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**Effectiveness of Glycyrrhizinic Acid  
in improving Molluscum Contagiosum  
in pediatric patient populations**



# **EFFECTIVENESS OF GLYCYRRHIZINIC ACID IN IMPROVING MOLLUSCUM CONTAGIOSUM IN PAEDIATRIC PATIENT POPULATIONS**

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## **Summary**

**Introduction:** Molluscum Contagiosum (MC) is a viral infection of the skin that mainly affects children; even though it is self-limiting, parents often seek help to alleviate their children's suffering.

**Objective:** Evaluate the effectiveness and the safety of the topical application of glycyrrhizinic acid (Glizigen) in patients with MC.

**Method:** An open, prospective, longitudinal pilot study was carried out on 55 patients aged 0-18, who had been clinically diagnosed with scattered MC on multiple parts of the body. The treatment consisted in washing the lesions three times the day with a bath gel containing glycyrrhizinic acid and then applying the same product in spray format on the lesions for 10 weeks. Their progress was monitored by the specialist at fortnightly check-ups. Their response to the treatment was assessed according to the relationship between the decrease in the number of lesions and the time taken for them to disappear, plus the occurrence of any adverse reactions.

**Excellent:** The MC had disappeared altogether by the end of the 10 week period. **Good:** More than 50% of the MC had disappeared at the end of the treatment.

**Normal:** The number of MC had decreased by less than 50%.

**Bad:** The clinical condition remained the same.

**Results:** All the lesions disappeared in 100% of the patients treated; the lesions of 88.2% disappeared in the first 8 weeks of treatment. No adverse reactions

were reported while the product was being used, there weren't any relapses either.

**Conclusion:** Glycyrrhizinic acid is an excellent option to cure scattered MC that is difficult to treat.

**Key Words:** *Molluscum Contagiosum*, glycyrrhizinic acid, Glizigen, viral skin infection.

## **Introduction**

Molluscum contagiosum (MC) is a viral skin infection that affects keratinocytes. It is produced by a brick-shaped poxvirus measuring between 150-350 nanometres with one internal membrane and an external one that surrounds a central nucleus. Moreover, it has two side bodies between the membranes, the viral genome is a single linear molecule of double-stranded DNA of about 190 kpb. There are two types of MC virus, VMC-1 and VMC-2, the former is the most common.<sup>(1)</sup>

The DNA replication only occurs in the epidermal cell cytoplasm. By carrying out a histological study of the lesion, the cells from the stratum spinosum can be distinguished from those of the stratum granulosum with multiple basophilic, cytoplasmic inclusions associated with the mature virions.

This virus is cosmopolitan.<sup>(2,3)</sup> In fact, it is a very common disease. It mainly affects children of any age up to adolescence, immunocompromised patients and the sexually active; notwithstanding this, some authors believe that adults build up a certain resistance to the infection.<sup>(4)</sup> Males and females of any skin colour are equally affected, although a higher incidence has been observed in individuals with personal or a family history of atopic dermatitis.<sup>(5)</sup>

The incubation period varies from one to a few weeks. It is very contagious; it is estimated that 35% of family members exposed to MC actually develop it afterwards.<sup>(1)</sup>

Epidemiological studies suggest that there are different factors associated with the transmission of the virus that include humidity, heat and poor hygiene. The viral infection is thought to spread through direct skin-to-skin contact or through fomites; swimming pools, public baths or showers and conglomerations all increase the risk of catching the skin disease.<sup>(5,6)</sup>

*MC is also known as Molluscum Contagiosum or Molluscum Sebaceum as the author Hebra called it. It is benign, it mainly affects children aged between 2 and*

12, it can clear up on its own within a period that ranges anywhere from 6 months to a few years in immunocompetent individuals. In clinical terms, it is characterised by papules of 3 to 6 mm in size that are pearly-white or skin coloured, shiny and umbilicated, with a caseous, fibrous plug, cell debris and infectious mature virions in the centre. On average, the majority of patients have 20 lesions that are spread out over the trunk, the abdomen, the limbs, the periocular area and the genitals. Patients with severe immunodeficiency disorders might suffer from the scattered or generalised forms of the skin disease and a common complication of such is a bacterial infection.

