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ORIGINAL ARTICLE
Pediatric/Craniofacial

Hair Transplantation in Migraine Headache Patients

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Background: Migraine headache is a primary neurologic disease affecting millions of people worldwide. As a consequence, quality of life is diminished, productivity suffers (through loss of work force), and treatment costs are substantial. The occurrence rate in the general population is quite high, with women accounting for 3 of every 4 cases.
Methods: Between January 2011 and May 2012, a total of 221 patients received hair transplants. Another 590 patients underwent hair transplantation between June 2012 and December 2016. Initially (first interval), patients were not questioned on migraine headaches in preoperative visits, but questioning was regularly done thereafter. Overall, 150 patients given transplants in the first period were surveyed by phone regarding preoperative migraine headaches. Aside from the 1 incidental discovery, no other instances of migraine emerged. Headache origins were occipital-frontal in 2 patients, occipital-temporal in 2 patients, and occipital-temporal-frontal in the 2 others. Donor/receiver areas in hair transplantation and migraine trigger zones shared locations. Headache frequencies ranged from 4 to 8 days per month (average, 6 days), and pain scores were 5–8 (10 being highest). Duration of pain was 3–5 hours (average, 4 hours). All six patients had used various medications, such as triptans, ergot, and nonsteroidal anti-inflammatory drugs, before hair transplantation. The 1 female patient was a 32-year-old seeking treatment for alopecia, with a 6-year history of migraine headaches. The male patients presenting with androgenetic alopecia (grade 4–5 by Norwood classification) had 6- to 20-year migrainous histories.
Results: After hair transplantation, each migraine sufferer was checked once in the first month and then once every 3 months. Those who could not appear in person after the first year were evaluated by phone every 3 months. Migraine headaches had ceased in all 6 patients, none of whom used medical treatments for migraines thereafter. The postoperative improvement each patient experienced was dramatic ($P < 0.001$). Overall, the mean intensity of headaches declined from 6.6 ± 1.47 to 0, on an analog scale of 1–10 ($P < 0.001$); and mean headache frequency was reduced from 5.83 ± 1.03/month to 0/month ($P < 0.001$). Likewise, the migraine pain index fell from a mean of 149.33 ± 19.21/month to mean of 0/month ($P < 0.001$).
Conclusions: This report details 6 patients who experienced abatement of migraine headache symptoms following hair transplantation. The positive effects of hair transplantation on migraine headache and potential mechanisms of action are also discussed. *(Plast Reconstr Surg Glob Open 2017;5:e1503; doi: 10.1097/GOX.0000000000001503; Published online 21 September 2017.)*

INTRODUCTION

Migraine headache is a primary neurologic disease affecting millions of people worldwide.[1] As a consequence, quality of life is diminished, productivity suffers (through loss of work force), and treatment costs are substantial. The occurrence rate in the general population is quite high,[2] with women accounting for 3 of every 4 cases.[3–5] Although men and adolescents are less often afflicted, the incidence of migraine in children is gradually increasing.[3–5] The current estimate of migraine prevalence among all pediatric patients is nearly 8%.[3–5] In addition, some sources indicate that 10.6% of children aged 5–15 years and 28% of adolescents aged 15–19 years have experienced at least 1 migraine headache.[3–5] Traditionally, patients with migraine headaches are treated and managed by neurologists.[6–8] Except in rare circumstances, a treatment consensus is lacking among plastic surgeons and neurologists. Moreover, many patients

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Received for publication April 18, 2017; accepted July 31, 2017.
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DOI: 10.1097/GOX.0000000000001503

