Methods: This was a parallel-group, single-center, randomised, two-armed effectiveness study. A 1:1 randomization was used to assign 50 patients with localised alopecia areata to either topical betamethasone diproprionate 0.05% lotion or topical latanoprost 0.005% ophthalmic solution. 44 of the 50 patients—21 in group 1 and 23 in group 2—finished the course of therapy.

Results: In the latanoprost group compared to the betamethasone group, the percentage decrease in area associated with alopecia areata at 16 weeks (primary endpoint) was lower (median [interquartile range], 11.1 [0–99.1] vs. 100% [13.6–100], P = 0.02). Compared to the betamethasone group, significantly fewer patients in the latanoprost group showed a full response to therapy (6 [24%] vs. 14 [56%], P = 0.02). When comparing the latanoprost group to the betamethasone group, the median (interquartile range) hair regrowth score was considerably lower (1 [0–4.5] vs. 5 [1–5], P = 0.02). The betamethasone group's subjects had a quicker decrease in the affected region.

Limitations: The study was limited by the brief treatment period and follow-up.

Conclusion: our findings imply that topical latanoprost 0.005% ophthalmic solution is a safer but less effective therapy for localised alopecia areata than topical betamethasone dipropionate 0.05% lotion.

Introduction

One type of autoimmune illness is alopecia areata. It manifests clinically as a well-defined, smooth-surfaced, round or oval, totally bald patch or patches of non-scarring alopecia[1].Despite mostly affecting the scalp, it may affect any place that bears hair. Alopecia areata therapy presents a difficult situation[2].

There is a deficiency of evidence-based information about different treatment approaches for alopecia areata. Topical corticosteroids are regarded as standard therapy among the numerous treatment options for localised alopecia areata[3]. Several clinical and animal model research studies have been conducted to investigate the possibility of latanoprost-induced eyelash hypertrichosis in glaucoma patients. This finding was made by

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coincidence and aims to better understand the condition's possible treatment options for alopecia areata[4,5]. Furthermore, latanoprost has a far better side effect profile than topical corticosteroids.

Methods:

This two-arm, parallel-group, single-centered, randomized efficacy trial was carried out at the department of dermatology, Vinayaka missions medical college between August 2023 to January 2024. Written informed consent was given by each patient.

Patient selection:

Thus, if proven effective, latanoprost may provide a safer alternative to topical corticosteroids for the treatment of alopecia areata. The current study compares the effectiveness of topical corticosteroid monotherapy, such as betamethasone dipropionate 0.05% lotion, with topical latanoprost 0.005% ophthalmic solution in treating localised scalp alopecia areata. Participants in this study were consecutive individuals with localised alopecia areata who visited this institute's dermatological clinic. Patients who satisfied the following requirements might be included in the study: (a) five or less alopecia areata patches that cover less than 40% of the scalp region and, The following patients may not be eligible for treatment: (b) those who have received oral or topical treatment for alopecia areata within the last month; (c) those who have any coexisting hair disorders (trichotillomania, androgenetic alopecia, telogen effluvium); (d) those who have any contraindications to topical corticosteroids (dermatitis, local skin infections); (e) women who are pregnant or in lactation period; and (f) those who are unwilling to provide informed consent.

Study protocol:

At baseline, a comprehensive history and clinical examination were performed on every patient. Before beginning therapy, each patient had a potassium hydroxide mount of their trimmed hair, thyroid function testing, and an indirect immunofluorescence test for antinuclear antibody presence. A urine pregnancy test was also administered to women who were potentially fertile. Alopecia areata was diagnosed based on a clinical assessment.

Patients were randomised 1:1 to receive topical betamethasone diproprionate 0.05% lotion (group 2) or topical latanoprost 0.005% ophthalmic solution (group 1). The assignments were placed in opaque, sealed envelopes, and the randomization sequence was created by a computer. Patients were told to apply either betamethasone propionate 0.05% lotion with fingers (group 2) or latanoprost 0.005% ophthalmic solution (group 1) twice daily to alopecia areata areas using a cotton tip applicator. Throughout the course of the trial, measurements and clinical assessments of the alopecia areata-affected region were made at baseline and then every 4 weeks.

