The Treatment of Axillary Odor: A Network Meta-Analysis

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Background: Axillary osmidrosis (AO) is common in plastic surgery. But there is no perfect way to treat AO. We systematically compared the efficacy of 10 AO treatments with network meta-analysis in order to provide reference for the clinical treatment of axillary odor.

Material/Methods: Chinese and English databases were searched by computer. Some relevant studies were collected for network meta-analysis.

Results: We identified 56 studies, including a total of 8618 patients for meta-analysis. The network meta-analysis showed that 21 out of 45 pairs of 10 AO treatments had no statistical significance. In statistical comparison, subcutaneous curettage and swelling suction subcutaneous pruning were better than a single treatment. In addition, the effects of both laser and electric ion therapy were inferior to those of other treatments. The order of therapeutic effects predicted by surface under the cumulative ranking (SUCRA), curve was swelling aspiration+subcutaneous pruning >subcutaneous pruning >subcutaneous curettage+subcutaneous pruning >spindle excision >botulinum toxin A injection >swelling aspiration >subcutaneous curettage >YAG laser therapy >CO₂ laser therapy >electric ion therapy.

Conclusions: In operative treatment of AO, swelling aspiration+subcutaneous pruning is the best operative treatment, and botulinum toxin A injection is the best in non-operative treatment. Overall, the effect of surgical treatment was more significant than that of non-surgical treatment.

MeSH Keywords: Meta-Analysis • Surgical Procedures, Operative • Treatment Outcome

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Background

Axillary osmidrosis (AO) is common in plastic surgery. The mechanism is that the unsaturated branched-chain fatty acids secreted by the apocrine sweat gland (ASG) gland in the axillary region are decomposed by bacteria distributed on the axillary skin to produce a special odor. AO does not result in injury to human physiological function. However, it often affects patients’ social interaction and even leads to psychological disorders, especially in Asia where the disturbance caused by AO is more obvious [1].

There are many clinical treatments for AO, but the principle is basically the same, that is, to reduce or completely clear the axillary ASG, reduce the secretion of unsaturated branched fatty acids to reduce or eliminate the special smell of axilla [2]. At present, the main methods of treatment for AO include surgical treatment and non-operative treatment. Surgical treatments mainly include subcutaneous curettage, fusiform skin excision, subcutaneous pruning, swelling aspiration and so on. And non-operative treatments mainly include CO$_2$ laser, YAG laser, electric ion therapy, botulinum toxin A injection, and so on. There are many studies comparing the curative effect of different treatment methods in the clinic setting, but most of them are 2 or 3 kinds of treatment methods, so it is not possible to evaluate the curative effect of each treatment method synthetically [3]. In order to help doctors to choose the treatment of AO better, we searched papers on clinical controlled studies of axillary osmidrosis which were published up to May 2018 for this network meta-analysis.

Material and Methods

This network meta-analysis was written in accordance with the requirements of the PRISMA extension statement [4].

Search strategy

We searched the PubMed, Embase, Cochrane Library, Wanfang Data Knowledge Service Platform, and China National Knowledge Infrastructure(CNKI) for studies published between January 1, 1990 and May 31, 2018. The search keywords were “Bromhidrosis”, “Underarm Odor”, “Osmidrosis”, “Bromidrosis”. In accordance with the request of PRISMA extended statement, the specific search strategy of PubMed is as follows: (((underarm odor) OR bromhidrosis) OR osmidrosis) OR bromidrosis. In this study, we retrieved articles published in English or Chinese only.

Inclusion and exclusion criteria

Studies were included in the network meta-analysis if they met the following criteria: 1) published studies on the treatment of AO; 2) in the same study, there were no statistically significant difference in age, sex, course of disease and severity of illness between different treatment groups. 3) interventions in the studies included 2 or more of these 8 items: subcutaneous curettage, fusiform skin excision, CO$_2$ laser, subcutaneous pruning, YAG laser, electric ion, swelling aspiration, and botulinum toxin A injection. 4) The evaluation index of the studies was the cure rate of the AO treatment. Reviews, case reports, comments, and ongoing trials were excluded.

