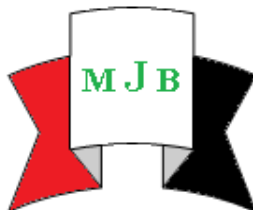


The Role of Vaccinia Virus Vaccination in Protection against Molluscum Contagiosum Infection

Wisam Ali Ameen

College of Medicine, Babylon University, IRAQ

E-mail:wisamali010@yahoo.com



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Abstract

Molluscum contagiosum virus (MCV) is classified within the Poxvirus family in a specific genus, the molluscipox and has features intermediate between the orthopox and parapox groups. The virus occurs throughout the world, most commonly causing disease in childhood. Infection with MCV is worldwide. Three groups are primarily affected: young children, sexually active adults, and immunosuppressed persons, especially those with HIV infection. Vaccinia virus vaccination protect against smallpox infection. The aim of this across secessional study was to assess the role of vaccinia virus vaccination in the protection against molluscum contagiosum infection.

Three hundred patients (165 male, 135 female) with molluscum contagiosum were included in this study their ages ranged from 1 to 80 years with a mean of 28.91 years $\pm 19.53SD$. The patients were divided in two groups, the 1st group including the age of the patients less than thirty five years. The 2nd group includes those patients equal and more than thirty five years. Complete history was taken regarding the age and sex and history of the recurrence of the same lesions. Complete physical examination was done including vaccinia vaccine scar, and BCG scar.

1st group those patient were their age less than 35 years were 150 patients with mean 8.38 years $\pm 7.97 SD$ which they already were unvaccinated with vaccinia virus vaccine, while in 2nd group which those patients were their age 35 years and older were also 150 patients with mean 46 years $\pm 7.88SD$. 110 (73.33%) patients of these group were unvaccinated with vaccinia virus vaccine, while the others 40 (26.66%) patients of these group were vaccinia virus vaccination scar positive, P value less than 0.001(highly significant).

BCG scar was found in 145 (96.66%) patients and the other 5 (3.33%) patients had negative BCG scar in group 1st group, while in 2nd group the BCG scar was found in 98 (65.33%) patients, p value less than 0.0001; confidence interval 95% = (0.2245,0.4021) and the other 52(34.66%) patients were had negative BCG scar.

History of the recurrence of the lesions were found in 51(34%) patients in the 1st group, while the recurrence of the lesions were found in 41 (27.33%) patients in the 2nd group, p value more than 0.05 not significant, confidence interval 95% = (- 0.0377, 0.1710). The result of the 2nd group was subdivided in to two groups, A and B.

Group A those unvaccinated with vaccinia virus vaccine patients with age equal and more than 35 years which were 30 (20%) patients, while group B patients with age equal and more than 35 years with positive vaccinia virus scar which were 11 (7.33%) patients, p value was 0.003 which is significant.

According to our knowledge, this study may be the first study in Iraq showed that the vaccinia virus vaccine may have the protective effect in the prevention of molluscum contagiosum and decrease recurrence rate of this infection.

Keywords: Molluscum contagiosum virus, vaccinia virus vaccination.

الخلاصة :

فيروس الملساء المعدية يُصنّف ضمن عائلة Poxvirus تحت جنس molluscipox وعِندَه المِيزَاتُ متوسطةٌ بين مجموعة orthopox ومجموعة parapox. الفيروس يحدث في كافة أنحاء العالم. المرض شائعاً جداً في الأطفال. عدوى فيروس الملساء المعدية بصورة رئيسية تكون في ثلاث مجموعات: الأطفال ، بالغون نشيطون جنسياً، وأشخاص قليلين المناعة. يُحْمِي تطعيمُ فيروس Vaccinia ضدَّ عدوى الجدري. هدف الدراسة هو تقيّم دور تطعيم فيروس vaccinia في الحماية ضدَّ عدوى الملساء المعدية.

ثلاثمائة مريض (١٦٥ ذكر، ١٣٥ أنثى) مصابين بالملساء المعدية اخذوا في هذه دراسة وكانت أعمارهم تتراوح من ١ إلى ٨٠. المرضى قُسموا إلى مجموعتين، المجموعة الأولى تضم المرضى الذين أعمارهم أقل من خمس وثلاثون سنة. المجموعة الثانية ضمت أولئك المرضى الذين

أعمارهم مساوي أو أكثر من خمس وثلاثون سنة. التاريخ الكامل للمرضى قد أخذَ بخصوص العمر والجنس وتأريخ تكرار نفس المرض. الفحص السريري الكامل اخذ متضمناً ندبة لقاح vaccinia، وندبة BCG.