Disclosure: *The author has no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the author.*

and some doctors are unaware of surgical treatment options, so referrals to plastic surgeons are uncommon. Despite the fact that medical treatment eases symptoms in many patients, drugs are not curative; and the precise pathologic mechanism of migraine has not been fully clarified.[9–13] On the other hand, success rates of surgical procedures are rising. The objective of surgical intervention in migraine headache is deactivation of trigger sites by either decompression or avulsion.[9–14] Although surgical treatment has proved effective in the 15 years of its use, the number of patients who cannot be completely treated is still very high.[9–15] Botulinum neurotoxin,[15] which has gained usage in recent years, provides temporary relief for some and helps identify candidates for surgery.[15–17] Throughout the world, many men (> 60%) and women (50%) suffer from androgenetic alopecia and irreversible hair loss,[18,19] which at present is frequently remedied by hair transplantation. In the past 10–15 years, a new hair restoration technique, known as follicular unit extraction, has been introduced.[20–22] A patient electing hair transplantation at our clinic (~5 years ago) brought to our attention during a 6-month follow-up visit that his migraine headaches had ceased, restoring quality of life. After this first chance discovery, we initiated both retrospective and prospective investigations, documenting similar outcomes in other patients (5 males and 1 female). This report details 6 patients who experienced abatement of migraine headache symptoms following hair transplantation. The positive effects of hair transplantation on migraine headache and potential mechanisms of action are also discussed.

SURGICAL TECHNIQUE

All procedures were performed under local anesthesia. First, the donor area was infiltrated with lidocaine, using a tumescent solution to then inflate the scalp. This maneuver facilitates graft collection and implantation. Grafts were collected via punch (0.8–0.9 mm), anchored to a micromotor. For each graft, the punch was inserted into scalp to an average depth of 4–4.5 mm, at a micromotor rate of 3,000–5,000 cycles/min. The sharp punch tip was advanced under loose areolar tissue. In this way, hair follicles buried in fatty substrate were easily released. Subcutaneous veins and nerves in the donor field invariably were destroyed. The average length of collected grafts was 5 ± 0.5 mm. Once graft collection was complete, the receiver field was cultivated and local anesthesia was administered in the same manner as that in the donor field. A sterile razor was used to open recipient channels (length, 7 mm; width, 1 mm). Secured in a clamp, the same razor served to create pores in the receiver field (~50 pores/cm^2). The average pore depth was 5 mm, incising scalp to level of periosteum. Grafts were then implanted manually, one by one. Vein and nerve damage within subcutis of receiver field was also typical.[23] After transplantation, the average vascularization period of grafts is 8 days. A total of 2,500 grafts were placed in our first patient. Graft totals in the other male patients ranged from 3,000–4,500 (Figs. 1–3). Grafts were collected via micromotor method, using temporal (right and left) and occipital scalp as donor