The alopecic patch was covered with a translucent sheet, which was then used to draw a two-dimensional image of each patch onto graph paper.

The alopecia patch's longest and shortest diameters were measured in order to determine the area affected by hair loss, which was given in cm^2. Additionally, photographs were taken at baseline and at 4-week intervals during the trial. An same assessor conducted each measurement. All patients received treatment for a total of sixteen weeks, or until full hair regrowth, whichever happened first. Patients who showed full hair growth at 16 weeks were monitored for an additional 8 weeks to look for signs of recurrence. After 16 weeks, the effectiveness of the therapy was assessed using a modified five-point semi-quantitative hair regrowth score: 1 indicates 1–24% regrowth, 2 = 25–49% regrowth, 3 = 50–74% regrowth, 4 = 75–99% regrowth, and 5 = 100% regrowth. 0 represents no change or further loss[6].

Study outcome:

Every side effect that the therapy caused that happened throughout the research period was also noted. The percentage decrease in the alopecia areata-affected region at 16 weeks was the study's main finding. The number of patients who experienced a complete response to the treatment (i.e., a regrowth score of 5), the median regrowth score, and the incidence of side events (such as dermatitis, erythema, skin atrophy, and telangiectasia) were among the secondary outcomes.

Sample size calculation:

Based on an estimate from a prior research, we estimated that the control group (betamethasone) would see an average percentage decrease of 50% throughout the superiority trial[7].A sample size of 17 individuals per group was needed to detect a 10% difference between the

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JCHR (2024) 14(3), 2819-2826 | ISSN:2251-6727

2 groups in the primary outcome (percentage decrease in the region associated with alopecia areata after 16 weeks) at a significance level of 5% and a power of 80%. In order to account for a 30% dropout rate, each group included of 25 individuals.

Statistical analysis:

The commercial statistical tool for social sciences for MS-Windows (Version 22, SPSS Inc, Chicago, IL) was used to do the statistical analysis. Descriptive data are shown as a number with a percentage or as a median with an interquartile range. The distribution's normality was assessed using the Shapiro-Wilk test. The chi-square test, also known as Fisher's exact test, was employed to examine variations across categorical variables, encompassing the percentage of participants who provided a comprehensive response. The primary outcome, which was the % reduction in area, and the regrowth score were among the continuous variables that were compared using the Mann-Whitney U test. Intention-to-treat and protocol-based analyses were carried out. The worst-case scenario—in which the individuals who were lost to follow-up were deemed to have no response to the study intervention—was taken into account for the intention-to-treat analysis. A repeated measure analysis of variance test was used to determine the trend related to the parameters that were observed over the time. Every statistical test was conducted at a significance threshold of $\alpha = 0.05$ and was two-sided.

Results:

Following an eligibility assessment of 78 individuals with localised alopecia areata, 50 patients (median [interquartile range] age, 24[14.5–34.3] years, 16[32%] women) were subsequently enrolled in the research [Figure 1]. Alopecia areata affected a median surface area of 7.5 (3–13) cm2, and the disease's median (interquartile range) duration was 3 (1.5–5.3) months [Table 1]. 21 patients (42%) had nail abnormalities, with leukonychia (11 [22%]), Beau's lines (7 [14%]), and pitting (5 [10%]) being the most prevalent.

The intention-to-treat analysis revealed a statistically significant difference between the latanoprost and betamethasone groups in terms of the median (interquartile range) percentage reduction in the alopecia areata-affected area at 16 weeks [Table 1] (11.1 [0–100] vs. 100 [13.6–100], P = 0.02). Comparing the latanoprost group to the betamethasone group, the percentage of patients who responded completely to therapy was considerably lower [6 [24%] vs. 14 [56%], P = 0.02; Figures 2 and 3]. At the conclusion of 16 weeks, the latanoprost group had a substantially lower median (interquartile range) regrowth score (1 [0–4.5] vs. 5 [1–5], P = 0.02) than the betamethasone group. Fourteen participants (sixteen in group 1 and twenty-three in group 2) finished a sixteen-week follow-up. Comparable outcomes were found in the protocol analysis [Table 2]. At the conclusion of the 24-week period, no patients in either group experienced a relapse. The sole side effect seen in the latanoprost group was erythema, but the betamethasone group also had erythema, skin atrophy, telangiectasia, dermatitis, and pustules [Table 3]. Between the latanoprost and betamethasone groups, there was no statistically significant difference in the number of participants reporting side events (4 [16%] vs. 4 [16%], P=1.00. Compared to latanoprost, topical betamethasone showed a faster rate of reduction in the affected region, indicating a quicker response [Figure 4].