Data extraction and quality assessment

Two reviewers (Sun and Wang) independently extracted data from the included studies. A special data extraction table was designed for the meta-analysis. The first author name, publication year, study location, surgery type, number of patients, and follow-up time were collected. The Newcastle-Ottawa Scale was used to evaluate the quality of the literature, which was evaluated from three aspects: patient selection, comparability, and outcome follow-up. The total score was 9. Less than 6 was classified as low-quality literature.

Outcome measure

The primary outcome was the cure rate of the AO treatment because these data were closely related to patient quality of life.

Statistical analyses

The network meta-analysis was performed using the Stata 14.0. First, 3 or more interventions were divided into all possible combinations of 2 intervention tests, and the software was used to map the evidence network of the intervention measures. Then, the inconsistency factor (IF) and its 95% confidence interval (CI) were used to evaluate the consistency of every closed loop in the evidence network graph. The lower limit of 95% CI equal to 0 was considered as consistency in the closed loop. Otherwise, it was considered that there was obvious inconsistency in the close-loop. The intergroup discrepancies for all outcomes were presented as relative risks (RRs) and 95% CIs respectively. Eventually, based on surface under the cumulative ranking (SUCRA) curve, efficacy of 10 treatments were ranked. The publication bias of the literature was evaluated using funnel diagrams.

Results

Characteristics of eligible studies

A total of 6817 relevant studies were identified in our database search and 1836 duplicate publications were deleted. We excluded 4726 studies due to titles and abstracts that suggested
the studies were obviously irrelevant. In addition, 199 articles (48 case series/reports, 52 literature reviews, 42 articles with no relevant data, 57 articles with no control group) were excluded by reviewing the full text of studies. Finally, 56 studies [5–60] were included in our network meta-analysis. The searching progress is shown in Figure 1.

In the network meta-analysis, 8618 participants were included and there was no significant difference in age, sex, or severity of disease. The included studies were published between 1994 and 2018. The research sites are all in China. The evaluation criteria were the cure rates. The shortest follow-up time was 1 month and the longest was 10 years. The characteristics of the included studies are shown in Table 1.

Meta-analysis

Network graph

Ten treatments formed 45 different pairings, 25 of which were direct pairwise comparisons and 20 were indirect pairwise comparisons. The point-to-point link indicated that there was

Table 1. Characteristics of the 56 included studies.

| First author | Year | Country | Surgery type | No. patients | Age | Follow-up (months) | Research type | Literature quality (star) |
|--------------|------|---------|--------------|--------------|-----|---------------------|---------------|--------------------------|
| Zong Yanxia  | 2005 | China   | a            | 88           | 25  | 6                   | Non-RCT       | 6                        |
|              |      |         | b            | 9            |     |                     |               |                          |
| Wang Jin     | 2014 | China   | c            | 52           | 27.2| 3                   | Non-RCT       | 6                        |
|              |      |         | d            | 68           |     |                     |               |                          |
| Cai Tiequan  | 1994 | China   | c            | 48           | 23.2| 8.2                 | Non-RCT       | 6                        |
|              |      |         | d            | 56           |     | 24.5                |               |                          |
| Chen Mingxing| 2002 | China   | c            | 58           | 18–35| 1                   | RCT           | 7                        |
|              |      |         | d            | 58           |     |                     |               |                          |
| Wang Shuhua  | 2003 | China   | c            | 140          | 25  | 12                  | RCT           | 6                        |
|              |      |         | b            | 140          |     |                     |               |                          |
| Yang Shulan  | 2008 | China   | c            | 50           | 13–60| 3–8                 | RCT           | 8                        |
|              |      |         | e            | 50           |     |                     |               |                          |
| Li Chaohui   | 2005 | China   | e            | 90           | 18–30| 3–12                | RCT           | 6                        |
|              |      |         | f            | 90           |     |                     |               |                          |
| Wang Weiping | 2007 | China   | a+d          | 145          | 27  | 3                   | Non-RCT       | 5                        |
|              |      |         | b            | 115          |     |                     |               |                          |
| Gu Shuguang  | 2010 | China   | c            | 40           | 18–40| 4–60                | Non-RCT       | 6                        |
|              |      |         | d            | 52           |     |                     |               |                          |
Table 1 continued. Characteristics of the 56 included studies.