In the majority of cases, the aforementioned lesions can be asymptomatic although sometimes moderate to severe itching might be experienced along with an eczematous reaction which might develop in the area affected by the molluscum contagiosum.

A clinical diagnosis is usually made and in more uncertain cases a skin biopsy might also be done for the histopathological study with H&E stain to identify either molluscum or Henderson-Paterson bodies; 90% of the patients have IgG antibodies. Diagnosis is carried out by means of electron microscopy, a polymerase chain reaction (PCR), ELISA, and immunohistochemistry.

Even though this skin disease is self-limiting, parents often seek help to alleviate their children's suffering. In the case of adolescents and adults, the fear of the infection spreading makes them seek immediate medical assistance to try and control it.

One question that must be asked in relation to patients affected by MC is whether treatment is absolutely necessary or not, which is why factors like the number of lesions, the location of such and the possibility of being able to provide the most non-invasive and painless treatment possible to try and cure the viral infection must all be taken into consideration.

Numerous types of therapy have already been tested to try and avoid having to use the more classic forms of treatment such as curettage of the lesions, liquid nitrogen or electrofulguration because although these are effective procedures, they can have both a physical and a psychological impact on the child in question.

Using a 0.9% cantharidin solution to treat Molluscum Contagiosum has had good results.<sup>(7)</sup> So has the aqueous solution of 15% potassium hydroxide used in another study, which produced encouraging results.<sup>(8)</sup> There are also reports of salicylic acid<sup>(9)</sup>, topical 5% imiquimod cream,<sup>(10)</sup> dynamic phototherapy and laser

therapy<sup>(11, 12)</sup>, griseofulvin and cimetidine, all being used to treat it.

In view of the aforementioned, we decided to test another type of user-friendly, non-invasive therapy for MC that has minimum adverse effects, for quite a short period of time to control or permanently remove the lesions.

Our treatment consisted in using a natural product that is directly extracted from liquorice root (*glycyrrhiza glabra*) by means of a biocatalytic process; it is currently one of the most popular medicinal plants available. It is very well-known for its anti-inflammatory and antiviral properties; it is also a demulcent, germicide and an antibacterial agent. The main active ingredient (glycyrrhizinic acid 0.1 g in 100 mg of the vehicle) interacts with the virus proteins and according to the actual stage of the viral infection this can result in the inactivation of extracellular free virus particles, the prevention of the intracellular decapsulation of infectious particles and the deterioration of the assembling capacity of the structural components of the virus.

Its beneficial effects are enhanced by molecular activation that considerably improves the biological activity of the antioxidizing molecules and that of all other molecules that contain carboxyl groups in their structure; it can also make antiviral activity up to 10,000 times as effective.<sup>(13)</sup>

For our study a combination of the topical application of this product was used (this consisted of spraying the product on the lesions and washing them with an enriched bath gel containing the same product to enhance the overall effect).

Our experiment was the first time that this type of therapy had ever been used on MC; the patients who took part in our clinical trial, who had had problems using other types of treatment or who had had frequent bouts of the MC infection previously, responded very well to our daily treatment.

Considering this and the fact that this is user-friendly and cosmetically acceptable product, it was decided that it should be used on patients suffering from MC who were being treated at the Dermatology unit of the Hospital Pediátrico Docente Juan Manuel Márquez in Havana, from September 2011 to March 2012.

The objective of this study was to evaluate the effectiveness and the safety of using glycyrrhizinic acid to treat MC and to determine whether any adverse reactions were experienced during the treatment.

## Method

An open, prospective, longitudinal pilot study (phase II clinical trial) was carried out from the 1st of July, 2011 to the 1st of February, 2012. The population under analysis consisted of patients aged 0 to 18 of both genders who were being treated at the outpatients unit of the Hospital Pediátrico Docente Juan Manuel Márquez (HPDJMM) in Havana, after they had been clinically diagnosed with MC and they had all given their written informed consent to take part.