المجموعة الاولى كانت أعمارهم أقل من ٣٥ سنة وكانوا ١٥٠ مريض متوسط أعمارهم ٨.٣٨ سنة ± ٧.٩٧ كلهم كانوا غير مُلقَّحون بلقاح فيروس vaccinia، بينما في المجموعة الثانية والذين كانوا أعمارهم مساوي أو أكثر من ٣٥ سنة وكانوا أيضاً ١٥٠ مريض متوسط أعمارهم ٤٦ سنة ± ٧.٨٨ . ١١٠ (٧٣.٣٣%) مرض من هؤلاء كانوا غير مُلقَّحون بلقاح فيروس vaccinia، والآخرين ٤٠ (٢٦.٦٦%) مرضا كان عنده ندبة تطعيم فيروس vaccinia.

وُجِدَتْ ندبة BCG في ١٤٥ (٩٦.٦٦%) مريضاً، والآخرين ٥ (٣.٣٣%) مرضا لم يكن عندهم ندبة BCG بالنسبة الى المجموعة الاولى، بينما في المجموعة الثانية، ندبة BCG وُجِدَتْ في ٩٨ (٦٥.٣٣%) مرضا، والمرض الآخرون ٥٢ (٣٤.٦٦%) لم تكن عندهم ندبة BCG رجوع المرض وُجِدَ في ٥١ (٣٤%) مرضا في المجموعة الأولى، بينما رجوع المرض وُجِدَ في ٤١ (٢٧.٣٣%) مرضا في المجموعة الثانية. المجموعة الثانية قُسمَتْ إلى مجموعتين، (أ) و (ب). مجموعة (أ) أولئك المرضى الغير مُلقَّحين بلقاح فيروس vaccinia وكانوا ٣٠ (٢٠%) مرضا، بينما مرضى مجموعة (ب) أولئك المرضى الملقَّحين بندبة فيروس vaccinia والذين كانوا ١١ (٧.٣٣%) مرضا.

وبحسب علمي، فإن هذه الدراسة هي الأولى في العراق التي بينت ان لقاح vaccinia لديه التأثير الوقائي في منع فيروس الملساء المعدية وتقليل نسبة تكرار المرض.

مفاتيح الكلمات: فيروس الملساء المعدية، تطعيم فيروس vaccinia

Introduction

Molluscum contagiosum virus is classified within the Poxvirus family in a specific genus, the molluscipox [1] The poxviruses are the largest animal viruses, being only slightly smaller than the smallest bacteria, and they are just visible by light microscopy. They are complex, double-stranded DNA viruses which replicate in the cytoplasm and are especially adapted to epidermal cells. Within the cytoplasm, they produce eosinophilic inclusion bodies (Guanieri bodies). [2]

The human is host for four genera: (2)

1- *orthopoxviruses*: variola (smallpox), vaccinia, monkeypox and cowpox, which are ovoid, 300 × 250 nm

2- *parapoxviruses*: orf and milker's nodule viruses, which are cylindrical, 260 × 160 nm

3- *molluscipox*: molluscum contagiosum, intermediate in structure and 275 × 200 nm

4- *yatapox*: tanapox virus.

Smallpox infection is now eliminated from the world and routine vaccination against it has been abandoned. Eradication of smallpox was accepted at the 23rd World Health Assembly in May 1980 [3].

Stocks of smallpox virus still exist in government agencies in the USA and Russia. Recent global terrorism has

reawakened concerns that the virus could be released as a biological weapon. This has led to a rapid increase in the number of medical and military personnel receiving vaccinia vaccination and an awareness of the clinical features of smallpox infection. [2]

In 1796 the English doctor Edward Jenner succeeded in preventing the development of smallpox in the 8 year old James Phipps by inoculation of contagious material from infected cows. A month and a half later he checked the vaccine effectiveness by injecting live smallpox virus into the boy, who stayed fully protected and did not develop any symptoms of the disease. Jenner introduced the vaccination as a method of immunization[4] The traditional variola vaccine is live vaccine from calves: Dryvax. Another type of traditional vaccine is tissue or cell type cultural vaccine, using vaccinia virus, which is comparatively non virulent. These vaccines are not applicable in immunocompromised humans. They can cause severe complications in some of the cases[5,6,7]

