

## Case Report

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# *Nigella sativa* and Saudi Honey Diminish Infections and Improve the Survival in a Kostmann's Syndrome Patient: Case Report

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### Abstract:

Severe chronic neutropenia is the main feature of infantile genetic agranulocytosis (Kostmann's Syndrome) associated with recurrent febrile bacterial infections episodes with fatal outcome. This study evaluated the effects of *Nigella sativa* seeds (Black seeds) and Saudi honey supplementation on the survival rate and frequency of febrile episodes of a Kostmann's syndrome patient. The patient was diagnosed with Kostmann's syndrome at 7 months of age and showed persistent neutropenia with an absolute neutrophilic count of  $0.2 \times 10^9/L$  and was admitted 26 times for infection in the first 2 years of his life. Unfortunately, he had no human leukocyte antigen matching donor for stem cell transplant and developed a cataract after being given granulocyte colony stimulating factor therapy Filgrastim. After supplementation with *Nigella sativa* and honey, the patient showed dramatic improvement. There was no admitting history to the hospital related to infection, and he has resumed a normal life style with regular school attendance. The patient is currently 15 years old. It would be concluded that a synergetic effect exists between *Nigella sativa* and honey which will improve the potency of the immune system with a marked reduction in infection and improved his survival. Further studies are needed to confirm the conclusion.

### Keywords:

Infection, Kostmann's syndrome, *Nigella sativa*, Saudi honey, survival

## Introduction

Kostmann's syndrome is a rare autosomal recessive disorder associated with severe congenital neutropenia resulting from the impairment of myeloid differentiation in bone marrow. Patients with this syndrome are susceptible to severe pyogenic infections resulting in their demise at a very early age.<sup>[1-7]</sup> The etiology of this syndrome is not yet fully elucidated.<sup>[8,9]</sup> Sepsis mortality is reduced by an advent of granulocyte colony stimulating factor (G-CSF) therapy Filgrastim.<sup>[4-6,10-12]</sup> It manifests itself in infancy with life-threatening bacterial infections.<sup>[1-7]</sup> The ongoing current treatment of Kostmann's syndrome includes the use

of G-CSF which results in the improvement of the patient survival. However, there are some long term complications with the use of G-CSF with the risk.<sup>[10-12]</sup> Hematopoietic stem cell transplant (HSCT) is the only curative option for patients with severe congenital neutropenia.<sup>[13]</sup> This is a case report of Kostmann's syndrome patient admitted to the Department of Hematology at King Abdulaziz University Hospital, a tertiary care medical center, Faculty of Medicine, at King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.

This patient developed cataract with recombinant G-CSF<sup>[11,12]</sup> and no matched stem cell transplant donor was found, the

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parents were advised and signed a consent to start traditional alternative therapy starting in 2004.

Alternative therapy included a combination of *Nigella sativa* seeds (Black seeds) and Saudi monofloral honey that was given on a daily basis with close follow up and monitor of any adverse outcomes, medication safety, patient/parent compliance, doses, and side effect.

### Case Report

A 15-year-old Yemeni patient diagnosed during the first few months of his life with Kostmann's syndrome.<sup>[1]</sup> On the 2<sup>nd</sup> day of his life, he was admitted to the pediatric intensive care unit with infection, followed by 26 inpatient admissions for bacterial associated infections between 2002 and 2004 with positive blood and urine cultures. At 7 months of age, he was referred to the pediatric hematology with high-grade fever persisting for 20 days and suffering from diarrhea lasting for 1 week. No sign of lymphadenopathy or organomegaly were noted. This boy was born to a 23-year-old mother with normal birth weight and Apgar scores. His parents were first-degree cousins. Patient has positive consanguinity and family history for a similar condition, elder brother died of sepsis during the 1<sup>st</sup> year of life. The complete blood count and blood film of both parents were normal with a normal morphology which excludes the other illness of familial febrile neutropenia.<sup>[1]</sup>

The patient was diagnosed with Kostmann's syndrome, followed by frequent admission for bacterial infections and persistent severe neutropenia, peripheral blood films with automated neutrophil count (ANC) range from 0.1 to  $0.2 \times 10^9/L$ , no blasts or dysplastic leukocytes were observed.

Bone marrow aspiration confirmed the diagnosis of Kostmann's syndrome and excluded other causes of congenital chronic severe neutropenia as Shwachman's syndrome and Glycogen storage disease. Genetic testing for ELA2 mutation was not considered due to unavailability at this stage yet diagnosis was confirmed by the typical clinical course and subsequent laboratory tests.

Blood sugar and electrolytes were within the normal ranges. Renal and liver function tests showed normal results. The aseptic screening was negative for fungal and other infections including: toxoplasmosis, other (syphilis, varicella-zoster, parvovirus B19), rubella, cytomegalovirus, herpes infections, for HIV 1 and 2 and Epstein-Barr virus.

