Dichloroacetate (DCA) in Cancer Care

Healthcare Provider Resource

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Developed by:

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General information

Proper Name
Dichloroacetate, Dichloroacetic acid

Common Name
Dichloroacetate (DCA)

Routes of Administration
Oral, Intravenous (IV)

Summary

Dichloroacetate (DCA) is a drug which has been investigated for its use in cancer. DCA acts primarily on cancer cell metabolism. Specifically, it inhibits pyruvate dehydrogenase kinase, which may convert metabolism from fermentative glycolysis back to oxidative phosphorylation. This process may induce cancer cell apoptosis through several mechanisms including increased oxidative stress and reduced lactate levels. DCA can be administered orally or intravenously. Clinical research on DCA in cancer is limited, consisting of one randomized controlled trial, five single-arm trials, and several case reports. Outcomes in these studies have been mixed. There is limited clinical trial evidence of disease stability with the use of DCA and a few encouraging case reports, but overall, there is insufficient evidence to support the efficacy of DCA as a cancer treatment. Although most studies have found DCA to be reasonably safe and well tolerated, one study and a couple of case reports have raised safety concerns. The most common side effect is reversible peripheral neuropathy. Typical doses range from 10-50mg/kg daily, with the most common oral dosing being 6.25-12.5mg/kg taken twice daily. DCA should only be administered under the guidance of a qualified healthcare professional and/or in a clinical trial. More research is needed to determine the efficacy and safety of DCA in cancer.

Background Information

Cancer cells have abnormal cellular metabolism, first described in the 1920s by a German physiologist and Nobel Prize laureate, Otto Heinrich Warburg. Warburg discovered that unlike normal cells that obtain 95% of their energy requirements via oxidative respiration in the mitochondria, cancer cells rely heavily on glucose in a process known as aerobic glycolysis occurring in the cytoplasm (1). This phenomenon, identified as the "Warburg effect", led Warburg to propose that cancer may be a result of mitochondrial malfunction. The process of glycolysis generates large amounts of lactic acid, which helps break down the extra-cellular matrix and further potentiates tumour growth and risk of metastases by activating angiogenesis and increasing cell mobility (2). Inactivating the mitochondria also gives cancer cells the unique ability to avoid apoptosis and the various pathways that would customarily signal abnormal cells to undergo apoptosis (3).

DCA is a by-product of water chlorination that has been used as an investigational drug in medicine for over 30 years (4), and may impact cancer cell metabolism (5). While experimental, DCA may be able to shift the metabolism of cancer cells away from anaerobic glycolysis towards the more normalized aerobic oxidative energy production which may enhance apoptosis. In 2006, a Canadian researcher from the University of Alberta, Dr. Evangelos Michelakis, began researching DCA as a cancer treatment (6). Michelakis and his research team hoped that DCA would selectively target cancer cells without affecting healthy cells. In his initial research using rats, after just 3 weeks of receiving DCA, cancer progression was stopped and tumours shrank by 70% (7).

DCA has been researched in adults and children for the treatment of severe metabolic disorders, lactic acidosis, diabetes, hypercholesterolemia, certain heart conditions, and cancer (6), but it remains experimental in all conditions.

Pharmacokinetics

DCA is a small water soluble molecule of 150 Da, allowing it to achieve 100% bioavailability when given either orally or intravenously (6). When given orally, DCA is readily absorbed in the gastrointestinal tract and less than 1% of the total given dose is excreted in the urine (4, 8, 9). Metabolism of DCA occurs in the liver and follows a simple one compartment pharmacokinetic model (4, 6, 9, 10).

Serum DCA levels rise rapidly after oral administration and exhibit a relatively short half-life. Following a single 25mg/kg oral dose, peak DCA concentration (median of 333 uM) was reached after a median of 1 hour, and had an elimination half-life of 92 minutes (11). After 8 days of continuous administration, peak serum concentrations were 2-fold what they were on day 1, and they peaked at approximately 2-hours rather than after 1 hour. Trough concentrations were also higher after 8-days of DCA than after a single dose (11), indicating a slower clearance from the body after multiple doses (12, 13). Another pharmacokinetics (PK) study found similar results; median peak concentrations were higher after 15 days of administration compared to after 1 day (14).. Although peak serum levels rise with continued use, there appears to be a plateau for this effect (7, 15, 16). The effect of food on DCA absorption has not been studied (11).

