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# Iron chelation therapy in myelodysplastic syndrome

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## EDUCATIONAL CASE REPORT

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Myelodysplastic syndrome (MDS) is a collective term for several clonal, pre-malignant or malignant bone marrow disorders characterized by impaired maturation of haematopoietic cells and cytopenia in the peripheral blood [\(1\)](#). Median survival depends on which sub-group the patient belongs to and also on the risk score. The cause of death is often transformation to acute leukaemia or direct complications of bone marrow failure [\(1\)](#).

Multiple blood transfusions and impaired erythropoiesis can lead to iron accumulation [\(2\)](#). Kiarash Tazmini and colleagues give a highly instructive description of serious clinical manifestations of this condition. They refer to a patient who had a prognostically relatively favourable type of MDS: refractory anaemia with ringed sideroblasts. She nevertheless required repeated blood transfusions, resulting in massive iron accumulation, and she developed severe multiple organ failure. High-dose iron chelation therapy had a favourable and possibly life-saving effect.

In transfusion dependent patients with MDS, one could consider prophylactic iron chelation [\(2, 3\)](#). Two drugs are approved in Norway for this indication. Desferroxamine is relatively cheap, but must be administered parenterally

using an infusion pump. Deferasirox is an oral preparation, but is extremely expensive and can cause adverse renal effects as well as problems with vision or hearing.

It has been well documented that median survival is shorter where iron accumulation is high rather than low (2). However, varying survival rates do not necessarily reflect an adverse effect of iron accumulation or a prognostic benefit from prophylactic intervention. Prognostic differences may simply depend on «the sickest being the sickest». Patients in an unfavourable prognosis group usually need repeat transfusions and thus accumulate more iron. Moderate iron overload is relatively harmless. In primary haemochromatosis, cardiomyopathy and liver cirrhosis are unusual at a ferritin level of < 4 000 µg/l and almost never occur at a ferritin level of < 1 000 µg/l (4). In MDS there may also be uncertainty as to whether the patient will live long enough for the iron accumulation to be clinically harmful.

Clinical studies should therefore be carried out on the appropriate use of prophylactic iron chelation in MDS, with the endpoints being prolongation of life, symptom improvement, adverse effects, costs, and quality of life. Retrospective data suggest a favourable effect in groups with reasonably long median survival and a high transfusion requirement (2, 5, 6). A retrospective multicentre study showed median survival of 124 months in a group that had received iron chelation therapy, compared with 53 months in a group that had not received such drugs (6). Since the study was neither prospective nor randomized, it is not possible to know whether the two groups were comparable. The findings are therefore uncertain.

The Nordic MDS Group's Guidelines for MDS recommend prophylactic iron chelation therapy for the group with a ferritin level of > 1 500 µg/l and an expected median survival of more than two years, although it is admitted that the documentation is insufficient (3). Many will probably consider this recommendation too liberal as long as the evidence is not stronger. Randomized, prospective studies will, it is hoped, show the right way forward.

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## LITERATURE

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