Molluscum contagiosum virus is classified within the Poxvirus family in a specific genus, the molluscipox [1] and has features intermediate between the orthopox and parapox groups. It infects humans, causing characteristic skin papules.(8) Restriction endonuclease and PCR analyses

of molluscum contagiosum DNA have identified two main types, MCV-1 and MCV-2, with two much rarer types, MCV-3 and MCV-4 [9,10] The virus occurs throughout the world, most commonly causing disease in childhood[11] The age of peak incidence is reported as between 2 and 5 years . A later incidence peak in young adults is attributable to sexual transmission with lesions more common in the genital area. The individual lesion is a shiny, pearly white, hemispherical, umbilicated papule which may show a central pore[11]

The aim of this study was to assess the role of vaccinia virus vaccination in protection against molluscum contagiosum infection.

Patients and Methods

This is across secession study was done in the out patient department of dermatology and venereology of Merjan teaching hospital for a period extended from September 2013 to September 2014. Three hundred patients (165 males, 135 females) with molluscum contagiosum were included in this study. Their ages ranged from 1 to 80 years with a mean of 28.91 years $\pm$ 19.53SD. The patients were divided in two groups, the 1st group including the age of the patients less than thirty five years and the 2nd group included those patients equal and more than thirty five years. The cause of taken this cut off period of age between the two groups is the routine vaccination of the Iraqi public against smallpox stopped in 1977. Complete history was taken regarding the age, sex and history of the recurrence of the same lesions. Any history of chronic illness (diabetes, malignancy, and other immune compromised) and molluscum contagiosum of genital area all were excluded. Complete physical examination was done including vaccinia vaccine scar, and BCG scar.

Statistical analysis

chi-square test and test of proportion were used to determine significant differences between the groups. P value < 0.05 was considered as level of significance.

Results

All patients were completed the study. The 1st group included those patient whom their age less than 35 years and were 150 patients with mean 8.38 years $\pm$ 7.97 SD. They were already unvaccinated with vaccinia virus vaccine. The 2nd group were those patients with age 35 years and older and were also 150 patients with mean 46 years $\pm$ 7.88SD. 110 (73.33%) patients of this group were unvaccinated with vaccinia virus vaccine, while the others 40 (26.66%) patients of this group were with vaccinia virus vaccination scar positive, P value less than 0.001 (highly significant).

BCG scar was found in 145 (96.66%) patients and the other 5 (3.33%) patients had negative BCG scar in the 1st group, while in the 2nd group the BCG scar was found in 98 (65.33%) patients, p value less than 0.0001; confidence interval 95% = (0.2245,0.4021) and the other patients 52 (34.66%) had negative BCG scar.

History of the recurrence of the lesions was found in 51(34%) patients in the 1st group , while the recurrence of the lesions was found in 41 (27.33%) patients in the 2nd group, p value more than 0.05 not significant, confidence interval 95%= (0.0377, 0.1710). The result of the 2nd group was subdivided in to two groups, A and B.

Group A those unvaccinated with vaccinia virus vaccine patients with age equal and more than 35 years which were 30 (20%) patients, while group B patients with age equal and more than 35 years with positive vaccinia virus scar in the 11 (7.33%) patients, p value was 0.003 which is significant.

Discussion

Molluscum contagiosum virus is classified within the Poxvirus family in a specific genus, the molluscipox[1] Infection with molluscum contagiosum virus is worldwide. Three groups are primarily affected: young children, [11] sexually active adults, and immunosuppressed persons, especially those with HIV infection. [12] The aim of this study was to

show the association between the vaccinia virus vaccine and molluscum contagiosum infection and if this vaccination may has protective effect against molluscum contagiosum infection in certain age group than others.

From this study the mean age of the 1st group is 8.38 years and this run with other published data which showed that one of the important groups is childhood age. [11,12]

So why this disease more common in this age group?