DCA metabolism is affected by glutathione transferase zeta 1/maleylacetoacetate isomerase (GSTZ1/MAAI) genotype status. Individuals with at least one wild-type haplotype metabolize DCA more rapidly and thus may be able to tolerate a higher dose with fewer adverse effects (17, 18). In one study, the presence of GSTZ1*A allele resulted in a shorter DCA half-life and lower area under the curve (AUC) (11). Conversely, a patient with the EGM/EGM genotype exhibited markedly higher plasma DCA levels and worsening peripheral neuropathy, leading to trial discontinuation (19).

Mechanism of Action

DCA primarily works on cancer cell metabolism. In normal cells, complete oxidation of one glucose molecule through mitochondrial oxidative phosphorylation generates about 30 molecules of ATP and produces reactive oxygen species (ROS). Conversely, cancer cells favor cytoplasmic glycolysis even in the presence of oxygen through a process known as aerobic glycolysis. Glycolysis involves a series of chemical reactions resulting in the conversion of glucose to lactate and the generation of 2 ATP molecules (20). This far less energy efficient metabolism also results in higher cellular production of lactate, and reduced production of ROS.

Reversal of cancer cell metabolism

DCA acts on the mitochondrial matrix of cancer cells, diverting metabolism from fermentative glycolysis back to oxidative phosphorylation (7, 20). DCA does this by activating the pyruvate dehydrogenase complex and inhibiting pyruvate dehydrogenase kinase (PDK). The shift from cytosolic metabolism of pyruvate to mitochondrial metabolism effectively reduces lactate levels by promoting the conversion of lactate into pyruvate (20, 21).

Decreased mitochondrial membrane potential

DCA administration results in the reopening of voltage and redox sensitive mitochondrial transition pores (22). This allows for the pro-apoptotic mediators, *cytochrome c* and *apoptosis-inducing-factor,* to be released into the cytoplasm, resulting in an apoptotic cascade selective to cancer cells which were previously operating under glycolysis (3).

ROS production

By relying heavily upon cytoplasmic aerobic glycolysis for energy, cancer cells can avoid the production of reactive oxygen species (ROS) via mitochondrial oxidative phosphorylation (20, 23, 24). DCA triggers the remodeling of mitochondrial metabolism, opening transition pores and increasing the levels of pro-apoptotic ROS through the activation of caspases (20, 21, 23). High levels of ROS (such as H_2O_2) can inhibit tumour growth and result in apoptosis (7).

Release of mitochondrial calcium

The lack of mitochondrial oxidative phosphorylation in cancer cells facilitates an increase in intracellular calcium (Ca++), resulting in an increase of proliferative transcription factors (25). Increased intracellular Ca++ is responsible for activating ornithine decarboxylase, the rate limiting enzyme in DNA synthesis, as well as the antiapoptotic nuclear factor of activated T lymphocytes (6, 25, 26). DCA causes a decrease in intracellular calcium, potentiating apoptosis in cancer cells and inhibiting proliferation (25, 26).

Mitochondrial K+ channel axis

Cancer cells exhibit down regulation of the potassium (K+) channel Kv1.5 by decreasing the tonic efflux of K+ down its intracellular/extracellular gradient (7). K+ exerts a tonic inhibitory effect on caspases, and K+ channel inhibition suppresses apoptosis in cancer cells. DCA activates mitochondrial Kv channels in cancer cells, promoting apoptosis.

Cancer stem cells

Although less well established, there is some evidence that DCA may be able to reduce stemness and induce differentiation in cancer stem cells through many of the same mechanisms already described, including shifting cells to oxidative metabolism (5).

Preclinical evidence related to effectiveness

Preclinical studies have demonstrated an anticancer effect of DCA in many cancer cell lines in vitro and in vivo, including glioblastoma (7, 27), colon (28, 29), breast (30, 31), prostate (22), ovarian (32), endometrial (26), cervical (33), lung (34), leukemia (35), and renal (36) cancer cells, and various mixed cancer cell lines (37). Limited in vitro data has also suggested that non-cancerous cell lines may also be susceptible to death when treated with DCA (37). Finally, there are also some preclinical studies which have produced mixed results or failed to show an anticancer effect of DCA, including one in colon cancer (25).

Clinical Evidence related to effectiveness

One randomized controlled trial, five single-arm clinical trials, and several case reports have evaluated the effect of DCA in cancer. Findings have been mixed for efficacy, tolerability, and safety. There is insufficient evidence to make an overarching comment on the efficacy of DCA as a cancer treatment.