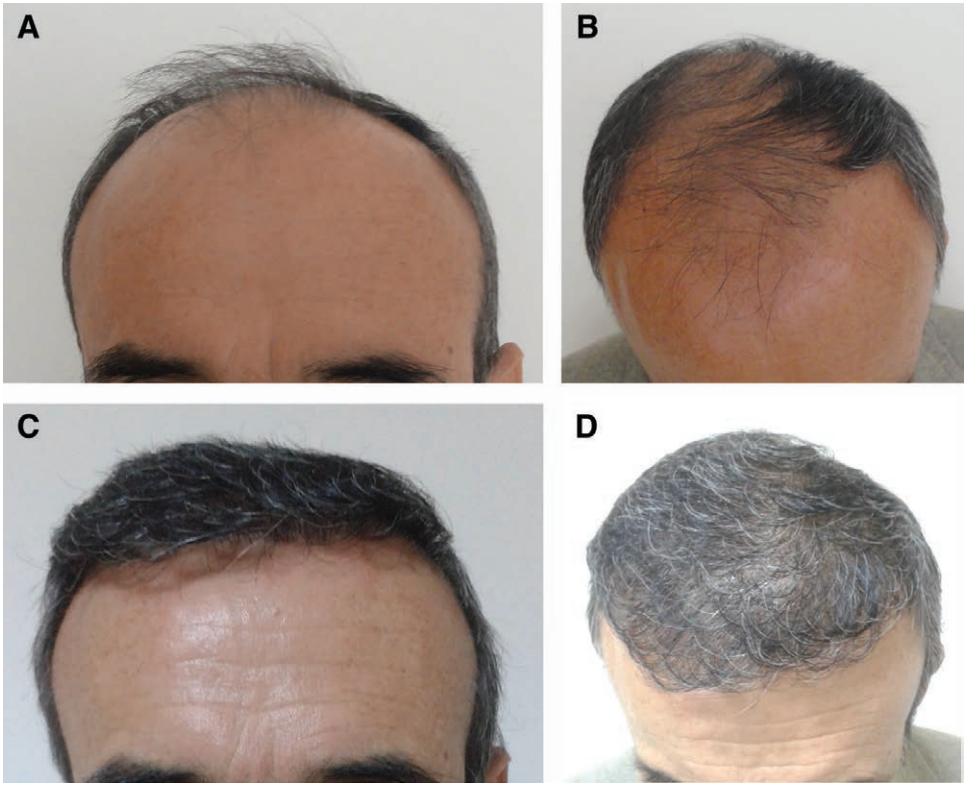

Fig. 1. The images of a male patient, 57 years old, who had migraine headache for 20 years. A, B, Preoperative appearances. C, D, Postoperative 2-year appearances.

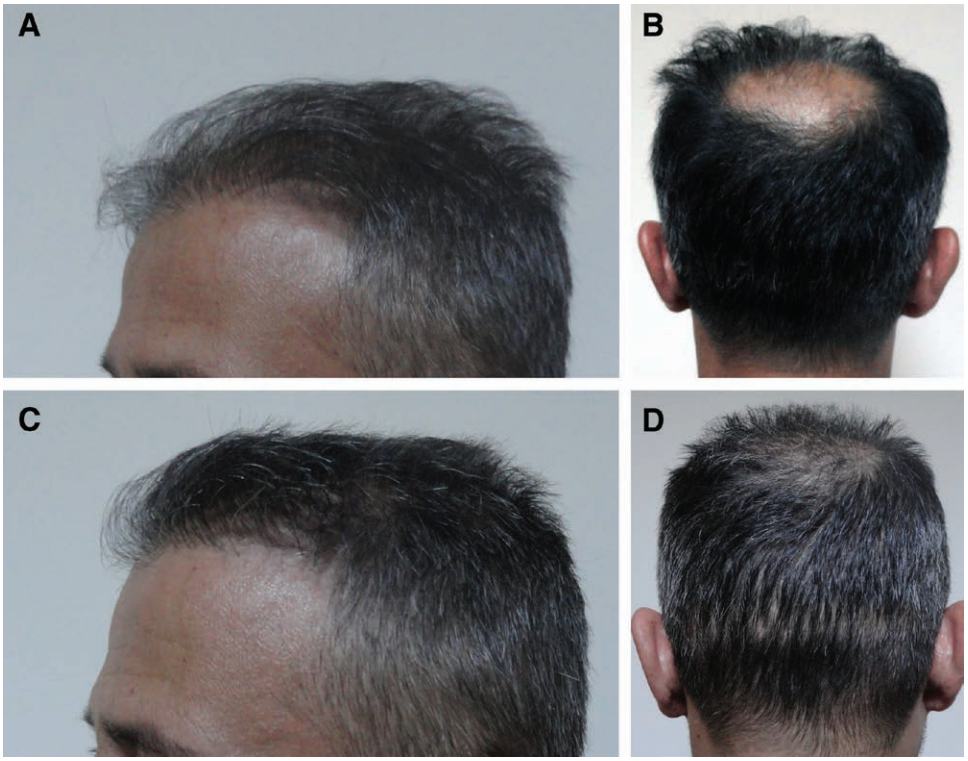

Fig. 2. The images of a male patient, 47 years old, who had migraine headache for 8 years. A, B, Preoperative appearances. C, D, Postoperative 3-year appearances.