Discussion:

This study has demonstrated that topical betamethasone dipropionate 0.05% lotion is more effective than topical latanoprost (0.005% ophthalmic solution) in treating alopecia areata. This is the first research to compare topical latanoprost and topical steroids head-to-head in non-eyelash alopecia areata and assess the effectiveness of topical latanoprost on non-eyelash alopecia areata of the scalp area. The effectiveness of topical latanoprost in treating eyelash alopecia areata has been assessed in all previous research.

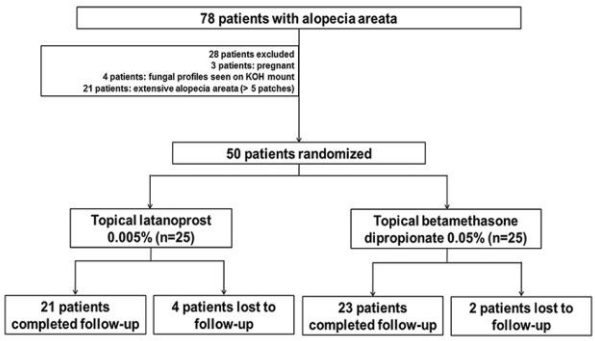

Figure 1: Flow diagram (CONSORT figure) depicting the study protocol and the participant inclusion process

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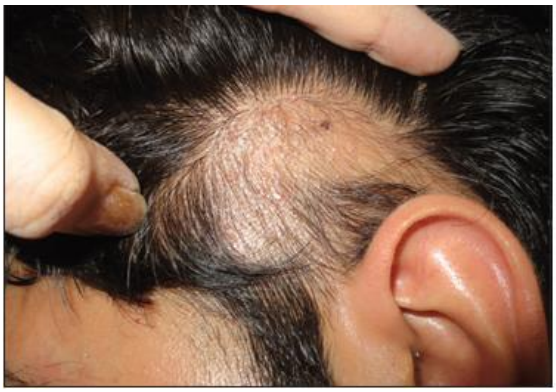

Figure 2a: Alopecia areata. A 27 year old man with scalp alopecia areata treated with betamethasone lotion. Alopecia areata patch at baseline

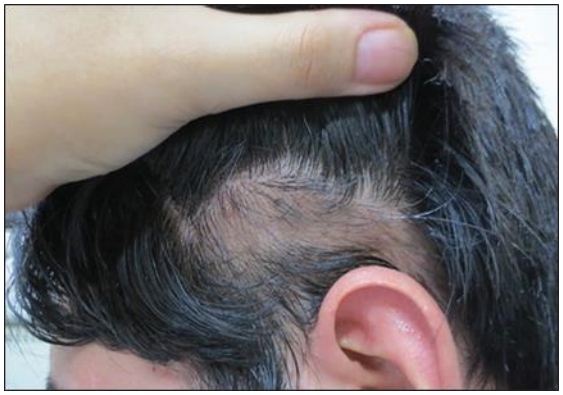

Figure 2b: Alopecia areata. A 27-year-old man with scalp alopecia areata treated with betamethasone lotion. After 4 weeks of therapy (initial response)

The initial purpose of topical latanoprost was to treat alopecia areata of the eyelashes. Dermal papilla and outer root sheath prostaglandin F2α receptors are expressed by eyelash hair follicles.

By binding to these receptors, latanoprost causes the telogen follicles to enter the anagen phase. Additionally, it extends the hair cycle's anagen phase.