Brain Cancer

Two small single-arm clinical trials have evaluated DCA for brain cancers. In the first, DCA was given to five patients with glioblastoma (38). In this small uncontrolled clinical study, two of the patients were also treated with standard therapy and three were considered palliative. After 15 months of oral DCA therapy, three of the five patients demonstrated regression of their glioblastoma on MRI and a fourth was considered clinically stable. Eighteen months after starting treatment with DCA, four of the patients were still living. The dose-limiting toxicity (DLT) was reversible peripheral neuropathy. There was no evidence of hematologic, hepatic, renal or cardiac toxicity from this therapy. The second study enrolled 15 people with recurrent stage III/IV glioma or brain metastases (39). The primary objective was to determine dose-limiting toxicity (DLT) from oral DCA after 4 weeks of use. DCA was given orally at an initial dose of 8.0 mg/kg every 12 h which was modified according to tolerance or glutathione transferase zeta 1/maleylacetoacetate isomerase (GSTZ1/MAAI) genotype status (which has been found to affect DCA metabolism). Eight patients completed 4-weeks of DCA, and no one escalated their dose. They remained clinically and radiologically stable and were on DCA for an average duration of 75.5 days (range 26–312). At the time of publication, three patients were alive, and five had died. No DLTs were identified, and adverse events were either grade 1 or 2 and included fatigue, gait abnormalities, hypersomnolence, and sensory peripheral neuropathy. The authors reported that DCA was safe, well tolerated, and feasible at the dose used.

One case report of a man with GBM treated with IV DCA and artesunate raised safety concerns following liver and bone marrow toxicity (40). After disease progression following surgery and radio-chemotherapy, the 52-year-old man received IV DCA (unknown dose) and artesunate (2.5mg/kg). Hepatic and bone marrow toxicities occurred a few days after infusion. The patient received supportive treatment at hospital; however, his condition deteriorated, and he died ten days after receiving the combined treatment. The Roussel Uclaf Causality Assessment Method (RUCAM) scoring system revealed reasonable probability that the combination of DCA and ART induced liver injury.

Other cancer types

Head and neck cancer:

The only randomized, placebo-controlled, double-blind study of DCA analyzed 45 patients with locally advanced head and neck cancer (HNC) who were randomized to DCA or placebo during concurrent chemoradiotherapy (CRT) (41). Patients received either DCA 12.5 mg/kg twice a day or placebo throughout the 5-weeks of cisplatin-based CRT. Overall, patients in both groups had similar tolerance to the concurrent CRT and there was no statistically significant difference in compliance to treatment. Compared to placebo, the DCA group experienced higher rates of fever (43% vs. 8%, $p = 0.01$) and low platelet counts (67% vs. 33%, $p = 0.02$), but there was no significant difference in grade 3 and 4 adverse events. Although the DCA group had significantly higher rates of complete response compared to placebo (71.4% vs 37.5%, $p = 0.036$), there was no difference in 5-year progression-free and overall survival.

Hematological malignancies:

One single-arm trial and two case reports assessed DCA in hematological malignancies. A single-arm phase II study was conducted to evaluate the use of DCA in patients with myeloma (11). Seven patients in a plateau phase or partial remission received DCA with a loading dose of 25 mg/kg orally for three days followed by a dose of 6.25 mg/kg BID from day four to 12 weeks (five patients also received concomitant maintenance chemotherapy). Of the six who were evaluable, three progressed, one responded, and two demonstrated partial response. The patients tolerated the treatment with no withdrawal or dose reduction due to the DCA given. One of the five patients who entered the trial with some degree of peripheral neuropathy developed a score of 3 in the Total Neuropathy Score (TNS), but this resolved within six months after DCA cessation.

A twenty-three-year-old male patient with refractory extramedullary acute myeloid leukemia (AML) was treated with DCA, arsenic trioxide (ATO), and hydroxyurea (42). The patient, who had previously received 8 lines of chemotherapy, received DCA at a dose of 12.5 mg/kg orally twice daily for 11 days, Arsenic trioxide (ATO IV starting 48 hours after the DCA for nine days, and hydroxyurea. The treatment was well tolerated; there was no tumor lysis syndrome, he experienced mild peripheral neuropathy, mild sore throat, and mild confusion when he was febrile. His leukocyte counts and blast percentage showed a decrease in the values starting seven days after the initial administration of the DCA. The patient was not followed long-term and thus the lasting effects of this combination are unknown. A case report was published regarding a patient with non-Hodgkin's lymphoma who relapsed after treatment with the chemotherapy regimen rituximab-CHOP (43). This patient then underwent a rigorous treatment cycle with DCA, alpha lipoic acid, and B vitamins and achieved complete remission of his cancer as evidenced by PET scans, CT scans, and laboratory testing. Four years later, the patient remained cancer free.