sites (Fig. 4A, B). Inflammation, proliferation, maturation, and remodeling phases of wound resolution proceeded without incident in receiver areas. The fact that thousands of microscopic tissue losses are sustained at donor locations is not unexpected. As receiver channels are developed through microincisions, cutaneous and subcutaneous structures are typically destroyed as well (Fig. 5C). All patients eventually recovered from transplant procedures, without long-term sequelae or complications. Hair growth in all patients was substantially complete within 6–8 months. Patient characteristics and methods between years 2011 and 2016, a total of 811 patients underwent hair transplantation by follicular unit extraction method. The vast majority (98%) were men (n = 796), the ages ranging from 32–57 years (average, 45 years). The 6 patients reported had suffered migraine headaches for 6–20 years. Our Research Ethics Committee granted approval for this retrospective clinical study, with consent of all patients involved. Between January 2011 and May 2012, a total of 221 patients received hair transplants. Another 590 patients underwent hair transplantation between June 2012 and December 2016. Initially (first interval), patients were not questioned on migraine headaches in preoperative visits, but questioning was regularly done thereafter. Overall, 150 patients given transplants in the first period were surveyed by phone regarding preoperative migraine headaches. Preoperative and postoperative surveys are given below. Aside from the 1 incidental discovery, no other instances of migraine emerged. Headache origins were occipital-frontal in 2 patients, occipital-temporal in 2 patients, and occipital-temporal-frontal in the 2 others. Donor/receiver areas in hair transplantation and migraine trigger zones shared locations. Headache frequencies ranged from 4–8 days per month (average, 6 days), and pain scores were 5–8 (10 being highest). Duration of pain was 3–5 hours (average, 4 hours). All 6 patients had used various medications, such as triptans, ergot, and

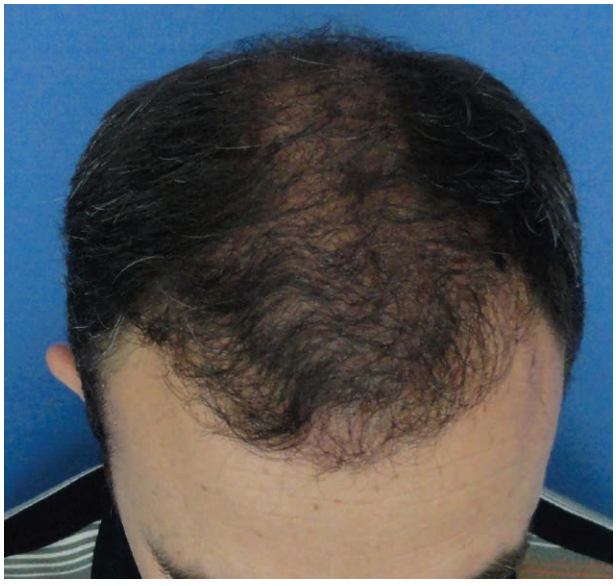

Fig. 3. Three-year postoperative male patient, 43 years old, who had migraine headache for 10 years.

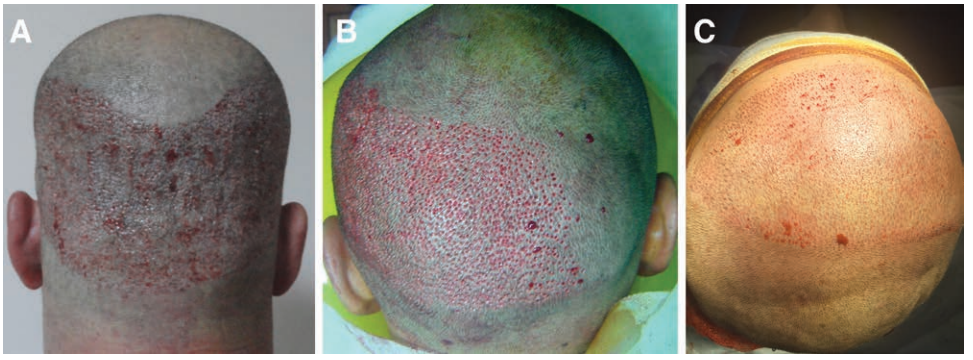

Fig. 4. Images of donor and recipient areas. A, Postoperative first day, appearances of temporal and occipital areas. B, Intraoperative, appearance of temporal and occipital areas. C, Intraoperative, appearance of frontal recipient area immediately after opened canal.