### Inclusion criteria

Patients who had been clinically diagnosed as having MC and as being immunocompetent, aged between 0 and 18, of both genders and any skin colour, who had given their written informed consent to take part prior to starting the treatment.

### Exclusion criteria

Patients with immunodeficiency disorders (infection caused by HIV-AIDS, anarcho-proliferative processes, those undergoing prolonged treatment with systemic steroids or immunosuppressive drugs and those with congenital or acquired immunodeficiency disorders). Patients that had received some kind of treatment one month before the day of the consultation or who were hypersensitive to the product.

### Criteria for leaving the trial

Missing two or more check-ups, experiencing a serious adverse reaction or intolerance to the product used or the patient requesting to stop use the treatment.

The end sample was made up of 55 patients clinically diagnosed as having MC who were being treated at the outpatient's Dermatology unit at HPDJMM. They were told to wash the area affected by MC three times a day with a bath gel containing glycyrrhizinic acid and then apply the same product in spray format on the lesions for a period of 10 weeks. Photos were taken of the lesions of each patient before and after the treatment (fig. 1), their general details and those of the follow-ups were all then included in their own individual data collection record. Descriptive statistical indicators and percentages were used as it was a small sample without a control group.

## Clinical therapeutic evaluation

Each patient had to go for a fortnightly check-up during the 10 weeks of treatment to assess their progress and their response to the treatment.

The disappearance or the decrease in the number of lesions and the occurrence of adverse effects were taken into consideration for the final evaluation of the treatment.

### Main variable

#### • Disappearance or decrease in the number of lesions

**Excellent (E):** When 100% of the lesions had disappeared by the end of the treatment period.

**Good (G):** When 50% or more of the lesions had disappeared by the end of the treatment period.

**Normal (N):** When less than 50% of the lesions had disappeared by the end of the treatment period.

**Bad (B):** When the clinical condition remained the same, unchanged, or if new lesions had appeared by the end of the treatment period.

### Secondary variable

#### • Time taken for all the lesions to disappear

**Excellent (E):** All the lesions had disappeared within 4 weeks of treatment.

**Good (G):** All the lesions had disappeared within 8 weeks of treatment.

**Normal (N):** All the lesions had disappeared within 10 weeks of treatment.

**Bad (B):** If the lesions were the same at the end of the 10 week treatment period or if new lesions had appeared within this period.

#### • Occurrence of adverse events or not

**Null (N):** No adverse events were experienced

**Mild (MI):** The adverse event does not interfere in any significant way with the subject's daily activities; it might cause transient discomfort or it might not require any treatment.

**Moderate (M):** The event does limit or interfere with the subject's daily activities, but it does not put their health at risk; treatment may be required to alleviate the adverse events.

**Quite severe (QS):** The adverse event significantly limits the subject's daily activities although it is not life-threatening; its clinical significance might be irrelevant, but it lasts quite a time, or the subject suffers from a very severe case of such and does not respond to the treatment administered or they might have to temporarily stop using the product that is being tested.

**Severe (S):** When the product being used is life-threatening.

The patients' gender (male, female), age, skin colour, number and type of lesions (periocular, face, neck, trunk, limbs, genitals and various places of the body) were all taken into consideration.

### Method of use of the treatment

The lesions on all of the patients were counted and then they were given the product to be used. The topical spray format of GA was applied on the affected area 3 times a day after the area in question had been washed with a bath gel containing the same product. The patients' progress was assessed at fortnightly check-ups during the 10 week treatment period.

### Results

The clinical trial was carried out on 55 patients. By the end of the 10 week treatment period, 51 patients were left, 4 had abandoned it during this period on their own free will.