Alopecia areata is a prevalent autoimmune hair condition characterised by a persistent pattern of relapses. There aren't many therapy alternatives accessible. There have been instances of eyelash hypertrichosis in glaucoma patients receiving latanoprost treatment. Consequently, the application of latanoprost in the management of eyelash

alopecia areata has been the subject of several investigations[4,8–17].However, the impact of latanoprost in scalp alopecia areata has not been investigated in any of the prior research. In order to examine topical latanoprost as a monotherapy option to topical corticosteroid, this is the first trial to compare its effectiveness against a powerful topical steroid for non-eyelash (scalp) alopecia areata.

The results of this study indicate that topical betamethasone dipropionate lotion is a more effective therapy for localised alopecia areata than topical latanoprost solution. The current study's findings are consistent with other research showing that latanoprost is less effective in encouraging hair growth in individuals with alopecia areata of the lashes and eyebrows[18–20].

Topical metastasone furoate cream was shown to be less effective than bimatoprost, a PGF2α counterpart, in treating localised alopecia areata in a recent research by Zaher et al[21]. These findings might be explained by a few things.

The topical corticosteroid employed in the current study, betamethasone propionate, is more potent than the steroid utilised in the study by Zaher et al., which explains why betamethasone produced superior outcomes in our investigation. Furthermore, compared to latanoprost, bimatoprost has been shown to

Table 1: Demographic Characteristics of Study Patients

BASELINE CHARACTERISTICS	TOPICAL LATANOPROST (*N*=25)	TOPICAL BETAMETHASONE (*N*=25)	TOTAL (*N*=50)	*P*
Age (years)	22 (11-37)	25 (16.5-33.5)	24 (14.5-34.3)	0.89
Gender (male:female)	17:8	17:8	34:16	1.00
Age of onset of disease (years)	22 (11-37)	25 (16.5-33.5)	24 (14.5-34.3)	0.87

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JCHR (2024) 14(3), 2819-2826 | ISSN:2251-6727

Total area involved by AA (cm^2)	5 (2.1-15.9)	9.9 (4.2-14.2)	7.5 (3-13)	0.19
Duration of disease (months)	3 (2-4.5)	3 (1-6)	3 (1-5.3)	0.79
Family history of alopecia	9 (36.0)	5 (20.0)	14 (28.0)	0.21
Family history of atopy	5 (20.0)	4 (16.0)	9 (18.0)	0.71
Personal history of atopy	9 (36.0)	5 (20.0)	14 (28.0)	0.21
Elevated TSH	3 (12.0)	1 (4.0)	4 (8.0)	0.30
Positive ANA	2 (8.0)	0	2 (4.0)	0.15

All values are expressed as median (interquartile range) or *n* (%). TSH: Thyroid-stimulating hormone, ANA: Antinuclear antibody, AA: Alopecia areata

TABLE 2: OUTCOMES OF THE STUDY

OUTCOME	**TOPICAL LATANOPROST**	**TOPICAL BETAMETHASONE**	**ESTIMATED DIFFERENCE (95% CI)**	***P***
Intention-to-treat analysis	*n*=25	*n*=25		
Primary outcome				
Percentage reduction in an area with hair loss between baseline and 16 weeks	11.1 (0-99.1)	100 (13.6-100)	-	0.02
Other outcomes				
Complete response	6 (24.0)	14 (56.0)	0.32 (0.05-0.53)	0.02
Hair RGS at 16 weeks	1 (0-4.5)	5 (1-5)	-	0.02
Per protocol analysis	*n*=21	*n*=23		
Primary outcome				
Percentage reduction in an area with hair loss between baseline and 16 weeks	71.7 (0-100)	100 (50.8-100)	-	0.03
Other outcomes				
Complete response	6 (28.6)	14 (60.9)	0.32 (0.03-0.55)	0.03
Hair RGS at 16 weeks	3 (0-5)	5 (3-5)	-	0.03

All values are median (interquartile range) or *n* (%). Rgs: regrowth score, ci: confidence interval

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JCHR (2024) 14(3), 2819-2826 | ISSN:2251-6727

