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Review Article

Osteosarcoma: A review

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ABSTRACT

Osteosarcoma (OS) is a type of cancer with onset in late childhood and peak at early adolescence.[1] OS is a typically is chemo sensitive cancer.[2] The treatment modalities include neo-adjuvant and adjuvant therapies with definitive surgery. Permutations and combinations of chemotherapeutics agents have been used.[3] However, in many clinical trial high dose methotrexate has been used as main drug with cisplatin and doxorubicin (MAP). In recent years, case studies have cited addition of fourth drug to the three drug regimen gives a detail of drug regimen being used over past years and discusses the successful treatment.[4]

1. Introduction

OS is most common malignancy of bone occurring in second decade of life. With advent of chemotherapy the 5 years event free survival has increased from <20% to 60% to 70%. Although not much improvement is evident in survival rate in last three decades.[5] The four most promising drugs used in OS are Methotrexate, Cisplatin, Doxorubicin and Ifosfamide. In north America and Europe high dose Methotrexate, Adriamycin and Cisplatin (MAP) are standard and show promising results. Non-HDMtx are being seldom followed now.[6]

2. Review and Case Reports

2.1. HDMtx-containing triple drug regimen (MAP[6–8]

With use of triple regimen containing HDMtx doxorubicin and cisplatin. There should be atleast 3 drugs regimen and as per case studies conducted by many research workers, a conclusion was sought with meta-analysis that there is no specific evidence to approve or disapprove HDMtx in OS. However, the three drug regimens including Mtx with Adriamycin plus cisplatin plus ifosfamide MAP (ifos) increased the survival rates. However as suggested by Rastogi et al, the uses of MAP and MAP (ifos) did not show much difference and also no significant difference with MAP plus etoposide.

2.2. Indian scenario with HDMtx chemotherapy regimen[9–11]

The HDMtx requires admission, rigorous hydration and leucoverin rescue with associated toxicities. In india, as per the case studies and opinion of Rastogi et al, the cost treatment is not economical and there is lack of facilities to measure Mtx levels. HDMtx is prevalent with 4% risk of renal failure and 2% mortality risk in developed countries. Secondly carboxypeptidase G2 the antidote for methotrexate intoxication is also less available in India.

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Table 1: Non-high dose methotrexate containing triple regimens

Patiets	Regimen	Median follow up	% overall survival
12	Cisplatin+doxorubicin+ifosfamide	5.5 years	83 (3 years) 75
32	Cisplatin+doxorubicin+ifosfamide (+ etoposide for per rise)	36 month	86 (2 years) 74
53	Cisplatin+cyclophosphamide+ vincristine+doxorubicin	151 month	71 (5 years) 60.4
32	Cisplatin+doxorubicin+ifosfamide	64 month	69 (5 years) 65
75	Carboplatin+doxorubicin+ifosfamide	5.1 years	78.9 (5 years) 66.7

2.3. Rise of non-HDMtx-containing three drug regimens[12,13]

Thus, to manage the treatment of OS in resources constrained situations, the three drug regimens containing non-HDMtx are rising and have good outcomes in non-metastatic OS. Majority of the non-HDMtx regimens include cisplatin as main drug OS the backbone and combined with doxorubicin with ifosfamide or cyclophosphamide. As studied by Daw et al., doxorubicin and ifosfamide were combined with carboplatin replacing cisplatin and the resultant survival rates of various regimens have been given table below.

It was concluded that used of carboplatin needed further trials to confirm as being active in multiple drug therapy. The use of carboplatin lessens the risk of hydration (as seen in cisplatin) and lessens the risk of electrolyte imbalance, nephrotoxicity and hearing loss. Thus, carboplatin, adriyamycin, ifofamide multidrug therapy may serve useful which does not include HDMtx.

2.4. Indian scenario[14]

According to data published non-metastatic OS treated non-HDMtx in teartiary care centers. On the back of percentage necrosis, patients with >90% necrosis received 3 cycles of cisplatin and doxorubicin or received cisplatin and doxorubicin alternatively for the next eight cycles in case they were poor response. The patients showed event free survival and overall survival rates at 5 years were 36% and 50% for those receiving two drug regimen (25%) and four drug regimen respectively. Necrosis was not a significant prognostic factor for final outcome. Such outcome includes unusually large tumor size, patients with poor performance status, the use of Non-HDMtx based chemotherapy or the use of double drug therapy.

2.5. Fourth drug and three drug regimen[10,11]

The use of ifosfamide to MAP chemotherapy i.e. the fourth drug addition to MAP (the three drug regimen) was not much beneficial.

2.6. Histologic response neoadjuvant chemotherapy[15]

The prognostic marker for chemotherapy being percentage necrosis assessment in non-metastatic OS. Patient with >90% necrosis: 5 year event free survival rate of approximately 70% to 80% Patients with <90% necrosis: 40% to 60% 5 years event for survival rate. The ultimate conclusion being ifosfamide or etoposide should be added to the poor responders.[16]

3. Conclusion

Thus, at a conclusion double drug regimen, three drug regimen and Non-HDMtx regimen should be compared whoever at some parts of the world the double drug regimen being a standard choice and hence all the regimens should conclude with evidence based clinical trial system.

4. Source of Funding

None.

5. Conflict of Interest

None.

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