Lung and breast cancer:

Patients with stages III and IV breast cancer (n=1) and non-small cell lung cancer (n=6) who progressed after previous conventional treatment were enrolled in a phase II, open-label uncontrolled clinical trial evaluating the use of DCA (44). The patients received oral DCA at a dose of 6.25 mg/kg twice daily for a median of 12 days (4-72 days). There was no clinical benefit from using the DCA among either population, and the study was closed

early due to safety concerns which included the death of two participants shortly after starting DCA. The relationship between mortality and DCA was uncertain. Adverse events (AEs) were reported in all patients. Four out of the seven patients developed AEs of grade 3 or greater including abdominal pain, lower extremity edema, elevated aspartate aminotransferase (AST), pulmonary embolism, hyponatremia, volume depletion, and sudden death.

Mixed cancers:

Twenty-four patients with refractory advanced solid tumors were included in a phase I study to test the tolerability of oral DCA, determine the maximum tolerated dose (MTD), and establish the recommended phase 2 dose (RP2D) (14). Patients received DCA orally for 28-day cycles with a standard 3+3 protocol with a starting dose of 6.25 mg/kg BID which escalated to 12.25 mg/kg BID according to tolerance. Among the 16 patients who were treated with 6.25mg/kg dose, only one patient had a dose-limiting toxicity (DLT) of grade 3 of neuropathy and fatigue, however 3 out of 7 patients who received the 12.25 mg/kg BID dose developed DLTs; grade 3 fatigue, nausea, vomiting, and diarrhea. Most of the grade 3 adverse events were neuropathy (13%) and fatigue (17.4%). According to the study, the MTD and RP2D were set at 6.25mg/kg BID. Eight of the 17 patients evaluated for response achieved stable disease at a median duration of 55 days (range 27–220 days).

A case report of a 57-year-old female with stage IV metastatic colorectal cancer to the liver and lung demonstrated disease stability on DCA (45). The patient received IV DCA weekly in escalating doses (started at 3000 mg) for six months with FOLFIRI (5-fluorouracil, irinotecan, leucovorin) chemotherapy, bevacizumab, oral metformin, and IV vitamin C. Following this, she received weekly IV DCA (4500 mg) without conventional treatment for three months followed by oral DCA 500 mg BID for two weeks on and one week off, for a total of 4 years. She also received supportive neuroprotective supplements (alpha lipoic acid, acetyl l-carnitine, and benfotiamine), and vitamins D and C. The patient remained stable for nearly 4 years while on DCA without any conventional treatments, and she survived for six years post diagnosis. She experienced tolerable and stable mild neuropathy which did not affect her daily activities, and she remained active with ECOG level 1.

A case report of a 35-year-old female with metastatic adenocarcinoma of the stomach treated with a combination therapy including DCA was published (46). The woman had advanced disease with peritoneal dissemination and was treated with palliative intent DCA (50mg tid orally), 5-aminolevulinic acid (50 mg tid), hyperthermotherapy and cellular immunotherapy. Her disease status remained stable while on this combination of treatments for 11 months. Furthermore, her quality of life improved significantly, and she was able to function and perform her work activities. Her survival time since diagnosis was one year and seven months. Given the multimodal treatment regimen, it is difficult to know what effect, if any, the DCA had.

In a young man with previously treated recurrent and metastatic melanoma, oral DCA was administered at a dose of 500 mg (17mg/kg orally) 3 times per day for two weeks on and one week off for four years (47). The patient received no conventional treatment but used several natural therapies (active hexose correlated compound, astragalus, curcumin, dandelion root, IV vitamin C, subcutaneous mistletoe injections), and daily oral neuroprotective supplements (alpha lipoic acid, acetyl l-carnitine, and benfotiamine). He achieved a complete radiological remission which lasted for over 4-years before relapse, and he continued with all his treatments during that time. The additional natural treatments were started 3-months prior to DCA, and during that time there was disease progression. Thus, the authors felt his treatment response was likely to be due to the DCA. During the 4-years on DCA, the patient experienced mild neuropathy and reduced ability to concentrate during his 2-weeks of treatment, but overall maintained a good quality of life.