| First author      | Year | Country | Surgery type | No. patients | Age    | Follow-up (months) | Research type | Literature quality (star) |
|-------------------|------|---------|--------------|--------------|--------|--------------------|---------------|---------------------------|
| Jiang Wei         | 2010 | China   | f            | 26           | 28.6   | 6–18               | Non-RCT       | 6                         |
|                   |      |         | g            | 30           |        |                    |               |                           |
|                   |      |         | d            | 50           |        |                    |               |                           |
|                   |      |         | a+d          | 50           |        |                    |               |                           |
| Zhang Likang      | 2014 | China   | a            | 60           | 23.4   | 2–6                | Non-RCT       | 7                         |
|                   |      |         | b            | 80           |        |                    |               |                           |
| Guo Xiaochuan     | 2008 | China   | a            | 114          |        |                    |               |                           |
|                   |      |         | b            | 52           |        | 15–47              | Non-RCT       | 6                         |
|                   |      |         | g            | 30           |        |                    |               |                           |
| Zhang Xiaotao     | 2013 | China   | b            | 45           | 23.98  | 6–12               | Non-RCT       | 7                         |
|                   |      |         | d            | 45           | 23.26  |                    |               |                           |
| Zhang Hui         | 2010 | China   | b            | 65           | 29.6   | 3                  | Non-RCT       | 6                         |
|                   |      |         | d            | 65           |        |                    |               |                           |
| Xie Qixuan        | 2004 | China   | a+d          | 85           | 25.7   | 3                  | RCT           | 5                         |
|                   |      |         | f            | 70           |        |                    |               |                           |
| Zhang Zhanzhao    | 2012 | China   | d            | 47           | 25.4   | 3                  | Non-RCT       | 6                         |
|                   |      |         | h            | 39           | 21.1   |                    |               |                           |
| Gu Tingmin        | 2012 | China   | b            | 113          | 24.5   | 6–12               | Non-RCT       | 7                         |
|                   |      |         | d            | 205          |        |                    |               |                           |
| Qian Jiang        | 2003 | China   | a            | 31           | 25     |                    | Non-RCT       | 6                         |
|                   |      |         | b            | 18           | 23.8   |                    |               |                           |
| Wang Wanzhi       | 2006 | China   | b            | 23           | 28.6   | 3                  | Non-RCT       | 5                         |
|                   |      |         | d            | 19           | 27.4   |                    |               |                           |
| Jing Liangyu      | 2010 | China   | a            | 46           | 27     |                    | RCT           | 7                         |
|                   |      |         | b            | 54           | 25     |                    |               |                           |
| Lei Tianbing      | 2014 | China   | a            | 40           | 16–40  | 6                  | RCT           | 6                         |
|                   |      |         | d            | 50           |        |                    |               |                           |
| Li Li             | 2015 | China   | d            | 45           |        |                    | Non-RCT       | 5                         |
|                   |      |         | g            | 45           |        |                    |               |                           |
| Zhang Jianzhuo    | 2014 | China   | d            | 40           | 22.51  |                    | RCT           | 6                         |
|                   |      |         | g            | 40           | 22.7   |                    |               |                           |
| Wang Qian         | 2011 | China   | d            | 90           | 23.53  | 6–12               | RCT           | 6                         |
|                   |      |         | h            | 100          | 20.65  |                    |               |                           |
| Zheng Ruo         | 2013 | China   | a            | 64           | 27.6   |                    | RCT           | 6                         |
|                   |      |         | d            | 64           | 27.2   |                    |               |                           |
| Jiang Bin         | 2012 | China   | a            | 136          | 28.7   | 3                  | RCT           | 7                         |
|                   |      |         | b            | 97           |        |                    |               |                           |
|                   |      |         | c            | 101          |        |                    |               |                           |
Table 1 continued. Characteristics of the 56 included studies.