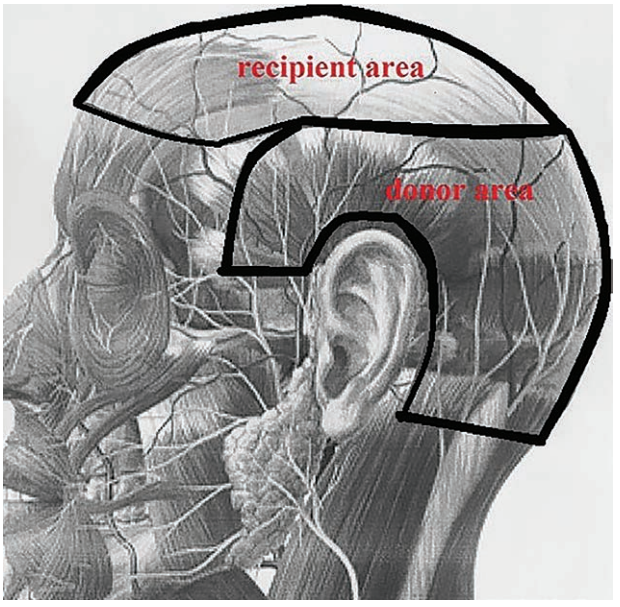

Fig. 5. Schematic illustration of the supraorbital, supratrochlear, occipital, auriculotemporal, and zygomaticotemporal branches of trigeminal nerves in the donor and recipient areas.

nonsteroidal anti-inflammatory drugs, before hair transplantation. The 1 female patient was a 32-year-old seeking treatment for alopecia, with a 6-year history of migraine headaches. The male patients presenting with androgenetic alopecia (grade 4–5 by Norwood classification) had 6- to 20-year migrainous histories. Patient characteristics and treatments are summarized in Table 1. Ages, genders, and symptoms of these patients were obtained from demographic records at first presentation. Once the first patient came forward, a migraine headache questionnaire was routinely requested of every patient, documenting headache frequency, duration, and severity. A migraine headache index was computed as (frequency: days/mo) × (duration in 24-hour period) × (pain score: 0–10), using survey responses and other collected data (Table 2). Quantifiable parameters were expressed as mean ± SD. To compare preoperative and postoperative variables, a 2-tailed t test was applied, setting significance at $P < 0.05$.

PREOPERATIVE SURVEY

1. Have you had headaches?
2. Did you get a migraine diagnosis? Who made the diagnosis?
3. How long do you have migraines?
4. How many migraine attacks do you have in a month?
5. How long does this pain last?
6. Does anyone have migraines in the family?
7. Do you have aura?
8. Do you have symptoms associated with migraine?
9. How would you classify the severity of your pain between 1–10?
10. Where exactly does migraine pain start?

[Behind the left eye, behind the right eye, the back of both eyes, left temporal side, right temporal side, in both temporal sides, above the left eyebrow, above the right eyebrow, above both eyebrows, left back of head, right back of head, both sides of the head.]

POSTOPERATIVE SURVEY

Does your pain continue?

Did you have any attack after surgery? Yes/No

If yes, is there a change in frequency?

When did your pain disappear? Immediately after, 1 month after, 6 months after.

Did you take medication? Yes/ No

Has your quality of life improved?

RESULTS

After hair transplantation, each migraine sufferer was checked once in the first month and then once every 3 months. Those who could not appear in person after the first year were evaluated by phone every 3 months. Migraine headaches had ceased in all 6 patients, none of whom used medical treatments for migraines thereafter. The postoperative improvement each patient experienced was dramatic ($P < 0.001$). Overall, the mean intensity of headaches declined from 6.6 ± 1.47 to 0, on an analog scale of 1–10 ($P < 0.001$), and mean headache frequency was reduced from 5.83 ± 1.03/mo to 0/mo ($P < 0.001$). Likewise, the migraine pain index fell from a mean of 149.33 ± 19.21/mo to mean of 0/mo ($P < 0.001$; Table 3).