A case series of three cancer patients highlighted the potential of DCA to have anti-cancer effects (48). This case series included a 79-year-old male with metastatic colon cancer, a 43-year-old male with metastatic

angiosarcoma, and a 10-year-old boy with metastatic neuroendocrine pancreatic cancer; all of whom were refractory after conventional treatment. In each case, DCA was given intravenously weekly with doses ranging between 2500 mg to 5000 mg per infusion. DCA treatment duration ranged between 3 weeks to 8 months. In addition, various supportive naturopathic therapies were used, and the patient with angiosarcoma received stereotactic radiotherapy and the patient with pancreatic neuroendocrine cancer received octreotide. In the patient with colon cancer, CEA dropped following DCA infusions, however treatment was only used short-term so the impact on disease progression or survival is not known. The patient with angiosarcoma experienced stability in some metastases and partial response in others after 5-months of treatment. No long-term follow up was available, and the patient discontinued DCA after approximately 8-months. In the patient with neuroendocrine pancreatic cancer, there was shrinkage of the hepatic metastases after 6 weeks of treatment. There were no significant side effects or organ toxicity. Overall, these cases demonstrate good tolerability of IV DCA and favourable responses.

A case report outlined the complete long-term remission of a patient with metastatic renal squamous cell carcinoma (49). After completing palliative radiation, this patient began a cyclical regimen of oral DCA for three months' time. Follow up imaging revealed no evidence of the disease and the patient remained cancer free five years after initially achieving remission following treatment with DCA (49).

A case report of a 51 year old male with a diagnosis of medullary thyroid carcinoma that metastasized to the lungs documented partial remission for seven years following treatment with numerous chemotherapies (50). However, his cancer eventually returned and resulted in the generation of metastases throughout his body. The patient was then started on DCA therapy, and had a positive reaction as evidenced by a reduction in his tumor marker, calcitonin, and a dramatic reduction in all tumors on his PET scan. At the time of publishing, the patient remained in remission and was continuing with DCA treatment (36).

One case report documented reductions in pain with the use of DCA. A 71 year old male with poorly differentiated metastatic carcinoma began using DCA in a palliative setting (51). After 5 months of treatment with DCA, the patient had improved quality of life through reduction of leg pain and he was able to stop using all pain medication (51).

Finally, one paper reported on three cases where DCA was used in addition to omeprazole, tamoxifen, and ivermectin in patients with metastatic and refractory breast cancer, osteosarcoma, and lung cancer (52). Given the various therapies used, it is not possible to discern the impact of the DCA. The authors exclusively report on symptom management, which they report improved substantially only after ivermectin was added to the regimen. The authors suggest that ivermectin was synergistic with DCA; however, given the lack of safety reporting, absence of objective outcomes or validated patient-reported outcomes, and small number of cases, this cannot be assessed.

Safety and adverse events

The majority of studies have found DCA to be safe and reasonably well tolerated (11, 38, 39, 41), however side effects are common. The most common side effect is reversible peripheral neuropathy, hypothesized to be due to the increased production in ROS when metabolism is shifted toward oxidative phosphorylation (5). Two case reports and anecdotal evidence suggest that co-administration with antioxidants may reduce this, but further research is needed (45, 47). Other side effects reported in clinical trials include fatigue, confusion, memory loss, sedation, tremors, gait abnormalities, central neuropathy, hallucination, agitation, depression, fever, diarrhea, heartburn (oral), and nausea (oral), liver enzyme elevation, thrombocytopenia, and hypocalcaemia (11, 12, 14, 39, 41, 53-55). Although these side effects were most often mild (grade 1-2), occasionally grade 3 adverse effects including neuropathy and fatigue have been reported. Side effects are typically dose-related, with higher doses producing

more frequent and severe adverse effects (14). One study in advanced cancer patients was discontinued early due to safety concerns, including several grade 3 or higher adverse events (abdominal pain, lower extremity edema, elevated AST, pulmonary embolism, hyponatremia, volume depletion, and sudden death) (56).

In an attempt to reduce side effects of DCA, some case reports have administered oral DCA in a 2 weeks on followed by 1 week off cycle (45, 47).

