Chinese Journal of Traumatology 18 (2015) 267–274

Contents lists available at ScienceDirect

Chinese Journal of Traumatology

journal homepage: http://www.elsevier.com/locate/CJTEE

Original article

An open air research study of blast-induced traumatic brain injury to goats

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ARTICLE INFO

Article history:
Received 29 April 2015
Received in revised form
13 July 2015
Accepted 16 July 2015
Available online 24 November 2015

Keywords:
Brain injuries
Explosive blast
Open-air field
S-100
Neuron specific enolase

ABSTRACT

Purpose: We once reported blast-induced traumatic brain injury (bTBI) in confined space. Here, bTBI was studied again on goats in the open air using 3.0 kg trinitrotoluene.

Methods: The goats were placed at 2, 4, 6 and 8 m far from explosion center. Trinitrotoluene (TNT) was used as the source of the blast wave and the pressure at each distance was recorded. The systemic physiology, electroencephalogram, serum level of S-100beta, and neuron specific enolase (NSE) were determined pre and post the exposure. Neuroanatomy and neuropathology were observed 4 h after the exposure.

Results: Simple blast waveforms were recorded with parameters of 702.8 kPa-0.442 ms, 148.4 kPa-2.503 ms, 73.9 kPa-3.233 ms, and 41.9 kPa-5.898 ms at 2, 4, 6 and 8 m respectively. Encephalic blast overpressure was on the first time recorded in the literature by us at 104.2 kPa-0.60 ms at 2 m, where mortality and burn rate were 44% and 44%. Gross examination showed that bTBI was mainly manifested as congestive expansion of blood vessels and subarachnoid hemorrhage, which had a total incidence of 25% and 19% in 36 goats. Microscopical observation found that the main pathohistological changes were enlarged perivascular space (21/36, 58%), small hemorrhages (9/36, 25%), vascular dilatation and congestion (8/36, 22%), and less subarachnoid hemorrhage (2/36, 6%). After explosion, serum levels of S-100β and NSE were elevated, and EEG changed into slow frequency with declined amplitude. The results indicated that severity and incidence of bTBI is related to the intensity of blast overpressure.

Conclusion: Blast wave can pass through the skull to directly injure brain tissue.

1. Introduction

It is reported that over 80,000 cases of US Armed Forces service members were diagnosed as mild or severe traumatic brain injury (TBI) during the surveillance period between 2000 and 2012 due to blast overpressure exposure.[1] Blast-induced TBI (bTBI) is the second most common cause of injuries from blast overpressure of explosive detonations, following amputations.[2] During Afghanistan and Iraq wars, prevalence of bTBI has been estimated as approaching 40%–60% of warfighters.[3] bTBI is not only a notable military health issue, but also a threat to civilians who experienced explosion without protective equipment.[4,5]

Injuries sustained from blast exposure can be categorized into four major types: primary, secondary, tertiary and quaternary, which are exceedingly complex due to the combination of explosion. Primary blast injury is associated with direct exposure of the head and body to blast wave, which is the unique injury mechanism. Secondary blast injury includes penetration by ejected materials, such as shrapnel. Tertiary blast injury is the result of inertially driven when the body is propelled by the blast into a surface. Quaternary blast injury is combined with other mechanisms, such as thermal, chemical, or radiation exposure.[6,7]

Usually, primary blast induces mild TBI (mTBI), which is much more common in the military operations in Iraq and Afghanistan, but frequently this injury is not recognized at the time of injury, as the symptoms are overlapped with post-traumatic stress disorder

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Peer review under responsibility of Daping Hospital and the Research Institute of Surgery of the Third Military Medical University.

http://dx.doi.org/10.1016/j.cjtee.2015.11.006

(PTSD) and the attentions are mainly focused on the moderate-to-severe TBI.[5] Therefore diagnosis of these individuals are often delayed, ranging from 1 h to several days in military medical evacuation to higher echelons of care.[8] During this time frame, secondary injuries including neurodegeneration and neuro-inflammation occur and the opportunities for timely therapeutic interventions to prevent progressive tissue damage after TBI are often lost.[9]

To date, the mechanism of bTBI has not been well understood. It is estimated that the incidence of bTBI is higher and the damage is more severe in an airtight space compared with an open-air field as blast wave can be reflected from the wall and armor of confined space.[10] We had used goats as the experimental animals to study bTBI resulted from detonation of 3 kg trinitrotoluene (TNT) in confined space, showing complex blast wave of 45 kPa-2.7 ms/71 kPa-2.367 ms can result in subarachnoid and parenchymal hemorrhage, perivascular space enlargement, vascular dilatation and congestion, accompanying abnormality of EEG and elevation of S-100β and neuron specific enolase (NSE) in the serum.[11] Here, bTBI was studied again in open field with the same animal model and methodology to determine its incidence and severity. Moreover intracranial blast overpressure on right temporal lobe was firstly recorded by our team. It was found that the blast wave reduced to 104.2 kPa, 0.60 ms after passing through the whole brain.

