Protection of Bortezomib-induced Neurotoxicity by Antioxidants

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Background

Although chemotherapeutic agents frequently cause severe peripheral neuropathy, very few studies have reported the effective strategy to prevent this side effect. Therefore, we investigated whether these drugs show higher neuropathy than other 15 anticancer drugs, and whether two popular antioxidants show protective effects.

Materials and Methods

Human oral squamous cell carcinoma (OSCC) and normal mesenchymal cells were cultured in DMEM supplemented with 10% heat-inactivated FBS. Rat PC12 cells were induced to differentiate into neuronal cells by repeated overlay of serum-free medium supplemented with nerve growth factor. Cells were treated for 48 h with samples, and viable cell number was determined by MTT method. Cells were sorted for apoptotic cells (distilled into subG1 phase) and cells at different stages of cell cycle (G1, S and G2/M).

Results

1. Among 19 anticancer drugs, bortezomib showed the highest cytotoxicity against PC12 cells regardless of differentiation stage.

2. Bortezomib, microtubule inhibitors and platinum analogs are expected to show higher neurotoxicity than other anticancer drugs, when used at clinical concentrations.

3. Antioxidants neutralized the neurotoxicity of bortezomib.

4. Bortezomib induced apoptosis in differentiated PC12 cell (Day6), which was inhibited by antioxidants.

Conclusions

- Bortezomib showed the highest neurotoxicity among 19 anticancer drugs via induction of apoptosis in differentiating PC12 cells.
- Oxidative stress may be involved in bortezomib-induced neurotoxicity.