Interactions with other therapies

Chemotherapy:

Several preclinical studies have demonstrated synergistic effects of DCA with chemotherapeutic agents, including carboplatin (34, 57), oxaliplatin (34, 57), 5-fluorouracil (29), paclitaxel (58, 59), doxorubicin (60), elesclomol (24), and sorafenib (61). Preclinical studies for cisplatin are mixed, with some finding benefit (3, 32, 62), one finding reduced efficacy (57), and one finding no effect with combined use (63). One preclinical trial found no effect on the efficacy of temozolomide (63).

Clinical data is limited. Oral DCA has been used with cisplatin and radiotherapy without apparently increasing the toxicity or decreasing efficacy of the treatment (64). A small study administered oral DCA to patients receiving various treatments including CyBorD (Cyclophosphamide, Bortezomib, and Dexamethasone), thalidomide, and lenalidomide, however it is not possible to deduce from that study if it had any impact on these treatments (11). One case report combined IV DCA with FOLFIRI and bevacizumab and the patient's condition was stable (45). A case report combined oral DCA with arsenic trioxide and hydroxyurea in AML with evidence of reductions in leukocytes and blasts (42).

Radiation therapy:

There is preliminary preclinical evidence that DCA may act as a radiosensitizer primarily by increasing levels of reactive oxygen species in tumour cells (5, 65). Two preclinical studies indicated that DCA is able to sensitize cancer cells to improve the efficacy of phototherapy and radiation (22, 66). However, despite promising in vitro data, some in vivo results have not demonstrated radiosensitization (67). Clinically, oral DCA has been used with cisplatin and radiotherapy without increasing the toxicity nor apparently decreasing efficacy of the treatment (64).

Due to the limited research available on combined conventional treatment with DCA, each case requires evaluation to determine the overall risks and benefits of proceeding with treatment.

Other medications:

Combined with artesunate one patient experienced fatal liver and bone marrow toxicity. Thus, until more is known this combination is likely best avoided (40).

There is insufficient evidence on the use of DCA with other medications, including other cancer treatments such as targeted therapies and immunotherapies.

Natural health products:

Alpha lipoic acid (IV and oral), acetyl l-canitine, and benfotiamine have been used in case reports to attempt to reduce the risk of DCA-induced neuropathy (45, 47).

Cautions and Contraindications

No studies have been conducted on the use of DCA during pregnancy or in lactation; therefore, pregnant and lactating individuals are advised to avoid therapy with DCA due to the unknown effects.

DCA is metabolized in the liver; therefore, caution is required when administering DCA in cases of compromised liver function or with hepatotoxic drugs. DCA has been shown to cause a reversible elevation in liver enzymes, and all patients undergoing DCA therapy

should be monitored for hepatotoxicity prior to initiating treatment and at frequent intervals during treatment (9).

Due to rarely-reported delirium with DCA use (54), it is recommended that DCA be used cautiously in patients also undergoing treatment with cannabinoids, benzodiazepines, or any other medications with potential neurological effects.

Because of the possible accentuation of cancer-cell death when administered in tandem with chemotherapy, there may be an increased risk of tumour lysis syndrome (TLS). TLS is most common in individuals being treated for leukemia and lymphoma or in cases of rapid tumour cell death as is commonly seen with bulky tumours (68). Close monitoring for symptoms of TLS such as nausea, fatigue, dark urine, reduced urine output, flank pain, numbness, seizures, hallucinations, muscle cramps, heart palpitations, kidney failure, and electrolyte imbalances is recommended.

DCA metabolism is affected by glutathione transferase zeta 1/maleylacetoacetate isomerase (GSTZ1/MAAI) genotype status (17-19). Thus, some patients, who have single nucleotide polymorphisms in these gene may not tolerate DCA as well due to reduced ability to metabolise the drug. Dose alterations may be necessary.

Dosing, frequency and length of treatment

DCA can be administered orally or intravenously. Dosing ranges from 10-50 mg/kg daily (5). When used orally, DCA is generally given twice daily, whereas IV use has generally been once weekly. In clinical trials, DCA has generally been administered orally at a dose of 6.25-12.5mg/kg BID (11, 14, 39, 41, 56). Some case reports have administered oral DCA in a 2 week on, 1 week off protocol with the aim of reducing adverse effects (45, 47). Patients may be started at a lower dose and slowly increased until benefit is observed or adverse effects become apparent. DCA has been administered for a few weeks up to several years with ongoing monitoring.

Disclaimer

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