| First author | Year | Country | Surgery type | No. patients | Age | Follow-up (months) | Research type | Literature quality (star) |
|--------------|------|---------|--------------|--------------|-----|-------------------|---------------|--------------------------|
| Zhang Kaiheng | 2012 | China   | b            | 33           | 24  | 5–72              | Non-RCT       | 6                        |
| Liu Cheng     | 2017 | China   | d            | 115          | 23.3| 6–9               | Non-RCT       | 6                        |
| Guo Qun       | 2007 | China   | g            | 12           | 28  | 6–72              | RCT           | 7                        |
| Mo Lue        | 2007 | China   | d            | 47           | 19–27| 6                 | RCT           | 5                        |
| Chen Jie      | 2011 | China   | b+d          | 177          | 15–40| 6–12              | Non-RCT       | 5                        |
| Chen Hui      | 2011 | China   | b            | 23           | 25  | 6                 | Non-RCT       | 6                        |
| Jing Liangyu  | 2010 | China   | b            | 34           | 27  | 6–60              | RCT           | 6                        |
| Liu Jianyi    | 2004 | China   | d            | 102          | 29.6| 6                 | RCT           | 7                        |
| Wu Weiping    | 2016 | China   | d            | 50           | 27.1| 3                 | RCT           | 7                        |
| Lin Xia       | 2012 | China   | g            | 45           | 26  | 6                 | RCT           | 5                        |
| Huang Haiyan  | 2011 | China   | a            | 105          | 24.6| 6–12              | Non-RCT       | 6                        |
| Liang Haisheng| 2014 | China   | b+d          | 75           | 25.5| 12                | RCT           | 6                        |
| Luo Wenyue    | 2010 | China   | c            | 69           | —   | 6–24              | Non-RCT       | 5                        |
| Wu Shuang     | 2014 | China   | d            | 50           | 37.2| 12                | Non-RCT       | 6                        |
| Zhou Jinghe   | 2015 | China   | d            | 108          | 17–39| 3–12              | RCT           | 5                        |
| Yang Xingang  | 2013 | China   | d            | 120          | 23.5| 6–12              | Non-RCT       | 6                        |
| Zhang Binyu   | 2012 | China   | d            | 58           | 29  | 3                 | Non-RCT       | 6                        |
direct evidence of comparison between the 2 interventions. Moreover, the larger the node was, the larger the sample size was. No link indicated no direct comparative evidence (Figure 2).

**Publication bias**

The funnel graph was used to detect the publication bias. From Figure 4, we can see that the funnel diagram was basically symmetrical and there was no publication bias.

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**Table 1 continued. Characteristics of the 56 included studies.**