Table 3: adverse effects of treatment in the study groups

ADVERSE EFFECT	TOPICAL (*N*=25)	LATANOPROSTTOPICAL (*N*=25)	BETAMETHASONETOTAL (*N*=50)	*P*
Any adverse effect*	4 (16.0)	4 (16.0)	8 (16.0)	1.00
Erythema	4 (16.0)	1 (4.0)	5 (10.0)	0.13
Skin atrophy	0	3 (12.0)	3 (6.0)	0.09
Telangiectasia	0	2 (8.0)	2 (4.0)	0.17
Dermatitis	0	1 (4.0)	1 (2.0)	0.33
Pustules	0	2 (8.0)	2 (4.0)	0.17

*There were more than one adverse effect in some study subjects

induce hypertrichosis earlier and more severely[22]. Compared to latanoprost, bimatoprost does not require conversion into an active metabolite in order to have pharmacological action, which may account for its better effectiveness. Furthermore, rather than discussing full hair restoration, Zaher et al. have merely remarked on the proportion of hair regrowth. On the other hand, full hair regeneration was one of our study's results, and this is a therapeutically more significant consequence when treating alopecia areata in a particular patient. The majority of patients tolerated latanoprost well; the sole side effect was erythema at the application site. Because vasodilatation acts on PGF2α receptors on dermal vessels, this is linked to it. Numerous more investigations have shown that the sole unfavourable impact at the latanoprost-treated locations is an erythematous response, or that there are no

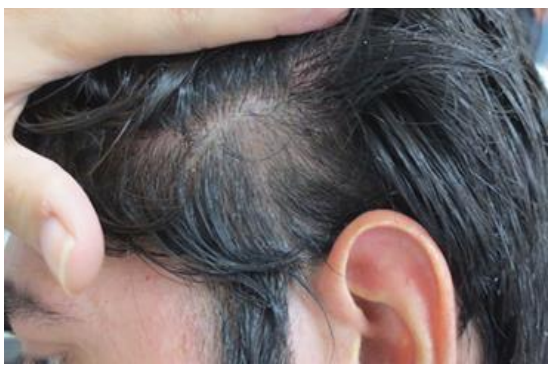

Figure 2c: Alopecia areata. A 27-year-old man with scalp alopecia areata treated with betamethasone lotion. After 8 weeks of treatment

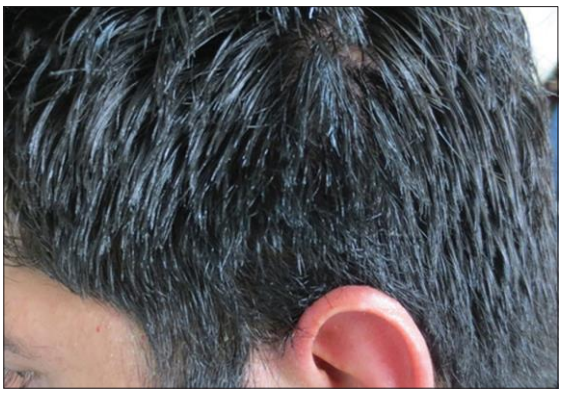

Figure 2d: Alopecia areata. A 27-year-old man with scalp alopecia areata treated with betamethasone lotion. Complete hair regrowth at 16 weeks

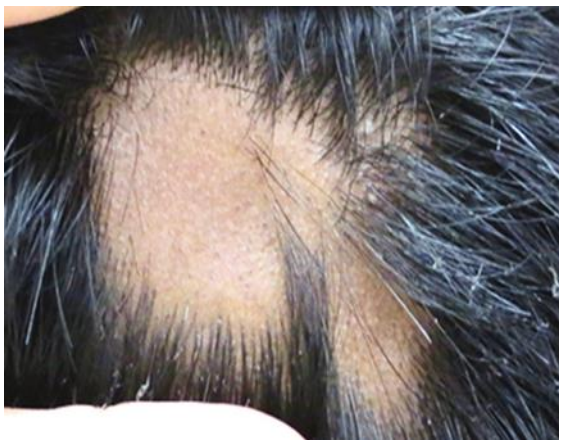

Figure 3a: Alopecia areata. A 35-year-old man with scalp alopecia areata treated with latanoprost solution. Alopecia areata patch at baseline