2. Materials and methods

All the experiments were approved by the Third Military Medical University (TMMU) and TMMU Institutional Animal Care and Use Committee.

2.1. Dynamite

TNT was used as dynamite for producing blast wave. Prior to use, 3.0 kg TNT was made into sphere by the manufactory. Blast wave from spherical dynamite propagates toward the periphery more even than blast evoked by other shape, hence bTBI may result from a consistent blast at the same distance in every direction. TNT ball was held by a steel supporter of 50 cm height and exploded by the electric detonator.

2.2. Animals and locations

Thirty-six male goats weighed about 25 kg were randomly divided into four groups ($n = 9$) and put at 2, 4, 6, and 8 m away from the explosion center. For each group, the experiment was repeated three times and the data were averaged for final analysis. Each goat was anesthetized with ketamine hydrochloride (2 mg/kg, iv) and restrained on a support frame with a flat board, which had four holes and a supporter to hold legs and head of the goat. The support frame was fixed to the ground to avoid movement during explosion. To maximize the pressure applied to the head during spread of the blast wave, the left side of the goat head was faced to the explosion. Before and after exposure, systemic physiology such as mental status, pupillary reflex, respiratory rate and heart rate were recorded besides examination of the general wound at 30 min after explosion.

2.3. Overpressure recording

The recording apparatuses consisted of transducers with sensitivity of 1.4181–1.4244 V/MPa (PCB Piezotronics Inc., NY, USA) and were protected by a steel circular plate fixed at the same height of the head of the goat. These recording apparatuses were held by a supporting pillar and a pedestal fixed on the ground (in a row with the animals) at distances of 2, 4, 6, and 8 m away from the explosion center. To prevent breakage by detonation, the recording wires were covered by the channel steel. For intracranial recording, a transducer with sensitivity of 3.36 pC/kPa was inserted into the right temporal bone and attached on the surface of the right temporal lobe of the brain. Before insertion, the animals were anesthetized with ketamine hydrochloride (2 mg/kg, iv), then the scalp was incised and a 6-mm hole was made on the temporal bone. After complete hemostasis, the transducer was inserted via the hole and fixed on the scalp and sutured by surgical lines (Fig. 1).

2.4. Electroencephalogram (EEG) recording

EEG was obtained before and within 1 h after injury. A neuroscan (Compumedics Neuroscan, 7850 Paseo Del Norte, Suite 101 EL Paso, TX 79912, USA) with four recording electrodes was used for EEG recording, whose leads of F3 and F4 were subcutaneously put at bilateral forehead prior to both horns, while P3 and P4 were inserted into the skin of the top occipitalis posterior to both horns in accordance with the 10/20 international system. The reference electrode and the ground electrode were located at the earlobe and the nasion respectively. The signals from continuous five-minute recording were analyzed using software Scand 4.3 in the laptop with low and high pass filter at 0.15 Hz and 50 Hz respectively (24 dB/octave).

2.5. Neuropathological observation

All animals were systemically examined for their consciousness, body position, respiration and heart rate, body wound, and hair burn in-theater. These items were re-examined carefully in the anatomical laboratory. Before pathoanatomical observation, the animals were deep anesthetized with 2% isoflurane, then the head skin was incised and the skull was opened to remove the brain. After gross anatomical examination slice by slice, the brain was sampled and fixed in 4% paraformaldehyde for 24 h at room temperature. The samples were embedded with paraffin and cut into 5 μm slices. The sections were stained with hematoxylin and eosin (HE) and mounted with Aqua Poly/Mount (Polyscience, Inc.). Thereafter they were examined using an Olympus microscope and photographed with DP71 digital camera and software.

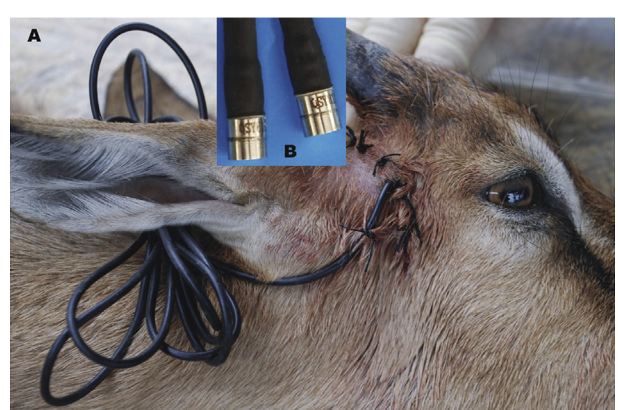

Fig. 1. Intracranial overpressure recording with the transducers (**B**) inserted into right temporal bone and attached on surface of right temporal lobe of the brain (**A**).