Immunophenotypic analysis of his lymphocyte profile revealed normal levels of T, B and natural killer lymphocytes.

The patient had normal immunoglobulin levels with a normal count and ratio of CD4 and CD8 cells. The patient has always had a 200–300 ANC.

The patient was initially treated subcutaneously with a daily dose of G-CSF at 5 µg/kg (mcg/kg) body weight for 7–10 days during admission for infection. On his discharge, the patient received G-CSF 5 mcg/kg once a week. As a result of G-CSF treatment episodes of febrile illness and hospital admissions were reduced. However, the neutrophil counts did not respond to G-CSF treatment and did not increase.

Four months later, the patient developed bilateral eye cataracts, more severe in the left eye, which required left lensectomy. Lens histology revealed chronic inflammation, presences of many macrophages and some fibrosis. Culturing the lens, revealed no evidence for bacterial, viral and/or fungal contamination.<sup>[11,12]</sup>

The G-CSF treatment was stopped and allogeneic hematopoietic stem cell transplantation (HSCT) was approved yet no matched human leukocyte antigen (HLA) donor was found.

The patient was admitted once again to the hospital with two incidents of respiratory tract infections and was treated using the regular febrile neutropenia protocol. The primary physician counseled the parents and advised them to be involved in a trial of alternative traditional medicine using *Nigella sativa* seeds and Saudi monofloral honey for the treatment of their child.

This traditional medicine was explained in details to the parents, and a consent form was signed by the parents to start the alternative treatment. The two combination of traditional/alternative medicine are well known for their anti-inflammatory and anti-microbial effect. Honey and *Nigella sativa* seeds: ancient cure or modern alternative therapy.<sup>[14-17]</sup>

### Materials and Methods

Saudi honey (monofloral) was given to the parent as small ready-made individual 100 g portions of Saudi honey.<sup>[18]</sup>

#### Preparation of *Nigella sativa* seeds

*Nigella sativa* seeds were purchased from the local market and prepared by the staff of the Hematology Research Laboratory at King Fahd Medical Research Center. A total of 100 g were dispensed into small bags and stored away from the light. The seeds were washed, dried, and crushed to a powder using an electric micro-mixer before being given to the parent who was informed and was aware on how to administer it to her son.

The patient responded well to the combined alternative therapy, and his safety was monitored for any side effects. Over the past 11 years, and without the use of G-CSF therapy and no transplant, the patient did not experience any febrile illness and was never admitted to the hospital as a result of infections. This is in spite of the fact that he had a persistent neutropenia with an ANC of  $0.2 \times 10^9/L$ .

The quality of life of the patient improved dramatically with no adverse side effects, with regular school attendance and normal healthy life.

## Discussion

The present study dealt with an alternative combined traditional therapy, including *Nigella sativa* seeds (Black seeds) and Saudi honey to treat a patient with Kostmann's syndrome at the Department of Pediatric Hematology.

The patient had no HLA matching for stem cell transplant and developed complications after being given G-CSF therapy.<sup>[11-12]</sup>

This alternative traditional medicine was effective and resulted in major improvement in his survival over the past 11 years.

Recent studies have shown that Saudi honey exerts anti-inflammatory, antioxidant, and antibacterial activity against multi drugs resistant bacteria and potentiates the efficacy of the immune system.<sup>[19-21]</sup>

Monofloral honey harvested from Saudi Arabia hives is derived from at least 55% of pollen from a single floral source. Most of those honey types have the ability to reduce the incidence of acute febrile neutropenia and potentiates the activity of the immune system through its antibacterial activity against most common bacterial strains.<sup>[18]</sup>

The wide antibacterial spectrum of Saudi honey against the main pathogens that are associated with severe neutropenia like *Pseudomonas aeruginosa* may explain the boost in the immunity of this patient.<sup>[18-21]</sup>

Recent studies have demonstrated that *Nigella sativa* seeds have antibacterial, anti-inflammatory, antioxidant activities, and are immune-modulators.<sup>[22-25]</sup>

A possible explanation for this treatment is likely to be due to the synergism that is produced on the combination of honey with *Nigella Sativa* seeds. This has resulted in the improvement of the immunity of this patient and kept the febrile neutropenia episodes under control. This activity is due to the anti-inflammatory, antimicrobial

potential of this combination. Such a combination may also potentiate the phagocytic functions and as such prevent the severe neutropenia.

## Conclusion

The most prominent effects of this combined traditional treatment were the ability of the patient to live a normal life and resume all his normal activities. No adverse health related or side effects were noted using *Nigella sativa* and honey combination. Natural products research is vital to come up with ways to improve the health of patients under controlled conditions in academic tertiary care medical centers. Future research is needed to elucidate the underlying mechanism of action of our treatment regimen for the improvement of the immune system. Further studies are needed to confirm the conclusion.

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## Conflicts of interest

There are no conflicts of interest.

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