| First author   | Year | Country | Surgery type | No. patients | Age | Follow-up (months) | Research type | Literature quality (star) |
|---------------|------|---------|--------------|--------------|-----|--------------------|---------------|--------------------------|
| Zhao Guilan   | 2010 | China   | a            | 90           | 18–40| 6                  | Non-RCT       | 5                        |
|               |      |         | f            | 85           | 6–24 |                    |               |                          |
| Shen Bin      | 2012 | China   | a            | 140          | 24   | 6                  | Non-RCT       | 6                        |
|               |      |         | d            | 140          |      |                    |               |                          |
| Tan Jianping  | 2003 | China   | a            | 62           | 16–49| 3–60               | Non-RCT       | 5                        |
|               |      |         | b            | 76           |      |                    |               |                          |
|               |      |         | f            | 48           |      |                    |               |                          |
| Cai Mei       | 2008 | China   | b            | 80           | 24.3 | 6                  | Non-RCT       | 5                        |
|               |      |         | d            | 82           |      |                    |               |                          |
| Huang Xiaodong| 2012 | China   | b            | 68           | 28.5 | 6                  | RCT           | 6                        |
|               |      |         | d            | 68           |      |                    |               |                          |
| Wu Hailong    | 2005 | China   | b            | 70           | 26   | 6                  | Non-RCT       | 5                        |
|               |      |         | c            | 70           | 30   |                    |               |                          |
| Liu Xiaofeng  | 2014 | China   | d            | 58           | 22   | 18–43              | Non-RCT       | 5                        |
|               |      |         | g            | 36           |      |                    |               |                          |
| Liu Jianzhong | 2008 | China   | d            | 138          | 28   | 3–6                | Non-RCT       | 5                        |
|               |      |         | g            | 55           |      |                    |               |                          |
| He J          | 2018 | China   | g            | 91           | 20   | 6–36               | Non-RCT       | 6                        |
|               |      |         | d+g          | 80           |      |                    |               |                          |
| Chen YT       | 2015 | China   | e            | 66           | 29.8 |                    | Non-RCT       | 6                        |
|               |      |         | g            | 19           | 37.5 |                    |               |                          |
| Cao Han       | 2016 | China   | a            | 71           | 26.8 | 6–24               | Non-RCT       | 6                        |
|               |      |         | d            | 73           |      |                    |               |                          |
| Li Weiwei     | 2010 | China   | g            | 120          |      | 3–24               | Non-RCT       | 5                        |
|               |      |         | h            | 50           |      |                    |               |                          |
| Yu Kefeng     | 2015 | China   | a+d          | 29           | 26.4 |                    | RCT           | 7                        |
|               |      |         | g            | 29           | 25.3 |                    |               |                          |

a – subcutaneous curettage; b – fusiform skin excision; c – CO2 laser treatment; d – subcutaneous pruning; e – YAG laser treatment; f – electric ion therapy; g – Swelling aspiration; h – botulinum toxin A injection; RCT – randomized controlled trial; non-RCT – non-randomized controlled trial.

**Inconsistent test**

There were 28 triangular rings and 5 quadrilateral rings in this network meta-analysis. The consistency of each closed loop study showed that the inconsistency factor (IF) was 0.01–1.43, and the lower limit of 95% CI was basically 0, which indicated that the consistency of each closed loop research was better, and the conclusion was more reliable (Figure 3).

**Publication bias**

The funnel graph was used to detect the publication bias. From Figure 4, we can see that the funnel diagram was basically symmetrical and there was no publication bias.
The network meta-analysis results

There was no statistical significance in 21 of the 45 items of the 10 treatments. In statistical comparison, the cure rate of surgical treatment in AO was better than that in non-operative treatment. And the curative effect of swelling suction subcutaneous pruning was more obvious in the surgical treatment. Among the non-operative treatment measures of AO, botulinum toxin A injection was more effective (Table 2).

Ranking of the therapeutic effects of AO

We used Stata 14.0 to plot the SUCRA curve and used the area under the curve (AUC) to predict the therapeutic effect. The larger the AUC was, the better the curative effect. Figure 5 shows that the therapeutic effects of treatments for AO were as follows: swelling aspiration+subcutaneous pruning > subcutaneous pruning > subcutaneous curettage > subcutaneous pruning > fusiform dermectomy > botulinum toxin A injection.
Table 2. The network meta-analysis results.

|   | a | (0.92,1.80) | 1.21 | (0.97,1.51) | 0.68 | (0.50,0.92) | 1.34 | (0.107,1.69) | 2.78 | (0.48,1.21) | 0.76 | (0.44,0.87) | 0.61 | (0.80,1.36) | 1.05 | (0.72,1.67) |
|---|---|-------------|------|-------------|------|-------------|------|-------------|------|-------------|------|-------------|------|-------------|------|-------------|
| p | 0.78 | 0.56 | 0.37 | 0.53 | 0.78 | 0.39 | 0.92 | 0.36 | 0.96 | 0.33 | 0.68 | 0.59 | 0.11 | 0.54 | 1.35 |
| b | 0.83 | 1.11 | 2.30 | 0.63 | 0.51 | 0.87 | 0.91 | | | | | | | | |
| c | 1.48 | 1.98 | 4.10 | 1.12 | 0.91 | 1.55 | 1.62 | | | | | | | | |
| d | 0.74 | 2.07 | 0.57 | 0.46 | 0.59 | 0.23 | 0.83 | 0.38 | 0.40 | | | | | | |
| e | 1.63 | 1.10 | 2.19 | 4.52 | 1.24 | 1.70 | 1.79 | | | | | | | | |
| f | 1.15 | 1.79 | 1.12 | 2.88 | | | | | | | | | | | |
| g | 0.96 | 1.23 | 1.15 | 0.65 | 1.28 | 2.65 | 0.73 | 0.59 | 1.05 | | | | | | |
| h | 0.91 | 1.17 | 1.10 | 0.62 | 1.22 | 2.53 | 0.69 | 0.56 | 0.95 | | | | | | |