Out of the 55 patients included in the clinical trial, the 1 to 5 year old age group, with 21 patients or 38.2%, was seen to be the most affected and 70.9% of them or 39 cases were white patients. There was no significant gender-related difference. (Table 1)

On analysing the distribution of the lesions, the trunk was the most frequently affected part of the body, standing for 32.7%, followed by scattered lesions on numerous parts of the body, representing 25%, and then the limbs, standing for 16 %. (Table 2)

On determining the number of lesions on the patients, 40% of them were seen to have between 1 and 10 lesions, 41.8% between 11 and 20 lesions, 10.9% between 21 and 30 lesions and 7.3% with more than 30

lesions, in one of the latter cases the patient had the lesions spread out in shetts. (Table 3)

In our clinical trial, 100% of the lesions of the 51 patients that made up the sample were seen to disappear altogether within the 10 week treatment period. (Table 4)

In terms of the time taken for the lesions to disappear, by the 4th week the lesions had disappeared altogether in 12 patients, which stands for 23.5% of the total population. By the 8th week, the lesions had completely disappeared in another 28 patients (54.9%). and by the end of the 10th week of treatment, all the molluscum had disappeared in the other 11 patients (21.6%). There were no relapses either in the patients whose lesions had cleared up in the first few weeks of treatment. (Table 4)

During the check-ups none of the patients treated mentioned or were seen to have experienced any adverse events to the product used.

### Discussion

On analysing the sociodemographic variables, the most affected age group was that of the children aged 1-5, which coincides with the results obtained by Dr. Hinostroza & cols. in a study carried out in Mexico where those in the 0-5 year old age group were the most affected.<sup>(14)</sup> This differs from the results obtained by Dr. Monteagudo & cols., where the most affected age on average was 10.7 and Dr. Vinder & cols, who reported that it was on average the 6 year old age group.<sup>(15)</sup>

According to the national annual statistics yearbook, the fact that it is mainly white patients who suffer from MC might be conditioned by the predominant skin phototype in our country;<sup>(16)</sup> no reports associated with skin colour were found in the literature review. Behaviour in terms of gender was similar, which coincides with some of the reports published by Monteagudo & cols.<sup>(15)</sup>, but not with what has been reported in other studies carried out in which females were seen to be most affected,<sup>(14)</sup> although in one study it was the male population.<sup>(17)</sup>

In our study, the majority of the lesions (32.7%) were located on the trunk, then on numerous parts of the body; this is in line with the observations made by Monteagudo & col., in which 58.6% of all the Molluscum Contagiosum where located in this area of the patients' bodies.<sup>(18)</sup> 7% of the lesions were found to be located on the genitals, this differs from the results obtained by

Dr. Laxmisha & cols., in which 14.5% of the lesions were located in this area. Incidentally, there was no history of sexual abuse or STI in either study where the patients had MC on their genitals.<sup>(17)</sup>

With regard to the most common number of lesions found, the majority of cases (81.8 %) had less than 20 lesions, which coincides with the data obtained from the literature review, in which the normal amount is usually less than 30 lesions in immunocompetent individuals.<sup>(19)</sup>

As for the response to the treatment in terms of the decrease or the disappearance of the lesions, they all cleared up in 100% of the patients treated by the end of the test period. This result is far better than that obtained by Arican, who found that in an experimental study on 12 children, there was a remission in a total of 7 cases treated with a cream containing 5% Imiquimod over a 16 week period.<sup>(20)</sup> A study carried out by Ross & Orchard showed that the combination of Imiquimod with Cantharidin produced a 90% improvement in 12 out of 16 patients within a period of 5 weeks.<sup>(21)</sup>

In another study in which topical treatment containing 20% KOH was used, the lesions were reported to have disappeared within a period of 17 days, although there were a lot of adverse effects,<sup>(22)</sup> which means that this type of treatment, that is quite a traumatic and aggressive procedure, is not suitable for small children as it might have both a psychological and aesthetic impact on them.

