

Analysis of factors influencing moxibustion efficacy by affecting heat-activated transient receptor potential vanilloid channels

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Factors of moxibustion (temperature, space and time); moxibustion intensity (a compound factor achieved through comprehensive control of the three individual basic factors mentioned above); and moxibustion quantity (the amount of temperature stimulation applied within a certain unit of time, including the total amount of moxibustion treatment). The results from present study show that the effect of moxibustion therapy appears to be determined by the activation of TRPV1-4, mainly TRPV1 and TRPV2. Temperature (the degree of heat stimulation), time and area (how long the treatment lasts and how many TRPV1-4 channels are activated) affect the intensity of moxibustion treatment to form effective moxibustion quantity; this should be considered in clinical moxibustion application.

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Key words: Moxibustion; Thermal stimulation; Thermoreceptor; Transient receptor potential channels

Abstract

Moxibustion is an important component part of Traditional Chinese Medicine (TCM). Among different kinds of moxibustion methods, thermal stimulation seems to be a pivotal impact factor to the therapeutic efficacy. Based on its thermal characteristic and treated area-skin, we hypothesize that the thermosensitive TRPV channels may involve in the mechanism of moxibustion. This study, by referring to various experimental and clinical data, analyzes the properties and features of transient receptor potential vanilloid (TRPV) subfamily 1-4 and the impact of moxibustion on these channels. The factors impacting the efficacy of moxibustion treatment were analyzed on three levels: the independent ba-

INTRODUCTION

Moxibustion is a Traditional Chinese Medicine treatment in which moxa is burnt to administer heat stimulation by altering local skin temperature and activating cutaneous thermoreceptors. Four thermosensitive ion channels have been reported as thermoreceptors in mammals; these primary channel effectors of mammalian thermal sensation all belong to the transient receptor potential vanilloid (TRPV) subfamily: TRPV1, TRPV2, TRPV3 and TRPV4.¹ As temperature sensation receptors, TRPV1-4 are expressed in primary sensory neurons (sensory nerves), keratinocytes, mast cells, and endothelial cells of the cutis.² Since the TRPV sub-

family contributes to temperature sensation, TRPV receptors potentially form essential part of the primary afferent pathway in moxibustion therapy. As well as being distributed in the cutis, the six TRPV channels in mammals are distributed in the cardiovascular, gastrointestinal, respiratory, urogenital, hematopoietic and immune systems.³ This review focused on the TRPV channels TRPV1-4 because the thermal activation thresholds of TRPV1-4 range from 27-52 °C, which is consistent with the temperature perceived by skin due to the heat stimulation of moxibustion.^{3,4} This review summarizes the factors impacting on the efficacy of moxibustion therapy according to the temperature sensation properties of TRPV1-4.

BASIC FACTORS INVOLVED IN MOXIBUSTION

Temperature

Warm-heat stimulation is the fundamental aspect of moxibustion that produces its therapeutic effect.⁵ Temperature plays a critical role in the effect of moxibustion therapy, and different temperatures produce different levels of efficacy; moxibustion at 46 °C was significantly better at lowering cholesterol in a mouse model of acute hyperlipidemia than moxibustion at 38 °C.⁶ Serial investigations into the effect of sandwiched moxibustion (using a divider, such as a piece of ginger, between the moxa and the skin) on hyperlipidemia-induced abnormal blood vessel function showed no significant difference between medicinal cake-separated and paper pad-separated moxibustion;⁷⁻¹¹ this implies that the temperature, rather than the divider, is essential to the therapeutic effect of moxibustion.

The TRPV channels that sense temperature changes can be identified through their distinct thermal activation thresholds: ≥ 43 °C for TRPV1, ≥ 52 °C for TRPV2, $> 34-38$ °C for TRPV3, and $>27-35$ °C for TRPV4.³ Hence, TRPV1 and TRPV2 are mainly sensitive to heat and noxious heat, while TRPV3 and TRPV4 are sensitive to warmth.¹²

The temperature sensed by skin during moxibustion ranges from 34-57 °C,^{13,14} corresponding with the thermal activation thresholds of TRPV1-4. The local skin temperature during moxibustion varies according to various factors such as the type of moxa material used, the distance between the moxibustion fire (burning terminal) and the skin, and the presence of dividers used in sandwiched moxibustion. The maximum human skin temperature of the contact surface was around 57 °C in sandwiched moxibustion when 2 g moxa was burned.¹³ The maximum temperatures achieved using traditional aconite cake-separated and ginger-separated moxibustion were 57.20 °C and 57.03 °C, respectively; while the peak skin temperature ranged from 45.2-45.5 °C in ginger-separated, direct and suspended moxibustion.¹⁵ In moxibustion using a moxibus-

tion-box, the average skin temperature was above 44 °C when the distance between the skin and the burning terminal was 4 cm, while it ranged from 44-49 °C when the distance was 3 cm.¹⁶ In mild moxibustion of Zusanli (ST 36), the skin temperature was 44.0-45.5 °C at a distance of 4 cm, and was 46.1-47.8 °C at a distance of 3 cm.¹⁶ In hyperlipidemic rats treated with different amounts of ginger-separated moxibustion, the regional temperatures of Zusanli (ST 36) in the six zhuang group (six moxa cones were burnt) and the nine zhuang group (nine moxa cones burnt) were 43.22 °C and 44.05 °C, respectively.¹⁷ The regional temperature in warming moxibustion was initially 34 °C and peaked at 40-43 °C.¹⁴

Temperature is the key to effective moxibustion therapy, because the curative effect is dependent on the skin reaching a certain temperature. According to research conducted on skin temperatures achieved during moxibustion and the thermal activation thresholds for TRPV1-4, we recommend that the peak temperature of moxibustion should be over 40 °C.

Space

The surface area of skin warmed during moxibustion also influences the effectiveness of moxibustion. Moxibustion is practically ineffective when the diameter of the moxa cone is less than 3 fen (3 fen = 0.57-0.72 cm, according to ancient literature).¹⁸ Moxibustion must thermally stimulate a certain area to produce a therapeutic effect. Horizontal three cun (cun is an ancient unit of measure where 1 cun=10 fen) of moxibustion is recognized as a relatively fixed area of thermal stimulation large enough to ensure a curative effect clinically.¹⁹ Neurons in the medullary subnucleus reticularis dorsalis (SRD) of rats were significantly more greatly activated by thermal stimulation at 44 °C in an area of 3.5-4.0 cm diameter, compared with the same temperature stimulation in an area less than 3.0 cm diameter.²⁰ Variation in the distance between the burning terminal and the skin in mild moxibustion, and the thickness of the divider in sandwiched moxibustion is effective in regulating skin temperature. The closer the moxa stick is to the skin, the higher the skin temperature is, and the greater the stimulus produced by moxibustion.

Time

The effectiveness of moxibustion therapy is affected by the duration of a single moxibustion treatment, the total time of the whole treatment course, and the interval time (the frequency of treatment). The duration of treatment in the form of time of each treatment and cumulative time of the whole treatment course influences the temporal summation of stimulation and the curative effect of moxibustion therapy. For example, moxibustion exhibits protective effects to vascular endothelial function only when the quantity of one treatment achieves a certain time period.²¹ Any kind of moxibustion treatment is a continuation of thermal stimulation

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