In order to answer this question we should know the way of transmission of this disease. Infection follows contact with infected persons or contaminated objects. [11,12]

So we will discuss this question. One of the important explanation that's the child is close contact with one another [11] but there is no difference between the contact of the adult with infected persons or contaminated objects and the contact of the children with the same things and the importance of epidermal injury is unknown[11]

other explanation is the lowest antibody prevalence was in children aged 6 months to 2 years (3%), and seropositivity increased with age to reach 39% in persons aged 50 years or older[13] But more recent study showed specific antibodies have been found in about 58–73% of adult patients with molluscum contagiosum, and, perhaps due to unrecognized infection (14) but these have not been demonstrated to have a role in disease clearance[11]

Also one of the important explanation is a clinical impression that molluscum contagiosum is commoner in patients with atopic eczema. [11] But more recent studies , 1st done in Japan, nursery school-based study of over 1100 children failed to find a statistically significant increase in molluscum contagiosum among the children who had a history of atopic dermatitis compared with children without atopic dermatitis[15]

Another 2nd study was dome in the Brazil was showed no statistically significant difference in the recurrence rates associated with molluscum contagiosum or in the

number of lesions between the patients who had atopic dermatitis and those who did not[16] All Our patients in the 1st group were unvaccinated with vaccinia virus vaccine, but more than 96% of them were BCG scar positive. The percentage of skin disease among BCG vaccinated individuals was significantly lower compared with healthy controls, these diseases include psoriasis, fungal infection, cutaneous leishmaniasis, and lichen planus, indicating that BCG decreases the frequency of skin diseases [17] ,and BCG is well known its important role in treatment of certain viral infection (wart) [18] but all our patients in this group are not taken vaccinia virus vaccine so BCG virus may not has a role in the protection from the molluscum contagiosum as like as wart. (18)

Other risk group for this viral infection is the sexually active adult and immunosuppressed patients[12] all our patients are apparently healthy and had no genital lesions, the 2nd group with our patients were their age equal and more than 35 years, 110 (73.33%) patients in this group were unvaccinated with vaccinia virus vaccine , where the others 40 (26.66%) patients in this group were positive scar for vaccinia virus vaccine, P value less than 0.001 (highly significant), while the BCG scar was found in 98 (65.33%) patients and the other 52 (34.66%) patients were had negative BCG scar. So the majority of our patients in this age group is unvaccinated with vaccinia virus vaccine (more than 73% of the patients).

So this may explain the role of the vaccinia virus vaccine in reduction risk of occurrence molluscum contagiosum infection in certain age group , and this can support the same finding of the previous multicentre case control study which has demonstrated a reduced risk of melanoma associated with Bacille Calmette Guerin (BCG) and/or vaccinia vaccination in early childhood due to immune surveillance effect of the vaccine [19] .The recurrence rate was found in 51(34%) patients in the 1st group, while the recurrence rate was found in 41 (27.33%) patients in the 2nd

group, p value more than 0.05, not significant, confidence interval 95% = (0.0377, 0.1710), while the recurrence rate in the group A (unvaccinated) patients of the 2nd group were 30 (20%) patients compared with group B(vaccinated) patients of the 2nd group were 11 (7.33%) patients, p value was 0.003 which is significant.

This finding may explain the role of the vaccinia virus vaccine in the reduction risk of molluscum contagiosum infection and decrease rate of recurrence of this disease. This results can explained as molluscum contagiosum shares a number of genomic similarities with other poxviruses, and approximately two-thirds of the viral genes are similar to those of vaccinia and variola virus[20] and this shearing of genomic material with vaccinia may result in cross protection to both smallpox and molluscum contagiosum in those patient with vaccinia virus vaccination. This fact was discovered by Edward Jenner (18th Century) who is observed that persons infected with cowpox did not contract smallpox. Jenner demonstrated that inoculating a person's skin with material from a human pustular lesion caused by the cowpox virus provided complete resistance to smallpox virus.(21) This new method, called vaccine (named from vacca [cow]), quickly gained popularity and was used all over the world by the early 19th century[22]

The other thing which may support our finding is the prevalence of molluscum contagiosum infection has risen significantly in the past several decades, with an 11-fold increase noted in one united state study of patient visits for this disorder over a two decade span [20] as the routine vaccination of the American public against smallpox stopped in 1972 after the disease was eradicated in the United States[23]

According to our knowledge, this study may be the first study in Iraq showed that the vaccinia virus vaccine may have the protective effect in the prevention of molluscum contagiosum and decrease recurrence rate of this infection.

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