Table 1. Migraine Headache and Hair Transplantation Patient Records

Patient Number	Sex	Disease Duration (y)	Age (y)	Drugs Preoperative	Follow-Up (mo)	Headache Satisfaction (%)	Medication	Symptoms Reduction (%)
1	Female	6	32	Triptans + nonspecific	58	100	None	100
2	Male	20	57	Triptans + nonspecific	36	100	None	100
3	Male	8	47	Triptans + nonspecific	26	100	None	100
4	Male	10	43	Ergot + triptans	21	100	None	100
5	Male	12	46	Triptans + nonspecific	18	100	None	100
6	Male	6	42	Ergot + triptans	6	100	None	100

O, occipital; F, frontal; T, temporal.
Nonspecific: anti-inflammatory drugs.

DISCUSSION

It is currently conceded that migraine headaches are not fully treatable through symptomatic medical intervention, and the possibility of better results by surgical means is echoed in recent studies.[10–16] In the past 15 years, various authorities (primarily Guyuron) have conducted numerous studies (e.g., anatomic, retrospective, prospective/randomized) aimed at surgical (or sham) treatment of migraine headaches.[10–16] Based on the 5-year follow-up data, it would appear that surgery is indeed effective,[9–16] but the underlying pathophysiology of migraines remains unclear. Related theories have implicated neuronal mediators, cortical neuronal hyperexcitability, peripheral and central activation of trigeminal nerves, and abnormal sensitization of the nociceptive system, the latter reflecting periaqueductal gray matter dysfunction.[24–27] Given these influences, meningeal inflammation ensues, activating trigeminal nerves and perivascular sensory fibers.[27–30] Vasodilation is then triggered through release of calcitonin gene-related peptide, substance P, and neurokinin A, all residing in trigeminal neurons.[31–34] The result is central sensitization and abnormal excitability.[35–39] However, the cause of neuropeptide release is not entirely understood. According to most current surgical studies, the target in migraine surgery is actually peripheral nerves. Chemodenervation of peripheral nerves by botulinum toxin and surgical decompression or avulsion (rarely ablation) have confirmed this.[10–16] Hair transplantation impacts peripheral nerves, thus explaining postoperative benefits in migraine sufferers. We have also observed fewer forehead wrinkles in most patients after hair transplantation, similar to botulinum toxin effect. The hair transplantation donor field starts at temporal region and is extended to nearby occipital area, moving toward opposite temporal zone (Figs. 4, 5). Destruction of nerves, veins, and soft tissue is unavoidable in doing so. Occasionally, the superficial temporal artery is injured if a large number of grafts are collected. In the donor field, particularly the area of greater occipital nerve domain, both auriculotemporal and zygomaticotemporal branches of trigeminal nerve may be destroyed bilaterally from excessive grafting.[38] Receiver areas for hair grafts are usually frontal area, apex, and vertex (Fig. 5). In these regions, approximately 50 pores (average depth, 5–6 mm) are opened in each square centimeter,[39] damaging veins, nerves, and soft tissues (Fig. 5). Depending on the nature of hair loss, the auriculotemporal and zygomaticotemporal branches of trigeminal nerve, the distal branches of supraorbital and supratrochlear nerves (extending toward frontal area), the distal branches of occipital nerve at vertex, and the arteries and veins accompanying these nerves may be damaged as well. In grafts incorporating 0.4 mm^2 of tissue (skin surface area), roughly 15 cm^2 of tissue is lost for every 3,000 grafts procured from donor areas (graft radius, r = 0.4 mm; area [$\pi r2$] = $3.14 \times 0.4 \times 0.4 \times 3{,}000$ grafts = 1,500 mm^2 = 15 cm^2). Such extensive tissue loss may alter occipital skin and subcutis, which then tightens. Hair transplants are composite in nature, combining skin, connective tissue, aponeurosis, and loose areolar tissue, so donor side tissue losses impact both appearance and contours.[39] The genetics of hair in occipital region differs from that in frontal region and apex. Hair follicles are capable of self-regulating responses to androgens through expressions of 5-alpha reductase and androgen receptors.[23,40,41] The latter elements quantifiably differ in areas of alopecia and hair-bearing scalp.[23,40–43] Accordingly, occipital hairs maintain resistance to male androgens when transplanted to vertex, and scalp hairs transplanted from vertex to forearm regress at the same pace as donor site.[44] Both tissue destruction and genetic underpinnings may account for differences within receiver fields. It is at these sites where migraine-triggering neurotransmitters are released, thus serving as points of neuromodulation. After hair transplantation, blood circulation increases substantially in both donor and receiver areas,[38] whereas disrupted vascular networks and fibrofatty tissues no longer

