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SCIENTIFIC ARTICLE

Evaluation of the effects of intra-arterial sugammadex and dexmedetomidine: an experimental study

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KEYWORDS
Sugammadex;
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Abstract
Background: Intra-arterial injection of medications may cause acute and severe ischemia and result in morbidity and mortality. There is no information in the literature evaluating the arterial endothelial effects of sugammadex and dexmedetomidine. The hypothesis of our study is that sugammadex and dexmedetomidine will cause histological changes in arterial endothelial structure when administered intra-arterially.
Methods: Rabbits were randomly divided into 4 groups. Group Control ($n = 7$); no intervention performed. Group Catheter ($n = 7$); a cannula inserted in the central artery of the ear, no medication was administered. Group Sugammadex ($n = 7$); rabbits were given 4 mg/kg sugammadex into the central artery of the ear, and Group Dexmedetomidine ($n = 7$); rabbits were given 1 μg/kg dexmedetomidine into the central artery of the ear. After 72 h, the ears were amputated and histologically investigated.
Results: There was no significant difference found between the control and catheter groups in histological scores. The endothelial damage, elastic membrane and elastic fiber damage, smooth muscle hypertrophy and connective tissue increase scores in the dexmedetomidine and sugammadex groups were significantly higher than both the control and the catheter groups ($p < 0.05$). There was no significant difference found between the dexmedetomidine and sugammadex groups in histological scores.
Conclusion: Administration of sugammadex and dexmedetomidine to rabbits by intra-arterial routes caused histological arterial damage. To understand the histological changes caused by sugammadex and dexmedetomidine more clearly, more experimental research is needed.
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PALAVRAS-CHAVE
Sugamadex;
Dexmedetomidina;
Intra-arterial;
Coelho;
Experimental

Avaliação dos efeitos de sugamadex e dexmedetomidina intra-arterial: estudo experimental

Resumo
Justificativa: A injeção intra-arterial de medicamentos pode causar isquemia aguda e grave e resultar em morbidade e mortalidade. Não há informações na literatura avaliando os efeitos endoteliais arteriais de sugamadex e dexmedetomidina. A hipótese de nosso estudo foi que dexmedetomidina e sugamadex causariam alterações histológicas na estrutura endotelial arterial quando administrados por via intra-arterial.
Método: Os coelhos foram randomicamente divididos em quatro grupos: grupo controle (n = 7), sem intervenção realizada; grupo cateter (n = 7), uma cânula foi inserida na artéria central da orelha e medicamentos não foram administrados; grupo sugamadex (n = 7), os coelhos receberam 4 mg/kg de sugamadex na artéria central da orelha; grupo dexmedetomidina (n = 7), os coelhos receberam 1 μg/kg de dexmedetomidina na artéria central da orelha. Após 72 horas, as orelhas foram amputadas e histologicamente examinadas.
Resultados: Não houve diferença significativa entre os grupos controle e cateter referente aos escores histológicos. Os escores do dano causado ao endotélio e à membrana e fibra elásticas, da hipertrofia do músculo liso e do aumento do tecido conjuntivo foram significativamente maiores nos grupos dexmedetomidina e sugamadex que em ambos os grupos controle e cateter ($p < 0,05$). Não houve diferença significativa entre os grupos dexmedetomidina e sugamadex nos escores histológicos.
Conclusão: A administração de sugamadex e dexmedetomidina a coelhos por via intra-arterial causou danos arteriais histológicos. Para entender as alterações histológicas causadas por sugamadex e dexmedetomidina com mais clareza, estudos experimentais adicionais são necessários.
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Introduction

Intra-arterial injection of medications may cause acute and severe ischemia and result in morbidity and mortality. The intra-arterial injection and cannulation incidence varies from 1/3440 to 1/56,000. Medications for sedation or general anesthesia, mainly, are mistakenly administered intra-arterially.[1,2] Intra-arterial injection of medications may cause acute and severe ischemia. It is difficult to fully determine the correct incidence of rare situations such as this.[1–3] After the intravenous forms of medications are given through intra-arterial routes, local ischemia and later tissue necrosis may develop in the artery. The physiopathological mechanisms of intra-arterial medication injection and development of ischemia are not clear. Among mechanisms blamed are formation of crystals of medication in small arteries, secondary hemolysis and platelet aggregation after intimal damage, and stasis, thrombosis and direct cytotoxicity in the artery. The tissue damage is essentially determined by the chemical structure and amount of the medication.[1–3]

The pathogenesis of formation of necrosis after intra-arterial injection of medication is not clear.[1,4] The rabbit ear model is a frequently used method to research the pathological process of intra-arterial injections. No matter how visibly different rabbit and human ears are, they are helpful to observe the tissue response to intra-arterial medications.[4]

Sugammadex is a medication newly entering anesthesia practice. It is a cyclodextrine-structured medication that selectively binds to aminosteroid-structure non-depolarizing muscle relaxants like rocuronium, ending their effects. It shows high selectivity especially for rocuronium and vecuronium. It may enter physicochemical reactions with different medications.[5]

There is no information in the literature evaluating the arterial endothelial effects of sugammadex and dexmedetomidine, two medications newly entering anesthetic practice. Only a single case report was found about dexmedetomidine mistakenly administered intra-arterially.[6]

The hypothesis of our study is that sugammadex and dexmedetomidine will cause histological changes in arterial structure when administered intra-arterially. To test this hypothesis in this planned study we used rabbit ear arteries to intra-arterially inject 4 mg/kg sugammadex and 1 μg/kg dexmedetomidine aiming to research the histological effects.

Method

The study was completed in Dokuz Eylül Universtiy Medical Faculty experimental animal laboratory after receiving permission from Dokuz Eylül University Medical Faculty Animal Experiments Ethics Committee (Meeting date: 08.01.2014 – Decision number: 115/2013). The research used 28 adult male New Zealand white rabbits weighing from 2.5 to 3 kg. The subjects obtained from DEUMF Experimental Animals Laboratory were fed with standard rabbit feed and water. The rabbits were housed in temperature-controlled (22–24 °C) illuminated rooms (12:12 h light/dark) before the

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