Studies in which the traditional curettage technique were used,<sup>(23)</sup> had a high incidence of relapses from the 4th to 8th week, unlike our study, in which there were no relapses or new lesions appearing throughout the treatment, even in the patients whose lesions had cleared up in the first 4 weeks.

In terms of the time taken for the MC lesions to disappear, the lesions of 12 out of the 51 patients treated (23.5%) disappeared in the first 4 weeks and within 8 weeks for another 28 patients (54.9%). The lesions of the rest (11 patients or 21.6%) had all cleared up by the 10th week of the treatment, which means that possibly an average time of 8 weeks is needed for the lesions to clear up. In the study carried out by Dohil & Prendiville, all the lesions cleared up in 10 out of the 13 cases treated with oral cimetidine after 8 weeks of treatment.<sup>(24)</sup> Ormerod & col. used nitric acid combined with 5% Salicylic acid in an occlusive dressing in their study which managed to cure 75% of the cases treated within about 2 months, although adverse effects were frequently reported.<sup>(25)</sup>

No adverse effects were experienced with the topical format of glycyrrhizinic acid during the treatment period of our clinical trial, unlike what has been reported in other publications when other types of therapy have been used.<sup>(22, 23, 24, 25)</sup>

## Conclusions

MC is a viral disease. It is a very common complaint that has to be treated at paediatric dermatology units because it mainly affects children and it's one that has increased the demand for health care in the last few decades. It is important that the specialist chooses the right type of treatment that suits the patient in question. Glycyrrhizinic acid (Glizigen) turned out to be a safe and effective topical treatment for *Molluscum Contagiosum*. Moreover, it is user-friendly and cosmetically acceptable.

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## ANNEXES

**Figure 1.** Photodocumentation of patients included in the clinical trial before and after the treatment with glycyrrhizinic acid (Glizigen)



Table 1.  
Baseline characteristics of the patients included in the study. Effectiveness of glycyrrhizinic acid in improving paediatric patients with MC. Hospital Pediátrico Docente Juan Manuel Márquez. July 2011-February 2012-

Variable	Number of patients	Percentage
<b>AGE</b>		
Younger than 1	0	0
1-5 years old	21	38.2
6-10 years old	20	36.4
11-15 years old	9	16.4
16-18 years old	5	9.1
<b>GENDER</b>		
Female	26	47.3
Male	29	52.7
<b>SKIN COLOUR</b>		
White	39	70.7
Mestizo	12	21.8
Black	4	7.3

Source: Data collection record. (N=55)



**Table 2.**

Distribution of patients according to the location of the lesions. Hospital Pediátrico Docente Juan Manuel Márquez. September 2011-March 2012

Location of the lesions	No. patients	Percentage
Periocular area	6	10.9
Face	3	5.45
Neck	1	1.85
Trunk	18	32.72
Limbs	9	16.36
Genitals	4	7.27
Multiple	14	25.45
Total	55	100

Source: Data collection record. (N=55)

**Table 3.**

Distribution of patients according to the number of lesions. Hospital Pediátrico Docente Juan Manuel Márquez. September 2011-March 2012

No. lesions	No. patients	Percentage
1-10	22	40
11-20	23	41.8
21-30	6	10.9
> 30	4	7.3
<b>Total</b>	55	100

Source: Data collection record. (N=55)

**Table 4.**

Evaluation of the response to the treatment. Hospital Pediátrico Docente Juan Manuel Márquez. September 2011 - March 2012

Evaluation according to the number of lesions that disappeared	Time taken for lesions to disappear		
	4 <sup>th</sup> week	8 <sup>th</sup> week	10 <sup>th</sup> week
<b>Excellent</b>	12 (23.5%)	28 (54.9%)	11 (21,6%)
<b>Good</b>	28 (54.9%)	11 (21.6%)	0 (0.0%)
<b>Normal</b>	11 (21.6%)	0 (0.0%)	0 (0.0%)
<b>Bad</b>	0 (0.0%)	0 (0.0%)	
<b>Total</b>	51		

Source: Data collection record. (N=51)