Table 2. Migraine Headache Index

Patient Number	Pain Frequency (d/mo)	Scale of Pain (with 10 being Highest)	Pain Duration (h/24)	Pain Index before Hair Transplantation	Pain Index after Hair Transplantation
1	4	8	5	160	0
2	5	7	4	140	0
3	6	7	4	168	0
4	8	5	3	120	0
5	7	6	4	168	0
6	5	7	4	140	0

Table 3. Comparison of Preoperative and Postoperative Symptoms

Characteristics	Before	After	*P*
Pain frequency	5.83±1.47	0±0	< 0.0001
Pain scale	6.66±1.03	0±0	< 0.0001
Pain duration	4±0.63	0±0	< 0.0001
Pain index	149.33±19.21	0±0	< 0.0001

contribute to vasospasm. As confirmed by Guyuron et al.,[13] transecting the zygomaticotemporal branch of trigeminal nerve and repositioning temporal soft tissues minimizes the potential for neural coaptation, diminishing migraine headache recurrence. Hair transplantation may affect receiver and donor areas in a similar manner. Given the enhanced regional blood flow, growth factors are apt to penetrate faster, facilitating wound recovery and maturation. Regenerating nerves also undergo change, especially myelin sheaths, leading to improved sequencing of neurotransmitter release and propagation and stem cells conveyed via perifollicular fat of composite grafts aid in tissue recovery. Trigger sites of migraine headaches in occipital, frontal, and temporal regions that occupy donor and receiver fields are likely impacted by tissue injury and posttransplantation hypoaesthesia.[23] In our patients, anesthesia and hypoesthesia (prominent in frontal region) typically lasted 3–6 months and dissipated gradually, with donor fields impacted comparatively less. Such developments were anticipated and were strictly temporary, not qualifying as complications.[23] From our perspective, the chief reason for rapid resolution of migraine attacks after hair transplantation is the hypoesthesia of donor/receiver fields that follows.[39] Subsequent benefit may be linked to regulatory control of perivascular sensory fibers. The positive effects of hair transplantation may well extend to psychosomatic aspects of migraine headaches. Although not an uncommon disorder, it was surprising that only 6 of our hair transplant patients were actual migraine sufferers, each treated medically for many years. Ultimately, all medications for migraine were abandoned during follow-up periods (6 months to 5 years), with no reported recurrences. The most striking part of this study is that the number of migraine patients is low compared with the hair plantation population. For this reason, we retrospectively and prospectively rescanned the patients more than once. But the rate did not change. This low rate can be entirely coincidental. Or, in patients who need hair transplantation, the rate of incidence of migraine may be low.

CONCLUSIONS

The seemingly curative effect of hair transplantation on migraine headaches has no clear explanation as yet. However, clinical and experimental studies of larger populations are surely forthcoming. Results were decisive in these few patients. It is remarkable that both alopecia and migraine headache may be easily remedied through a simple and easily applied procedure. As a result of this study, hair plantation in bald migraine patients may be an alternative to migraine treatment. In nonbald patients, the mechanism of action of hair transplantation may be a guide for migraine treatment. Previously, various mechanisms of central and peripheral origin have been emphasized in the treatment of migraine. In recent years, however, the focus has been on the origin of peripheral nerves. This study supports that the main cause of migraine originates from peripheral nerves. This study shows that migraine symptoms may improve in patients who do not need hair transplantation when they are damaged in the transcutaneous peripheral nerve, both in donor and recipient areas, as in hair transplantation. Our work will be a reference for such a study on patients in the future.

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