Figure 5. Ranking of therapeutic effects of axillary osmidrosis.

Axillary osmidrosis is mainly treated by 2 kinds of methods: non-surgical treatment and surgical treatment. The main applications of non-surgical treatments are botulinum toxin type A injection, CO₂ laser therapy, and electric ion therapy.

Discussion

At present, AO is mainly treated by 2 kinds of methods: non-surgical treatment and surgical treatment. The main applications of non-surgical treatments are botulinum toxin type A injection, CO₂ laser therapy, and electric ion therapy.
treatment and physical therapy such as laser, electric ion, and so on. The main methods of surgical treatments include subcutaneous pruning, subcutaneous curettage, swelling aspiration, fusiform dermectomy, swelling aspiration+subcutaneous pruning, subcutaneous curettage+subcutaneous pruning, and so on. The non-surgical treatments have the advantages of less injury, faster recovery, and less complications, but may result in easier recurrence of AO, which increase the medical burden of the patients. Although surgical treatments of AO have the advantage of being more thorough, surgical interventions may cause physical damage, form scarring, and have more complications. At present, there are no perfect treatments of AO, and clinical treatment methods have both advantages and disadvantages, which also increases the difficulty for doctors to choose the treatments of AO.

Through our network meta-analysis, we found that swelling aspiration+subcutaneous pruning was the best reported treatment of AO. The second was subcutaneous pruning, but there was little difference between subcutaneous pruning and subcutaneous curettage+subcutaneous pruning. There was no significant difference in the effect of fusiform excision, swelling aspiration, and subcutaneous curettage. Botulinum toxin type A injection was the best in non-surgical treatments. There was no significant difference in the effect of CO\textsubscript{2} laser therapy, YAG laser therapy, and electric ion therapy.

Through the inconsistency test, we found that 28 trilateral rings and 5 quadrilateral rings formed good consistency. And funnel diagram was basically symmetrical, which showed there was no publication bias in the included literature. The results of these 2 tests showed that the network meta-analysis of 10 treatments was reliable.

A total of 56 articles including 8618 patients were included in this meta-analysis, and the conclusion was shown to be highly credible. However, this study also had limitations. First, in this study, the cure rate of AO treatment was analyzed only, and the incidence of complications and the effective rates were not comprehensively evaluated, thus the conclusions were limited. Second, because of different cultures and customs, there were few similar studies available in other countries. Chinese patients were the main research groups in our meta-analysis, so we cannot effectively evaluate the curative effect of different treatment measures in other countries. Third, there is uneven quality of the literature may affect the reliability of the final conclusions. Fourth, although there was no obvious publication bias as shown by the funnel graph, the existence of potential bias of publication was not excluded.

Conclusions

The network meta-analysis evaluated the treatment measures of AO objectively. The results showed that swelling aspiration+subcutaneous pruning was the best in surgical treatments of AO. Botulinum toxin A injection was the best in non-surgical treatments of AO. Overall, the effects of surgical treatments were more significant than that of non-surgical treatments. In the future, doctors should choose treatment methods of AO according to the conclusion of this study and their own experience. However, due to the limitations of this study, the conclusion of this network meta-analysis still needs to be further confirmed by some well-designed randomized controlled trials.

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