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JCHR (2024) 14(3), 2819-2826 | ISSN:2251-6727

side effects at all.[8,21,23] This contrasts with the steroid therapy, which has a number of unfavourable side effects, including minor local atrophy, telangiectasia, pustules, and acneiform face eruptions.[24]

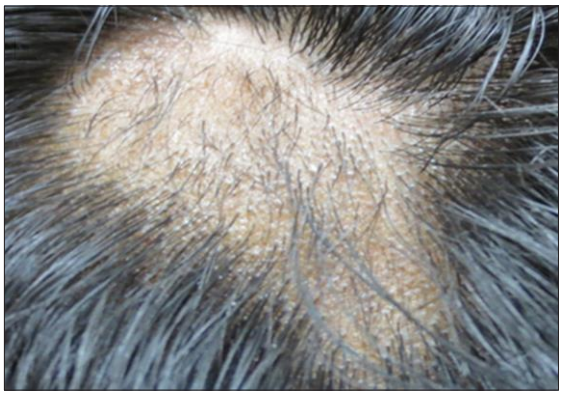

Figure 3b: Alopecia areata. A 35-year-old man with scalp alopecia areata treated with latanoprost solution. After 4 weeks of therapy (initial response)

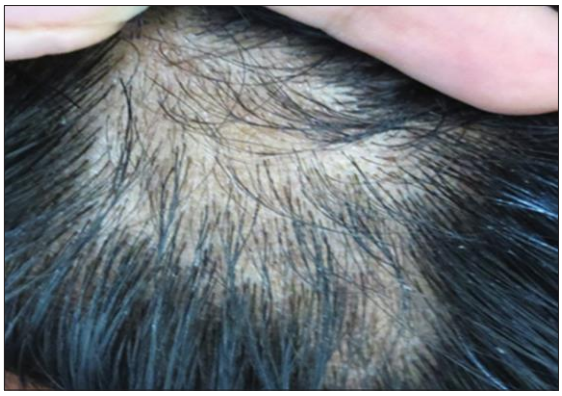

Figure 3c: Alopecia areata. A 35-year-old man with scalp alopecia areata treated with latanoprost solution. After 8 weeks of treatment

Strengths and limitations:

Our study's primary strength is that it is randomised. This is the first investigation on latanoprost usage for alopecia areata. A major disadvantage of our study is that there were neither multiple assessors nor assessor blinding. brief treatment duration and brief post-therapy follow-up are the other constraints. The major outcome that we measured was the actual percentage reduction in the hair loss area.

The Severity of the Alopecia Tool (SALT) score, a more popular and reliable way to gauge hair loss in alopecia areata, was not evaluated by us. There might have been a few reasons for the patients' subpar latanoprost response in our investigation. The primary concern is inadequate absorption into the follicular bulb because the formulation utilised in the research was intended for ocular usage, primarily in the treatment of glaucoma.

This restriction may be addressed by increasing the potency of latanoprost and altering the vehicle such that the medication can penetrate as far as the dermal papilla and outer root sheath of the hair follicle, which contain prostaglandin receptors. Additionally, by giving the medication a minimal amount of time to take effect, extending the length to six months or beyond may have improved the outcomes.

It is also necessary to investigate the efficacy of other prostaglandin analogues, such as bimatoprost and tramaprost, in encouraging hair regeneration.

Discussion:

Topical betamethasone is a more effective treatment option for treating scalp alopecia areata than topical latanoprost. In this investigation, topical latanoprost was also linked to fewer side effects. Larger trials with longer treatment durations and follow-up periods are necessary to determine the actual therapeutic potential of this approach for this persistently relapsing illness.

Declaration of patient consent:

The authors attest that they have all the necessary patient permission documents. The patients have agreed on the form that their pictures and other clinical data may be published in the publication. The patients are aware that although every attempt would be made to keep their identities hidden and that their names and initials will not be disclosed, anonymity cannot be ensured.

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